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Does Long-Term Medication Use Improve the Academic Outcomes of Youth with Attention-Deficit/Hyperactivity Disorder?

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Abstract Youth with Attention-Deficit/Hyperactivity Disorder (ADHD) frequently experience academic impairment, including lower grades than their peers and elevated risk for grade retention and school dropout. Medication is the most commonly used treatment for youth with ADHD, and it is therefore essential to understand the extent to which medication use improves long-term academic functioning. This paper reviews the literature on the relation between long-term medication use and the academic outcomes of youth with ADHD. A systematic literature search was conducted to identify pertinent studies published since 2000 that followed youth with ADHD for 3 or more years. Academic outcomes of interest included school grades, achievement test scores, and grade retention. Nine studies were identified reporting on eight distinct longitudinal samples (N across studies = 8,721). These studies demonstrate that long-term medication use is associated with improvements in standardized achievement scores. However, the magnitude of these improvements is small and the clinical or educational significance is questionable. Evidence for long-term improvements in school grades and grade retention is less compelling. This review highlights methodological considerations in providing directions for future research. The importance of using multiple sources to gather information about medication adherence is discussed, including use of methodologies such as electronic monitors, rather than relying solely on parent report or chart review. Future research should also examine a range of medication adherence definitions in order to determine whether age of onset, duration of use, dose, and/or consistency of use moderates the relation between long-term medication use and academic outcomes.

Keywords ADHD · Long-term medication use · Academic achievement · School performance

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Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a common childhood neurobehavioral disorder that frequently persists into adulthood (Wilens et al. 2002). Children and adolescents with ADHD exhibit significant functional impairment across multiple domains of functioning (American Psychiatric Association 2000). The negative impact of ADHD on academic functioning is especially profound (DuPaul and Stoner 2003). In comparison with their peers without ADHD, children with ADHD have significantly lower school grades and achievement scores and higher rates of grade retention and school dropout (Barkley 2006; Loe and Feldman 2007). These differences are not only statistically significant, but clinically meaningful as well. The gap between children with and without ADHD on standardized achievement tests is substantial ($d = .71$; Frazier et al. 2007), up to 30 % of children with ADHD repeat a grade in school, and between 10 and 35 % drop out of school (Barkley 2006).

Prescription medication is the most common treatment for children with ADHD, with up to 60 % of children with ADHD prescribed psychotropic medications (Centers for Disease Control and Prevention 2003). Numerous studies

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have documented that ADHD medications have a significant short-term impact on objective measures of academic functioning. Significant improvements with medication have been found on classwork productivity, quality of completed work, number of problems completed on tests, and improved quiz scores (Evans et al. 2001; Pelham et al. 2001; Rapport et al. 1989; Schachar and Tannock 1993; Swanson et al. 1991). However, it remains unclear whether long-term medication use improves the academic outcomes of children with ADHD. That is, if children with ADHD take medication over a period of years, is there a significant positive impact on important long-term academic outcomes such as grades, achievement scores, and grade retention?

The impact of long-term medication use on academic functioning is a highly significant research and clinical question. Grades and achievement scores largely determine whether or not students are accepted into college and strongly predict academic performance in college (Wolf 2001; Zwick and Sklar 2005). As college education becomes increasingly important, students who fail to finish college exhibit higher rates of unemployment, more frequent job changes, and lower rates of professional satisfaction (Biederman et al. 2006; Office of Juvenile Justice and Delinquency Prevention 1995; Wolf 2001). Not surprisingly, the long-term benefits and side effects of medication use are issues of great importance to families of children with ADHD (Hansen and Hansen 2006; LeFever et al. 2002), and physicians need to be able to make evidence-based recommendations. Unfortunately, until recently, there has been insufficient research to determine whether long-term medication use improves the academic outcomes of youth with ADHD.

Challenges Inherent to the Study of Long-Term ADHD Medication Use

There are a number of significant challenges inherent to research on the long-term effects of ADHD medication. These challenges may partly explain why it has been difficult to draw definitive conclusions from the studies that have been completed in this area. Many of these challenges are related to the fact that it is unethical to force participants to remain in randomly assigned treatment groups for extended periods of time. That is, the most internally valid method for answering questions about the long-term effects of medication use would be to randomly assign participants to receive medication or not, and then to follow these participants during childhood and throughout adolescence. This design ensures that the comparison, or reference group, remains clear over time and does not become contaminated (i.e. comparison group stays off medication and analyses examine between group differences). In this ideal study design, medication would also be managed by research study doctors, doses administered following best practice protocols, and adherence monitored through a multi-method approach.

In reality, all studies of long-term ADHD medication use are either community-based and do not involve random assignment or involve random assignment initially prior to transitioning to a non-random naturalistic designs after a period of 1–2 years (e.g. MTA Cooperative Group 1999). As a result, controls surrounding medication prescription practices and adherence are minimal, and there is often no clear reference group. Specifically, participants being followed longitudinally frequently go on and off ADHD medications for various periods of time (e.g., Molina et al. 2009; Thiruchelvam et al. 2001). This creates a situation where the reference group, and therefore the primary research question of interest, is no longer obvious, and it is up to investigators to develop internally valid ways of evaluating the impact of long-term medication use. Specifically, since no clear on and off medication groups exist, participant groupings must be established using cut-points based upon criteria such as consistency of medication use over an identified period of time or adherence to prescribed medications (e.g., Charach et al. 2004—adherent versus nonadherent; MTA Cooperative Group 1999—% of days medicated).

Alternatively, investigators can treat medication use as a continuous variable and examine the relationship between percentages of time on ADHD medication (e.g., days, weeks, or years) with outcomes in a single group (e.g., a regression approach). However, because the definition of on versus off medication and the quality of the measurement tools used to make these determinations varies from study to study (e.g., a group approach based upon cut-points versus an examination of dose versus an examination of duration of use), it can be difficult to summarize results and to draw conclusions across studies. These issues are discussed in more detail below as they have significant bearing on the internal validity of reported findings and therefore on the conclusions drawn in this review paper.

Measuring ADHD Medication Use and Adherence

As noted above, studies of long-term medication use are primarily completed in the community using naturalistic designs which means that adherence to prescribed medication regimens is largely in the control of the child/adolescent and their family. This is a major challenge for the study of long-term medication use, as across disorders, non-compliance with pharmacotherapy is common, especially during the period of adolescence (Cooper et al. 2009). In terms of ADHD medication use, adherence estimates range from 50 to 75 % depending upon how adherence is defined (Hack and Chow 2001). For example, more than 50 % of children who take ADHD medications are either nonadherent (Thiruchelvam, Charach, and

Schachar) or eventually discontinue treatment altogether (Perwien et al. 2004). Further, approximately 50 % of children prescribed ADHD medications fill only the first prescription (Olfson et al. 2003).

Poor levels of adherence to ADHD medications have also been found using objective measures. Specifically, in the MTA study, collection of salivary samples demonstrated that only about 50 % of participants assigned to the medication and combined treatment groups were consistently adherent, and medication nonadherence had deleterious effects on outcomes (Pappadopulos et al. 2009). Similarly, Charach et al. (2004) found that at 2- and 5-year follow-up assessments, participants that were adherent to ADHD medication showed significantly greater improvement in teacher-reported ADHD symptoms in comparison with participants who were nonadherent (see Charach et al. 2004 for specific definition of adherence). Given that nonadherence to ADHD medications appears to be the norm rather than the exception and that adherence clearly impacts outcomes, studies of the long-term impact of ADHD medication must carefully monitor medication adherence and consider adherence in the analyses.

