Published in final edited form as:
Exp Clin Psychopharmacol. 2009 October ; 17(5): 291–301. doi:10.1037/a0017259.

The Effects of Methylphenidate on Discounting of Delayed Rewards in ADHD

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Abstract

Impulsivity is a central component of attention-deficit/hyperactivity disorder (ADHD). Delay discounting, or a preference for smaller, immediate rewards over larger, delayed rewards is considered an important aspect of impulsivity, and delay-related impulsivity has been emphasized in etiological models of ADHD. The current study examined whether stimulant medication, an effective treatment for ADHD, reduces discounting of delayed experiential and hypothetical rewards among 49 children (age 9–12 years) with ADHD. Following a practice day, participants completed a 3-day double-blind placebo-controlled acute medication assessment. Active doses were long-acting methylphenidate (Concerta), with the nearest equivalents of 0.3 and 0.6 mg/kg TID immediate-release methylphenidate. On each testing day, participants completed experiential (real-world money in real time) and hypothetical discounting tasks. Relative to placebo, methylphenidate reduced discounting of delayed experiential rewards, but not hypothetical rewards. Broadly consistent with etiological models that emphasize delay-related impulsivity among children with ADHD, these findings provide initial evidence that stimulant medication reduces delay discounting among those with the disorder. The present results also draw attention to task parameters that may influence the sensitivity of various delay discounting measures to medication effects.

Attention-deficit/hyperactivity disorder (ADHD) is a heterogeneous disorder characterized by developmentally inappropriate and impairing levels of inattention and/or hyperactivity and impulsivity (see American Psychiatric Association, 2000; Swanson et al., 1998). Etiological models of ADHD implicate cognitive and motivational processes, and an integration of these processes as in the dual-pathway model of ADHD (Sonuga-Barke, 2002, 2005). Within this model, impulsive behavior is characterized in part as a rational choice to avoid delay because it is experienced as aversive. Delay aversion is considered an important pathway in the development of ADHD, along with executive function deficits such as inhibitory control (Willcutt, Sonuga-Barke, Nigg, & Sergeant, 2008). The delay aversion hypothesis emphasizes the negative motivational and emotional significance of delay for children with ADHD as an expression of a broader motivational style, which results in a preference for immediate over delayed rewards (Sonuga-Barke, Sergeant, Nigg, & Willcutt,

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2008). The consideration of delay aversion in theoretical accounts of ADHD has contributed to the shift towards multi-process rather than single-deficit etiological models.

Neurobiologically, delay aversion is thought to be related to impairments in the neural signaling of delayed rewards and to involve brain reward circuits linking the ventral striatum to frontal regions (Sonuga-Barke et al., 2008; Willcutt et al., 2008). Dopamine is considered a key neuromodulator in sending signals for reward (i.e, information regarding incentive value and availability) and regulating behavioral processes under conditions of delayed reward. Similarly, Sagvolden and colleagues (Sagvolden, Johansen, Aase, & Russell, 2005) have postulated that a hypofunctioning mesolimbic dopamine branch gives rise to delay aversion and impulsivity by altering reinforcement and causing deficient extinction of previously reinforced behavior.

Developmentally, delay aversion may emerge out of an impulsive drive for immediate reward (Sonuga-Barke et al., 2008), a construct closely related to the phenomenon of delay discounting, (Rachlin & Green, 1972). Delay discounting refers to “the change in the value of a reward as a function of its temporal proximity” (Green, Fry, & Myerson, 1994, p. 33). Behaviorally, delay discounting is operationalized as a preference for smaller, immediate rewards over larger, delayed rewards. Delay discounting tasks are employed to model impulsive behavior in substance use and gambling (Reynolds, 2006), as well as ADHD (Barkley, Edwards, Laneri, Fletcher, & Metevia, 2001; Scheres, Lee, & Sumiya, 2008; Sonuga-Barke, Taylor, Sembi, & Smith, 1992).

Several measures have been developed to assess delay-related impulsivity in humans and animals. In humans, delay discounting tasks have been categorized as hypothetical, real-reward, or real-time tasks; this distinction depends on the extent to which the individual actually experiences the delays and rewards associated with his or her choices (Reynolds, 2006). Hypothetical discounting tasks are generally question-based and involve imaginary delays and rewards (see Green & Myerson, 2004). Real-reward discounting tasks utilize a similar approach to hypothetical discounting tasks, but the participant receives one of the choice responses from all of the choices made (e.g., Kirby, 1997; Richards, Zhang, Mitchell, & de Wit, 1999). Real-time assessments require participants to experience the consequences of each of their choices (e.g., delays and rewards). It has been suggested that real-time discounting measures provide a more sensitive tool for examining short-term changes in delay discounting (McDonald, Schleifer, Richards, & de Wit, 2003; Reynolds & Schiffbauer, 2004). Real-time tasks also may be better suited for use with children because the choices are less abstract (Reynolds, 2006) than for hypothetical or real