It is important to acknowledge that measuring adherence is complicated and that some methods are more valid, or at least more comprehensive, than others. For example, estimates of adherence vary based upon the source of the evidence, with self- and parent-report leading to overestimates relative to more objective measures such as salivary samples or pill counts (Pappadopulos et al. 2009; Wagner and Rabkin 2000). Perhaps an even more important issue is whether medication use/adherence is assessed prospectively or retrospectively. It is unclear exactly how far back into the past parents can accurately report on their children's medication use, and it is likely that the specific time period varies based upon the question being asked. For example, it is unlikely that parents could report on day-to-day or week-to-week medication adherence from 3 years ago, but they might be able to report broadly whether or not their child took ADHD medication at all 3 years ago (i.e., yes/no). Irrespective of these specific time limitations, it is clear that frequent prospective reporting on medication use/adherence will produce more accurate results in comparison with retrospective reporting (Rapoff 2009).

Another important consideration is how comprehensive a definition of medication adherence is utilized. Medication adherence is best conceptualized along a continuum rather than as a dichotomous yes/no question. Specifically, Gearing et al. (2011) have proposed a comprehensive model of long-term medication adherence separated into six phases depending on when the nonadherence occurs. Briefly, Gearing et al. (2011) note that nonadherence can occur early in the medication initiation process (e.g., a prescription is only filled once), in the middle of the process (e.g., following completion of a titration trial), or during the maintenance phase of treatment (e.g., intermittent use over a period of years). The authors note that the reasons/causes for each of these types of nonadherence likely differ (e.g., dosReis et al. 2009) and that each type of nonadherence may have different implications for long-term outcomes. Accordingly, reviews of the long-term medication use literature such as this one need to pay particular addition to the level of detail with which adherence was defined and measured.

Defining the Outcome of Interest and Relevant Covariates

The present review examines whether long-term ADHD medication use has an impact on academic outcomes. As such, it is important to define what is meant by academic outcomes and, also, to consider variables known to be associated with academic outcomes that could confound results. In terms of defining academic outcomes, it is sometimes assumed that a child's school grades and achievement test scores are highly related and that results from one academic outcome will translate to another. The validity of this assumption has direct implications for whether or not findings from long-term medication use studies can be combined and summarized across academic outcomes.

Broadly speaking, standardized achievement tests are examinations of academic knowledge, whereas school grades are a combination of students' academic knowledge, performance, classroom participation, effort, behavior, attendance, and homework performance (Bowers 2011; Randall and Englehard 2009). School grades and achievement test scores are correlated at approximately the .5 level in general education samples (Bowers 2011) and at the .15–.27 level in ADHD samples (Langberg et al. 2011), meaning that they explain at most, 25–35 % of each other (Bowers 2009). Further, school grades are strongly associated with other academic outcomes such as school dropout, whereas standardized achievement scores are not (Allensworth and Easton 2007; Balfanz et al. 2007; Rumberger and Palardy 2005). In addition, high school grade point average (GPA) is a stronger predictor of college performance than achievement scores (Zwick and Greif Green 2007). Nevertheless, standardized achievement test performance is critically important given the rise in the accountability movement. Specifically, these test scores typically get reported to state and federal levels and, in some cases, have implications for school funding (Bowers 2009). Given that achievement scores and school grades exhibit low to moderate correlations, it is important for studies to acknowledge that medication effects in one area may not translate into effects in another area. Further, reviews of the literature such as the present study should summarize findings separately by academic outcome.

Another important issue is ensuring that the sample is well defined and that potential confounds are measured and addressed. There is substantial evidence supporting the assertion that background variables such as parent education level, intelligence, and student gender are associated with academic outcomes (Klapp Lekholm and Cliffordson 2008; Langberg et al. 2011; Mayes et al. 2009; Rumberger 2004). The strength of these relations depends on the academic outcome being examined. For example, in a sample of 436 adolescents with ADHD, Langberg et al. (2011) found that intelligence was highly correlated with achievement scores, whereas correlations between intelligence and school grades were small. Similarly, Mayes and colleagues found that intelligence was the single strongest predictor of achievement scores both in general education (Mayes and Calhoun 2007a) and ADHD samples (Mayes and Calhoun 2007b). Across studies completed with typical children, IQ has been found to account for between 52 and 76 % of the variance in achievement scores (Swanson et al. 2003). Accordingly, potential confounding variables such as intelligence are particularly important to consider in studies of academic outcomes.

Aims of this Review

There have been multiple literature reviews focusing specifically on the impact of long-term medication use on academic outcomes, although all were published before the mid-1990s. Each of these early reviews concluded that either there were no long-term benefits (Barkley and Cunningham 1978; Pelham 1986) or there was not enough research from which to draw conclusions (Schachar and Tannock 1993; Swanson et al. 1991). Fortunately, the past decade has seen a renewed interest in research examining the impact of long-term medication use on academic outcomes. The current review has two primary aims. The first is to evaluate whether or not long-term ADHD medication use improves the academic outcomes of youth with ADHD. Three separate academic outcomes will be examined in this review: school grades/GPA, achievement test scores, and grade retention/school dropout, and findings will be summarized separately for each outcome. The second aim is to evaluate the strength of the current literature as related to the challenges to internal validity described above, and to identify shortcomings as a way of offering promising avenues for future research.

To be included in this review, children with ADHD needed to be followed for a minimum of 3 years. There have been multiple reviews of randomized controlled trials documenting that with consistent medication use and monitoring, improvements with ADHD symptoms and academic outcomes can be maintained up to 2 years post-medication initiation (Huang et al. 2011; van de Loo-Neus et al. 2011; Van der Oord et al. 2008). It is clear that when participants are consistently monitored over a 1–2 year period, and medication is actively titrated, improvements in ADHD symptoms and academic outcomes are frequently maintained (Hechtman et al. 2004; MTA Cooperative Group 1999). In contrast, this review focuses on studies of children with ADHD who have received medication management in the community over an extended period of time. This is an important distinction as care provided in the community is typically quite different than care provided in intervention studies, often involving less frequent monitoring and titration (Epstein et al. 2008, 2010).

Only studies published after 2000 are included in this review since earlier studies followed relatively small samples of participants diagnosed using *DSM-II* or *DSM-III* criteria. Further, most of these samples were followed in the 1970s and 1980s when medication prescribing patterns were markedly different and long-acting medications were not in use (Bhatara et al. 2004). In sum, studies prior to 2000 are not included as the results have already been summarized and deemed inclusive (Schachar and Tannock 1993) and would be difficult to compare with more recent longitudinal research.

Method

Searches were performed using PubMed, Academic Search Complete, and Google Scholar databases. Articles published between January 2000 and September 2011 were included, using all possible combinations of the keywords: ADHD, Attention-Deficit, extended treatment, long-term, medication, methylphenidate, stimulants, psychotropic medication, and psychostimulants. These studies were first reviewed to evaluate whether participants were followed for a minimum of 3 years. Studies meeting this criterion were then reviewed to determine whether data on academic outcomes were reported. The academic outcomes of interest in this review were school grades and GPA, standardized achievement scores, and grade retention/dropout. Studies focusing on micro-level aspects of academic performance (e.g., homework problems; Langberg et al. 2010) or only on behavior at school (e.g., ADHD symptoms; Charach et al. 2004) were not included.

The reference section of each of the identified articles was examined for additional relevant studies that may have been missed with the database searches. In total, the search resulted in nine articles reporting on eight distinct longitudinal samples and a combined participant sample of 8,721 children and adolescents. These studies are summarized in Tables 1 and 2. The review is separated according to the academic outcome examined given evidence that achievement scores, school grades, and dropout/retention are overlapping but distinct constructs. Throughout, particular attention is given to

Table 1 Summary of sample and methods of studies included in the review

Authors (Year)	ADHD sample N	Source of ADHD diagnosis	Sample type	Potential confounding variables examined	Length of follow-up	Definition of medication use/adherence	Source of medication use/adherence data
Scheffler et al. (2009)	594	Parent report	Community Naturalistic	Gender, race, intelligence, income, parent education, and school services were included in models	K-5th grade	Medication use defined as number of years on medication	Retrospective parent report Parents interviewed at 5th grade follow-up regarding medication use during study
Barnard et al. (2010)	2,844	Parent report and school records	Community Naturalistic	Tested for group differences (subtypes) on gender, ethnicity, income, and location	5 years; Age range at baseline = 6–12 years	Medication use defined as on medication at all 3 time points compared to no medication; Intermittent stimulant users not included	Prospective parent report Parents interviewed three times during study period and asked if child is on ADHD medications (yes/no)
Massetti et al. (2008)	125	Study completed parent diagnostic interview with teacher ratings	Clinic Naturalistic	Intelligence, age, sex, family, income, race/ethnicity, and comorbid disorders included in models	8 years; Age range at final follow-up = 11–13 years	Medication variable examined is whether or not child received medication in the 12 months prior to each assessment point	Prospective parent report Parents interviewed yearly to obtain medication use data
Barbaresi et al. (2007)	370	School and medical records	Community Naturalistic	Tested for group differences on parent education level, parent age, and marital status; gender, subtype, comorbidities, school interventions, and maternal education included in models	Birth cohort; Median age at last follow-up = 18.4 years	Medication variables examined include: duration (months); average daily dose, age of onset, and any treatment (yes/no)	Medical chart and school record review
Powers et al. (2008)	90	Study completed parent diagnostic interview with teacher ratings	Clinic Naturalistic	Tested for group differences on age, SES, intelligence, and race/ethnicity	M = 9.13 years; M age at follow-up = 18.4 years	Medication use defined as consistent use for >1 year; sample M = 5.33 years	Retrospective parent report Services Received Interview administered to parents at follow-up
Molina et al. (2009)	436	Study completed parent diagnostic interview with teacher ratings	Clinic intervention to Naturalistic	Tested for group differences on parent education, gender income, age, race/ethnicity, marital status; Intelligence included in models for academic outcomes	8 years; M age at follow-up = 16.8 years	Medication variable is the proportion of days on medication in the past year	Prospective parent report Monthly medication visits during intervention phase followed by administration of SCAPI interview at all follow-up assessments
Langberg et al. (2011)	436	Study completed parent diagnostic interview with teacher ratings	Clinic intervention to Naturalistic	Intelligence, parent education, gender, income, race/ethnicity, and service utilization included in models	8 years; M age at follow-up = 16.8 years	Medication variable is average percentage of days on medication from baseline to 8 year follow-up	Prospective parent report Monthly medication visits during intervention phase followed by administration of SCAPI interview at all follow-up assessments
Markus and Durkin (2011)	3,543	School and medical records	Community Naturalistic	Gender, race/ethnicity, school level, comorbid disorders per medical record, learning disability per school record included in models	5 years; Grades 1–8	Medication use variable represents the number of marking period days with a stimulant prescription; Considered stimulant adherent if >70 % of days on medication	Medicaid claims reviewed to obtain prescription fill dates, refills and days' supply during each school marking period

Table 1 continued

Authors (Year)	ADHD sample *N*	Source of ADHD diagnosis	Sample type	Potential confounding variables examined	Length of follow-up	Definition of medication use/adherence	Source of medication use/adherence data
Biederman et al. (2009)	140	Study completed parent diagnostic interview with teacher ratings	Clinic Naturalistic	Tested for group differences on intactness of family of origin, ADHD severity, comorbid disorders, SES	10 years; *M* age at follow-up = 22 years	Participants classified as medication users if they reported a lifetime history of use and onset of treatment was before grade retention	Retrospective participant report Participants interviewed at follow-up to obtain age of onset of medication, name of medication, and age of treatment termination

ADHD attention-deficit/hyperactivity disorder, *CT* ADHD combined type, *DBD* disruptive behavior disorder, *GPA* grade point average, *HI* ADHD predominantly hyperactive type, *IA* ADHD predominantly inattentive type, *NOS* ADHD not otherwise specified type, *SCAPI* the services use for children and adolescents-parent interview

differences in how medication use/adherence was assessed (e.g., parent report versus medical record review; retrospective versus prospective). Further, differences in how medication use was defined (e.g., percent of days on medication, years on medication, and medication dose) are highlighted given that these differences could impact findings. Finally, potential confounds considered in the analyses are noted for each study given the strong association between variables such as intelligence and achievement scores (Mayes et al. 2009). Given the importance of these issues (i.e., definition and assessment of medication use/adherence, covariates examined), this information is summarized for each study reviewed in Table 1.

Results

Standardized Achievement Test Scores

The literature search produced seven studies that included an evaluation of the impact of long-term medication use on standardized achievement scores. Scheffler et al. (2009) used data from the Early Childhood Longitudinal Study (ECLS-K) to examine the impact of long-term medication use on achievement test scores. The ECLS-K followed the academic progress of a nationally representative sample of children from kindergarten through fifth grade. In the ECLS-K sample, 1,195 children were diagnosed with ADHD according to parent report. Specifically, at four of the five assessment points, parents were asked whether their child had been diagnosed with ADHD by a "professional". If a parent responded *yes* at any time during the study, the child was considered to have an ADHD diagnosis. Of the 1,195 students with ADHD, 594 (75 % female, 72 % White) had complete medication and academic achievement data and were included in the analyses.

Standardized math and reading achievement tests were administered five times during the course of the study (twice in Kindergarten and once in 1st, 3rd, and 5th grades). ADHD medication use was assessed using parent report when participants were in the fifth grade. Specifically, parents were asked to retrospectively report whether their child was taking medication for ADHD, and if so, had they taken medication for a period of .08–1 year, 1–2.5 years, 2.5–4.5 years, or greater than 4.5 years. The midpoint of the range selected (e.g., 3.5 for range of 2.5–4.5) was the variable used in the analyses. Analyses controlled for child demographic characteristics such as gender and race and also controlled for income, intelligence, and receipt of school services.

Analyses showed that medicated children's math achievement scores were on average 2.9 points higher than unmedicated children's scores. The mean improvement in math for the entire sample over the 6-year study period

Table 2 Summary of findings for long-term medication use by academic outcome examined

Authors (Year)	ADHD sample *N*	Measurement of academic outcomes	Findings for standardized achievement	Findings for school grades	Findings for retention/dropout
Scheffler et al. (2009)	594	Standardized achievement test administered five times between K-5th grades	Medicated participants are 2.9 points higher on math achievement than non-medicated, a .19 school year difference Medicated participants are 5.4 points. higher on reading achievement, a .29 school year difference Difference for reading only significant when comparing participants with >2 years medicated to participants with <2 years	NA	NA
Barnard et al. (2010)	2,844	Standardized achievement test administered at each of the 3 time points	Participants taking ADHD medications at all three time points did not differ significantly from those not taking ADHD medications on achievement scores Examined differences by subtype; Positive association between medication and reading for IA, HI, CT, and negative association for NOS group (less severe)	NA	NA
Massetti et al. (2008)	125	Standardized achievement test administered at all time points	Medication use *not* associated with achievement scores, $p > .10$	NA	NA
Barbaresi et al. (2007)	370	School record review to obtain reading achievement scores (statewide achievement test), absenteeism, and grade retention	Average daily dose associated with last reading score $r = .15$, $p = .012$; Duration of treatment and age of onset of treatment are *not* associated with reading achievement	NA	Participants treated with stimulants (yes/no) 1.8 times less likely to have been retained Average daily dose, duration of treatment, age of onset, and treatment (yes/no) are *not* associated with dropout
Powers et al. (2008)	90	Standardized achievement test administered at follow-up; school transcripts collected for half of sample to obtain grades; parents interviewed about grade retention	Non-ADHD group performs better than ADHD medicated and ADHD unmedicated at follow-up Medicated performs better than unmedicated on reading and math achievement scores, $p < .05$	Medicated youth significantly higher GPA (2.0) compared to unmedicated (1.4)	No significant differences on grade retention
Molina et al. (2009)	436	Standardized achievement test administered at each time point; School transcripts reviewed and coded for data on school grades and retention	Medication use in the past year positively associated with math standardized achievement scores at the 8 year assessment but not with reading or spelling	Medication use in the past year not associated with overall GPA	Medication use in the past year not associated with grade retention
Langberg et al. (2011)	436	Standardized achievement test administered at each time point; School transcripts reviewed and coded for data on school grades and GPA	Lifetime medication use positively associated with math and spelling achievement but not reading	Lifetime medication use not significantly correlated with school grades for any core class subject or with GPA	NA

Table 2 continued

Authors (Year)	ADHD sample *N*	Measurement of academic outcomes	Findings for standardized achievement	Findings for school grades	Findings for retention/dropout
Markus and Durkin (2011)	3,543	School transcripts reviewed and coded for data on school grades and GPA	NA	Stimulant-adherent marking periods were associated with significantly higher GPAs ($M = 2.18$ for adherent and $M = 1.99$ for nonadherent). Within-student analyses show a significant association between adherence and GPA over time. Small effect size ($d = .15$) and a .108 higher GPA	NA
Biederman et al. (2009)	140	History of grade retention collected through interviews with participants at follow-up	NA	NA	$M = .63$ grades retained for no-stimulant group compared to $M = .26$ for lifetime group; $p < .001$

ADHD attention-deficit/hyperactivity disorder, *IA* inattentive type, *HI* hyperactive impulsive type, *CT* combined type, *NOS* not otherwise specified, *GPA* grade point average, *DBD* disruptive behavior disorders

(K-5th grade) was 90.2 points. Given this trajectory, the authors calculated that a 2.9-point difference was equivalent to 0.19 school years. In contrast to math, analyses with reading scores did not reach statistical significance when comparing mediated to unmedicated children. However, children who were medicated $\geq$2 time points had significantly higher reading scores than unmedicated children. The 5.4-point difference between groups was estimated as comparable to 0.29 school years. The results did not change when parents' marital status, education, and income were added to the models, and there also was no effect of gender. However, the difference between children who were medicated or unmedicated was significantly reduced in both reading and math among children with Individualized Education Plans (IEPs). The authors concluded that despite significant improvements associated with medication use during elementary school, gains were modest and did not eliminate the achievement gap between children with and without ADHD in the ECLS-K Study.

Next, Barnard et al. (2010) used data from the Special Education Elementary Longitudinal Study (SEELS) to examine the impact of stimulant medication use on academic achievement over a 4-year period. SEELS is a nationally representative sample of 9,747 students between the ages of 6 and 12 eligible for special education services, of which 2,844 had a diagnosis of ADHD as reported by parents and supplemented with school records (77 % male, 73 % White). At each of the three study time points, a standardized achievement test was administered and parents were asked whether their child was currently taking ADHD medications. In the analyses, the authors compared children receiving stimulant medication at all three assessment points to children who never received stimulant medication (children who used stimulant medication at some time points but not at all three were dropped from analyses). Analyses only included the stimulant medication variable and did not control for demographic or child variables. Initial analyses demonstrated that children with ADHD who did or did not receive stimulant medication at all three time points did not differ on any measure of academic achievement.

The authors followed up these initial analyses by evaluating whether there were differences according to ADHD subtype classification. Based on teacher-reported symptom profiles, participants were placed into four ADHD groups: Predominantly Inattentive Type (IA), Predominantly Hyperactive/Impulsive Type (HI), Combined Type (CT), and Not Otherwise Specified (NOS). Children classified as NOS had less severe symptom profiles, but academic achievement scores were statistically equivalent across the four subtype groups. The authors also demonstrated that these four groups were equivalent on a number of important demographics characteristics, including gender, ethnicity, income, and geographical location. Results demonstrated a significant positive association between stimulant medication use and academic achievement across time for children classified as IA, HI, and CT. The association between stimulant use and achievement was negligible for the HI type (.11), small for the IA type (.21), and moderate for the CT type (.38). In contrast, there was a significant negative association (−.33) for children classified as ADHD NOS. The authors concluded that for a majority of children with ADHD, extended use of stimulant medication is associated with small improvements in academic achievement. The authors also suggest that given the negative response witnessed in the NOS group (17.5 % of sample), differences in response to stimulant medication as a function of ADHD subtype is an area that warrants additional investigation.

Massetti et al. (2008) completed a naturalistic longitudinal study examining the validity of the ADHD subtype classifications in predicting academic achievement. The sample consisted of 125 children diagnosed with ADHD between the ages of 4 and 6 and followed for 8 years (80 % male, 71 % White). Academic achievement was measured using standardized achievement test scores assessed yearly during the study. The authors were primarily interested in the validity of the ADHD symptom subtypes in predicting achievement but also examined a number of additional predictors as covariates in the model, including ADHD medication use.

ADHD medication use was assessed yearly during the study using parent interviews. The medication use variable of interest in this study was dichotomous, indicating whether or not the child took medication in the past 12 months. The authors also examined additional covariates, including but not limited to, family income, intelligence, and oppositional defiant/conduct disorder symptoms. The authors found that ADHD medication use was not associated with academic achievement ($p > .10$).

Barbaresi et al. (2007) examined modifiers of long-term school outcomes in a sample of 370 children with ADHD (75 % male) followed from birth as part of the prospective, population-based, Rochester Epidemiology Project (REP; $N = 5{,}718$). School records were reviewed for all participants to obtain data on reading achievement. In addition, medical records were collected which provided data on type of ADHD medication, dose, age of treatment initiation, and medication start and stop dates. Children were diagnosed with ADHD using a comprehensive review of school records and medical records designed to document the presence of *DSM-IV* symptoms of ADHD. The sample included children enrolled in public, private and parochial schools and children who were home-schooled.

The stimulant medication variable used in the analysis was average daily dose. The average daily dose variable was calculated by weighting each dose by the duration of use as determined by start and stop dates. In addition, the authors examined the total duration of treatment with stimulants in years. There was considerable variability in the sample in terms of duration of treatment with 59 youth treated from 1 to 3 years, 50 youth treated from 3 to 5 years, and 76 youth treated for greater than 5 years. The median duration of stimulant use was 30.4 months. Every 2 years, reading achievement was assessed using the California Achievement Test (CAT). The CAT score used in the analysis was the last available score in the data set when participant M age was 12.8. The authors reported no differences between participants treated with stimulants ($N = 272$) and participants who were not treated with stimulants ($N = 77$) on maternal or paternal age or education, marital status, or the presence of comorbid disorders. Further, the authors examined associations between gender, ADHD subtype, comorbid conditions, type of educational interventions, and maternal education with academic outcomes.

Analyses revealed that reading achievement scores at follow-up were not statistically different when comparing participants treated with stimulant medication to those who were not. However, there was a small significant correlation between the average daily dose of stimulant medication and reading achievement ($r = .15$), and children on the highest stimulant doses tended to have higher reading scores, although this difference was not statistically significant. Finally, duration of stimulant treatment was not significantly associated with reading achievement scores.

Powers et al. (2008) completed a 9-year follow-up of a subsample of 90 children (88 % male, 24 % White) who had been diagnosed with ADHD between the ages of 7–11 (baseline M age = 9.11, follow-up M age = 18.41). Children who did not participate in the follow-up or who were lost to follow-up (total = 47 % of sample) did not differ from those who participated in the follow-up on SES, IQ, or ADHD ratings at the initial assessment. At the follow-up assessment, academic achievement and parent interviews were conducted. Academic achievement was assessed using the Word Reading, Pseudoword Decoding, and Numerical Operations subtests from a standardized achievement test. Parents provided information during the follow-up interview about whether participants had ever repeated a grade in school. Parents were also asked about their child's medication use history, including when treatment was initiated, duration of treatment, and type of treatment.

Prior to conducting analyses, participants were divided into two groups: ADHD medicated and ADHD unmedicated. Participants were placed in the ADHD medicated group if they had received stimulant medication treatment and complied with the prescribed treatment regimen for at least 1 year ($n = 48$). On average, participants in the ADHD medicated group had been taking medication for 5.33 years. The data were analyzed with and without age at initial evaluation and baseline teacher ratings of ADHD symptoms as covariates. The two groups did not significantly differ on intelligence scores, gender, age, SES, or race/ethnicity (differences on parent education level were not reported).

Analyses comparing the achievement scores of medicated children to unmediated children revealed that although ADHD medicated children scored higher on all three academic achievement subtests, the differences were not statistically significant. However, when the two groups of children were compared controlling for age at initial evaluation and childhood ADHD symptom ratings, significant differences were found for all three achievement subtests with higher achievement scores among the ADHD medicated participants. Analyses examining change in achievement scores from baseline to follow-up (i.e., as opposed to group differences at follow-up) revealed that both groups' standard scores declined over time with no significant group main effect or group × time interaction present. However, when examining the subscales individually, the ADHD unmedicated group did have a significantly greater drop in Word Reading scores over time compared with their medicated peers ($p = .04$); no significant differences emerged for the other subtests.

As summarized in Table 1, Molina et al. (2009) reported on the 8-year follow-up of the Multimodal Treatment Study for Children with ADHD (MTA) sample (MTA Cooperative Group 1999). The MTA study began as a 14-month randomized intervention trial followed by a prospective naturalistic study with participants ($N = 579$) receiving services in the community. All significant group differences associated with the intervention trial were gone by the 36-month follow-up and participants remained significantly worse than a comparison control group at the 8-year follow-up on 91 % of measures. Participants were between the ages of 7–9 at entry into the MTA study (80 % male, 61 % White) and the mean age at the 8-year follow-up was 16.8 years.

Participant medication use was tracked using a structured parent interview completed at each of the MTA measurement time points: baseline, 14 months, 24 months, 36 months, 6 years, and 8 years. The medication variable examined in the Molina et al. (2009) study was the proportion of days that children received any medication for ADHD in the past year. Thirty-two percent of the MTA sample had taken ADHD medications more than 50 % of days in the past year. A majority of participants taking medication at the 8-year follow-up (75 % of sample) had also been taking medication when the study ended at the 14-month time point. To evaluate academic achievement, participants ($N = 436$) completed the reading, math and spelling subtests of a standardized achievement test. Medication use during the past year was treated as a time-varying covariate in the analyses. The proportion of days participants were on medication was not associated with reading or spelling achievement scores but was positively associated with math achievement scores at the 8-year follow-up. The authors concluded that because medication use in the past year largely reflected continuous use (i.e., the majority of participants medicated at 8-years were also medicated at 14-months), the association suggested a benefit of long-term medication use on math achievement.

Langberg et al. (2011) expanded upon the Molina et al. (2009) study by examining lifetime ADHD medication use as a predictor of standardized achievement scores in the MTA sample ($N = 436$ at the 8-year follow-up). Further, the Langberg et al. (2011) study examined a wider range of predictor variables shown to impact academic performance, including homework problems, teacher ratings of children's academic competence, SES, child ethnicity, IQ, parent education, family income, receipt of school services (e.g., IEPs), and ADHD symptom severity.

In this study, lifetime medication use was defined as the percentage of days the child took ADHD medications between the MTA baseline and the 8-year follow-up. This information was gathered through parent interviews completed at each of the MTA time points. Homework problems were measured using the parent-completed Homework Problems Checklist (HPC; Anesko et al. 1987; Power et al. 2006), academic competence with the teacher-completed Social Skills Rating Scale (SSRS; Gresham and Elliott 1990), and ADHD symptoms with the SNAP-IV rating scale (Swanson 1992).

On average, MTA participants were on ADHD medication for 43 % of the days between baseline and the 8-year follow-up. This variable was significantly correlated with math and spelling achievement at the 8-year follow-up but not with reading achievement. Crucially, however, when the medication use variable was included in a regression model with all of the predictor variables of interest, it was no longer significantly associated with math and spelling achievement scores. Rather, ratings of participants' homework materials management and academic competence in elementary school were the strongest predictors of achievement scores in adolescence. Intelligence, family income, and parental education were also significant predictors in the final model, demonstrating the importance of controlling for these variables in studies of ADHD medication use.

Strengths and Weaknesses of Studies of Achievement Test Scores

A strength of this group of studies is that all considered potential covariates known to be associated with academic outcomes, such as intelligence, income, and parent education level. In terms of ADHD diagnoses, participants in four of the seven studies were diagnosed with ADHD using a comprehensive multi-informant evaluation conducted as part of the research study (Langberg et al. 2011; Massetti et al. 2008; Molina et al. 2009; Powers et al. 2008). Two additional studies employed a multi-method approach using medical records and school records (Barbaresi et al. 2007) or parent report in combination with school records (Barnard et al. 2010). Only one study relied solely on parent report (Scheffler et al. 2009).

For mediation adherence data, four studies gathered information through prospective parent report (Barnard et al. 2010; Langberg et al. 2011; Massetti et al. 2008; Molina et al. 2009). Two studies gathered this information through retrospective parent report, both asking parents to recollect back multiple years (Powers et al. 2008; Scheffler et al. 2009). Finally, Barbaresi et al. (2007) utilized a review of medical records to gather information about the type and dose of medications prescribed to participants.

There was considerable variability in how medication use/adherence was defined across the studies focused on academic achievement. Barbaresi et al. (2007) provided the most comprehensive examination, evaluating use/adherence in three ways: (1) comparing medicated to unmedicated participants; (2) grouping participants based upon the number of years on medication; and (3) examining outcomes as a function of the average daily dose of medication. Three of the studies examined medication use as a continuous variable, as a percentage of days medicated either in the past year or in the lifetime (Langberg et al. 2011; Massetti et al. 2008; Molina et al. 2009). Scheffler et al. (2009) examined whether academic outcomes varied depending on the number of years participants had been taking ADHD medications. Finally, Barnard et al. (2010) and Powers et al. (2008) both took a yes or no approach, dividing participants into two groups. Using a yes/no approach meant that somewhat arbitrary cutoffs were applied. For example, the unmedicated group in the Powers et al. (2008) study was any participant medicated less than 1 year, and in the Barnard et al. (2010) study, participants with intermittent medication use were dropped from the analyses.

School Grades

Markus and Durkin (2011) retrospectively analyzed Medicaid and school records from a sample of 3,543 1st–8th-grade children (75 % male, >50 % African American). Children in the sample had one or more stimulant prescriptions and had been diagnosed with ADHD according to Medicaid records and school records (excluding children with documentation of developmental delay, mental retardation, autism, speech/language impairment and/or traumatic brain injury). School grades were the academic outcome of interest with participants' English, mathematics, social studies, and science grades averaged to create a GPA variable on a scale from 0 to 4.0.

Stimulant medication records and grades were collected over a 4-year period. Participants' grades were collected at each marking period, with three marking periods occurring during each school year. The authors first compared mean GPA during stimulant adherent and non-adherent marking periods and then examined variation in individual participants' GPA over time as a function of stimulant adherence. Participants were coded as either stimulant adherent or stimulant non-adherent for each marking period using prescription fill data. Specifically, the number of marking period days for which participants had a supply of stimulant medication was divided by the total number of days in the marking period to create a continuous stimulant adherence variable ranging from 0 to 1.0. The authors considered a marking period stimulant adherent if the ratio was $\geq$.70. Each marking period was also coded to represent whether the participant's prescription was new (absence of a prescription in the previous 90 days) or continuing.

Across the entire sample, results showed that mean GPA was significantly higher during stimulant adherent marking periods (19 % of marking periods; $M = 2.19$) in comparison with stimulant non-adherent marking periods ($M = 1.99$). Further analyses indicated that the association between stimulant use and GPA was stronger among children in middle school in comparison with children in elementary school, and also for new stimulant treatment periods in comparison with continuous use. In the within student analyses, stimulant adherence was also significantly associated with GPA. Stimulant adherence was associated with a .11 higher GPA, a small effect ($d = .15$). The pattern of results was consistent across participant race/ethnicity. The authors noted that although results were statistically significant, the differences between the stimulant adherent and non-adherent groups were small and potentially lacked clinical or educational significance.

The Langberg et al. (2011) and Molina et al. (2009) studies described in detail above also involved an examination of school grades in the MTA sample ($N = 436$ at the 8-year follow-up). Molina et al. (2009) examined the impact of medication use in the past year on overall GPA at the 8-year follow-up and did not find a significant effect. Langberg et al. (2011) completed additional analyses to examine the impact of lifetime medication use on school grades examined separately by subject area (e.g., math, reading) and also as a predictor of overall GPA. The average percentage of days on ADHD medication between baseline and the 8-year follow-up in the MTA sample was not significantly correlated with school grades for any of the core class subjects examined. Rather, ratings of participants' homework materials management and academic competence in elementary school were the strongest predictors of grades.

Powers et al. (2008; described in detail above) also collected school transcripts for a portion of the sample ($N = 43$; 48 %) to examine participant GPA in high school. Analyses demonstrated that medicated participants had a higher high school GPA in comparison with unmedicated participants after controlling for age at evaluation and ADHD symptom ratings. The authors concluded that long-term stimulant medication use (>1 year) does improve academic functioning as measured by GPA. However, the authors noted that the magnitude of the effects was modest and academic functioning was not normalized with medication (e.g., M high school GPA for ADHD medicated participants = 2.0).

Strengths and Weaknesses of Studies of School Grades

Three of the studies of school grades diagnosed ADHD using a comprehensive evaluation (Langberg et al. 2011; Molina et al. 2009; Powers et al. 2008) and one study relied on a review of school and medical records (Markus and Durkin 2011). All four studies either accounted for potential covariates or examined whether patterns of results varied as a function of demographic characteristics such as child ethnicity (Markus and Durkin 2011). Three of the studies relied on parent report for medication use data, with two using prospective report (Langberg et al. 2011; Molina et al. 2009), and the other retrospective report (Powers et al. 2008). Markus and Durkin (2011) obtained information about ADHD medication prescriptions through a review of medical records. Finally, Markus and Durkin (2011) examined medication use prospectively at multiple time points. Further, they specifically examined the question of medication adherence, defining adherence as a participant holding a prescription for medication at least 70 % of the days during a marking period.

Grade Retention/Dropout

Biederman et al. (2009) completed a 10-year prospective longitudinal study of 140 boys with ADHD. The primary purpose of the study was to determine whether extended stimulant medication use protected against the development of comorbid psychopathology. However, the authors also examined the impact of medication use on grade retention. Participants ranged in age from 6 to 17 years at baseline and from 15 to 30 years at the 10-year follow-up. At the follow-up ($N = 112$), participants were interviewed about their ADHD medication use. Participants were asked to report on the names of medications taken between baseline and follow-up, age of treatment onset, and age at treatment termination. During the follow-up interview, participants were also asked about grade retention.

The authors created a dichotomous (yes/no) lifetime stimulant use variable. Participants were placed in the lifetime stimulant group if they reported a history of stimulant treatment and the stimulant treatment began before the reported outcome of interest. Five participants whose grade retention and stimulant use started at the same time were dropped from the analyses because they could not be categorized. Seventy-three percent of the sample that completed the 10-year follow-up met criteria for the lifetime stimulant use category. The mean age of treatment onset in the sample was 8.8 years and the mean duration of treatment was 6 years. The authors reported that the two groups (medication yes/no) did not differ on parent marital status, ADHD symptom severity, baseline psychopathology, or SES. Group differences on intelligence and standardized achievement scores were not examined and the no-stimulant use group was significantly younger at the 10-year follow-up. Results showed that participants in the lifetime stimulant use group were significantly less likely to have been retained a grade ($M = .26$ grades retained) as compared to participants in the no-stimulant use group ($M = .63$ grades retained). The authors concluded that long-term stimulant treatment had a protective effect against the occurrence of grade retention.

Barbaresi et al. (2007; described in detail above) also collected school records data on absenteeism, grade retention, and school dropout. School record data on retention, absenteeism, and school dropout were obtained for as long as participants were in school, with the median age at the last follow-up being 18.4 years. The authors reported a significant association between stimulant use and school attendance. Specifically, children treated with stimulants were absent from school significantly less of the time compared with untreated children, and greater stimulant use duration was associated with fewer absences from school. Children treated with stimulants were also 1.8 times less likely to be retained a grade but did not differ from nontreated children in school dropout rates. Higher maternal education served as a protective factor for both grade retention and school dropout.

Finally, Molina et al. (2009) and Powers et al. (2008; both studies described in detail above) also examined the impact of medication use on grade retention. No effects for medication use were found either for percentage of days medicated in the past year (Molina et al. 2009) or for differences between medicated and unmedicated participants (Powers et al. 2008). These null results were not due to a lack of variability, as approximately 25 % of the MTA sample had been retained at least one grade by the 8-year follow-up.

Strengths and Weaknesses of Studies of Grade Retention/Dropout

The Biederman et al. (2009) study included participants who were comprehensively diagnosed with ADHD. Another strength of the study is that potential covariates such as SES were examined. However, medication use data were obtained through retrospective report with participants being asked to recall medication use over a 10-year period. Further, analyses of adherence were conducted by dichotomizing the sample into yes/no rather than as a continuous variable. In contrast, the Barbaresi et al. (2007) sample was diagnosed based upon a review of medical and school records and also examined the role of potential covariates. Barbaresi et al. also examined medication adherence in four separate ways. Finally, Molina et al. (2009) and Powers et al. (2008) included samples comprehensively diagnosed with ADHD and covariates were considered. In the Powers et al. (2008) study, medication use was examined as yes/no and these data were obtained through retrospective parent report. In contrast, in the Molina et al. (2009) study, medication use was defined as the percentage of days on medication in the past year and these data were obtained through prospective parent report.

Discussion

Longitudinal research evaluating the relation between long-term ADHD medication use and the academic outcomes of youth with ADHD has improved substantially in the past 10 years, in terms of the number of studies completed, sample size and sample diversity, and quality of research methodologies employed. During this time, the impact of long-term medication use on standardized achievement scores has been examined in six longitudinal samples, on school grades in three samples, and on grade retention in four samples (total ADHD participant $N = 8{,}721$). All studies included in this review followed children with ADHD for a minimum of 3 years ($M =$ 8.13 years across studies reviewed). Four of the studies reviewed followed participants from childhood into early adolescence, and five studies followed children into late adolescence or into adulthood.

Evidence now exists to support the assertion that long-term ADHD medication use is associated with improvements in standardized achievement scores. A positive association between long-term medication use and academic achievement was documented in six of the seven studies that examined this relation (see Table 2). However, there is also substantial evidence to suggest that although the gains in achievement produced by long-term medication use are statistically significant, the magnitude of these gains is small [e.g., Barbaresi et al. (2007) medication with reading = .15; Langberg et al. (2011) medication and math = .14]. Further, whether the size of the improvements in achievement is clinically or educationally significant remains unclear.

Scheffler et al. (2009) examined this question by examining the association in terms of the typical trajectory of achievement and found that over a 5-year period, long-term medication use produced gains equivalent to .19 school years for math and .29 school years for reading. However, in terms of educational significance, it is important to note that positive associations between medication and achievement scores do not necessarily reflect actual changes in academic knowledge. Specifically, gains in achievement scores may largely be due to improvements in test taking behaviors, such as an increased ability to maintain focus during the testing. Regardless of whether the gains are educationally meaningful, it is clear that long-term medication use does not normalize achievement, as demonstrated by each of the studies in this review that included a non-ADHD comparison group (e.g., Massetti et al. 2008; Molina et al. 2009).

Research examining the relation between long-term medication use and school grades is less conclusive. One study found a modest difference in grades between participants who were medicated (GPA = 2.0) and those who were not (GPA = 1.4), but the sample size was very small ($N = 43$ with grade data; Powers et al. 2008). Another, much larger study ($N = 3{,}543$) found that children who were stimulant adherent had significantly higher grades in comparison with non-adherent children, but the magnitude of the effect was small ($d = .15$; Markus and Durkin 2011). Finally, data from the 8-year follow-up of the MTA sample (Langberg et al. 2011; Molina et al. 2009) showed no significant relationship between either lifetime medication use or past year medication use and school grades. Of these studies, the Markus and Durkin (2011) study is the strongest of the four studies reviewed because it included a large diverse sample, controlled for a number of important covariates (e.g., SES, ethnicity, comorbid psychopathology), and used medication prescription records to define medication use rather than parent report. Accordingly, the best evidence collected to date suggests that there may be a small positive relationship between long-term medication use and grades. However, as noted by the authors, it is not clear that this difference ($d = .15$) has clinical or educational significance.

Two of the four studies that examined the association between long-term mediation use and grade retention found significant group differences. Barbaresi et al. (2007) found that long-term stimulant users were 1.8 times less likely to be retained. Similarly, Biederman et al. (2009) reported that lifetime stimulant users (retained .26 times on average) were significantly less likely to be retained compared with non-stimulant users (retained .63 times on average). In contrast, neither Powers et al. (2008) nor Molina et al. (2009) found an association between medication use and grade retention. It is difficult to discern why these studies produced such different results. Of the two studies that found an effect on grade retention, one was a naturalistic community sample (Barbaresi et al. 2007) and the other was a clinic-based sample (Biederman et al. 2009), and so sample type is not a plausible explanation. In addition, sample sizes are nearly equivalent (total $N = 510$ for studies with an effect and total $N = 496$ for studies without an effect). Further, in all four studies, the sample was followed into high school, and so differences in duration of time in school are not a likely explanation. It is noteworthy that in the Barbaresi et al. (2007) study, there was an effect of stimulant use (yes/no) on grade retention, but there was not an effect on school dropout. This finding again highlights the importance of not lumping academic outcomes together and assuming that effects on one outcome will translate into effects for another. In summary, more research is needed before conclusions can be drawn about the relation between long-term medication use and grade retention and school dropout.

It is interesting to consider why improvements in academic outcomes over a follow-up period of a minimum of 3 years (i.e., studies in this review) are relatively small, when larger improvements have been documented in shorter-term studies (e.g., Evans et al. 2001; Hechtman et al. 2004; MTA Cooperative Group 1999; Pelham et al. 2001). The most likely explanation is that in the studies with relatively short follow-up periods, medication was managed as a part of the study and included rapid titration and frequent monitoring and adjustment. In contrast, in the studies included in this review, participants had their medication managed in the community. In community settings, placebo controlled trials are rarely used to rapidly titrate medication and adjustments occur infrequently (Epstein et al. 2008, 2011). It is clear that these differences in medication management procedures have a significant impact on child outcomes, with children receiving consistent monitoring and titration performing significantly better across a range of functional outcomes in the short-term (MTA Cooperative Group 1999).

However, it is also important to note that even when children receive a rapid titration trial, the gains achieved through this process are not automatically maintained. Specifically, in two of the studies included in this review (Langberg et al. 2011; Molina et al. 2009), participants received a placebo controlled titration trial and frequent monitoring for a period of 14 months before transferring to medication management in the community. The fact that the improvements associated with the MTA medication management protocol were no longer present at the 6- or 8-year follow-ups (Molina et al. 2009) highlights the importance of consistent, on-going, medication monitoring and adjustment above and beyond the importance of rapid titration. It may be that if academic outcomes are consistently monitored over a period of years, and medication titrated in accordance with these outcomes, children with ADHD could experience long-term benefits. At this point, however, there is not enough research to address this possibility.

An alternative explanation for the lack of robust effects for medication on academic performance is that medications are frequently titrated based upon behavioral outcomes rather than cognitive or academic indicators (Hale et al. 2011; Swanson et al. 1991). In an earlier review of the literature, Swanson et al. (1991) concluded that there is no evidence to suggest that medication use improves the long-term academic achievement of children with ADHD. The authors suggested that children with ADHD may not experience significant academic improvements because they are often on higher than optimal doses. That is, the ideal dose of medication for cognitive/academic functioning may actually be lower than the ideal dose for behavioral functioning (i.e., ADHD symptoms). Hale et al. (2011) recently tested this hypothesis using double-blind placebo controlled methodology with 52 children with ADHD. The authors found that the best dose for neuropsychological functioning was usually lower than the best dose for behavioral functioning. This finding is important as it suggests that physicians may need to help parents prioritize and make conscious decisions about which functional outcomes to target in terms of monitoring and titrating medication.

Methodological Considerations

There were some significant methodological differences across the studies reviewed that had an impact on the findings. These differences are reviewed below as they have important implications for future longitudinal research on the relation between long-term medication use and academic outcomes.

Assessment of Medication Use

The majority of studies in this review ($N = 7$; 78 %) gathered information about medication use through either parent or participant interview. The studies that used parent interview varied greatly in how frequently medication use was assessed and the period of time for which parents were asked to retrospectively recollect their child's medication use. For example, in some studies (Massetti et al. 2008; Molina et al. 2009), parents were queried yearly about medication use, reporting on use since the time of the last study assessment. However, in other studies, parents were asked to retrospectively recall medication use onset and start and stop dates from the past five (Scheffler et al. 2009) to ten (Biederman et al. 2009) years. The manner in which medication use is assessed is important because parents have been shown to overestimate adherence as compared to data collected using more objective techniques (e.g., saliva samples, Pappadopulos et al. 2009; electronic monitoring, Rapoff 2009). Further, parents' ability to retrospectively recall detailed information regarding medication start and stop dates over 5–10-year periods is questionable at best. Future studies of long-term medication use should be prospective, should assess use frequently (e.g., monthly), and should employ multiple measures of tracking medication adherence such as pill counts, medical record reviews (Barbaresi et al. 2007; Markus and Durkin 2011), and parent interview.

Definition of Medication Use

There was considerable variability in how medication use was defined in the studies reviewed. As shown in Table 1, definitions of medication use included lifetime use, past year use, use during a school marking period, and number of years on mediation. This is important because the definition appears to have a significant impact on study outcomes. Specifically, Barbaresi et al. (2007) took a comprehensive approach and defined medication in four ways: (1) treatment with stimulants (yes/no); (2) average daily dose of stimulants; (3) duration of treatment with stimulants; and (4) age of onset of stimulant treatment. Markedly different results were reported based upon the metric used. For example, average daily dose was significantly positively associated with reading achievement but the associations between yes/no, duration, and age of onset with reading achievement were not significant (Barbaresi et al. 2007). This is a particularly interesting finding because one of the main differences in medication managed through study protocols versus medication managed in the community is related to the daily dose of medication prescribed. Specifically, children tend to be titrated up to significantly higher doses in research titration trials in comparison with the community (e.g., MTA Cooperative Group 1999). These findings highlight the need for future research to move away from dichotomous yes/no categorizations of medication use and to look at more micro-level variables such as daily dose of medication instead. The most clinically useful information will likely come from future studies that examine a range of medication definitions and durations.

As shown in Table 1, the studies reviewed also differed in terms of how long participants had to take medication to be placed in the medicated group. For example, in the Powers et al. (2008) study, participants had to use medication consistently for at least 1 year, whereas in the Barnard et al. (2010) study, participants had to be medicated at all three time points (approximately 3 years) in order to be placed in the medicated group. This distinction is particularly important given that differences in outcome were found based upon the duration of medication use. Specifically, in the Scheffler et al. (2009) study, participants were grouped based upon the number of years they had taken stimulant medication, with durations ranging from less than 1 year to greater than 4.5 years. Only participants who were medicated for a minimum of 2 years were higher on reading achievement than their non-medicated peers. These findings again demonstrate the need for a more micro-level measurement approach, such as examining a range of years on medication rather than simply classifying participants as medicated or unmedicated. Future studies should also consider examining the impact of variables such as type of medication, mode of delivery, and/or the use of long-acting versus short-acting mediations.

Conclusions and Future Directions

In conclusion, it is clear that long-term medication use is positively associated with improvements in standardized achievements test scores, but the clinical and educational significance of this association is questionable. In contrast, evidence for an association with grade retention and school grades is less compelling and more research is needed in this area before firm conclusions can be drawn. Overall, research on the impact of medication on academic outcomes such as grades and achievement scores is in contrast to research on the impact of medication on objective measures such as productivity which have previously shown robust effects (Evans et al. 2001). These findings are also in contrast to data from randomized controlled trials which show that improvements in functioning from medication use can be maintained for a period of up to 2 years (Hechtman et al. 2004; MTA Cooperative Group 2004). As discussed above, these discrepancies are likely due to differences in the frequency with which medication is monitored and titrated in intervention trials versus in the community (Epstein et al. 2008, 2011).

Future research on long-term medication use in children with ADHD should use multiple sources to gather information about medication adherence, including methodologies such as electronic monitors, which are commonly used in other areas (e.g., Hommel et al. 2009) but infrequently used in ADHD research. Further, when parent interviews are used, they should be completed frequently, rather than asking parents to recollect about past use across a period of years. Future research should also include a wide range of medication adherence definitions to determine whether age of onset, duration of use, dose, and/or consistency of use is the most important factor for improving the academic outcomes of children and adolescents with ADHD. As described in the introduction, comprehensive models of medication adherence have been proposed (Gearing et al. 2011) based upon the fact that adherence is a dynamic concept. Gearing et al. (2011) note that *when* medication nonadherence occurs (e.g., following a titration trial versus after a period of years) likely has a significant impact on outcomes. These types of questions were not examined in the studies reviewed and this is an important area for future research.

Future research should also move beyond evaluation of whether or not children with ADHD are adherent to medication to examining moderators and mediators of long-term adherence. There is already some promising research in this area, suggesting that it may be possible to predict which children/families will have difficulties with adherence. For example, Thiruchelvam et al. (2001) found that an absence of teacher-rated oppositional defiant disorder, more teacher-rated ADHD symptoms, and a younger age at baseline predicted adherence in a sample of 71 children with ADHD followed for 3 years. Additional research on moderators and mediators of ADHD medication adherence may serve to identify families that could benefit from interventions to promote adherence.

It will also be important for future research to consider the developmental trajectories of youth with ADHD in conjunction with medication treatment and academic functioning, including aspects of medication compliance, developmentally distinct academic demands (e.g., transition to multiple classes in middle school and the possibility of school dropout in high school), and the full continuum of ADHD symptomatology. For instance, Bussing et al. (2010) examined the adolescent functioning of children diagnosed with ADHD and found that subthreshold ADHD in adolescence, but not full ADHD, increased risk for grade retention. Adolescents with subthreshold ADHD also had the lowest graduation rates. As such, these students with subthreshold ADHD are certainly in need of research and clinical attention. As reviewed above, Barnard et al. (2010) examined the effect of stimulant medication on academic achievement scores across subtypes of ADHD and found that the ADHD NOS group of children with less severe ADHD symptomatology, in contrast to the subgroups of children with full ADHD, had a *negative* medication response in relation to academic achievement. This is a perplexing finding, and additional work is clearly needed across the range of ADHD symptom levels, particularly as youth with subthreshold ADHD are less likely receive ADHD medication treatment (Barbaresi et al. 2002; Reich et al. 2006) or be eligible for special education or other school services, perhaps leaving these youth underidentified and at unique risk for school failure (Bussing et al. 2010).

Finally, it is important to note that only a few of the studies reviewed examined trajectories over time (i.e., most examined group differences at points in time). One study that did examine trajectories found that reading achievement scores declined over time for both the medicated and unmedicated groups (Powers et al. 2008). This finding has significant implications for how questions about the impact of long-term medication use are framed. Specifically, it may be that medication does not lead to improvements in academic outcomes but does stem the tide and prevents academic functioning from deteriorating. This is an important question that can only be answered through longitudinal research that collects academic outcomes at multiple time points. In summary, in the next generation of research examining long-term medication use and the academic outcomes of children and adolescents with ADHD, attending to developmental, measurement, and other methodological factors will not only increase our ability to draw conclusions about the effects of long-term medication use on academics, but in turn, also inform empirically based prevention and intervention efforts.

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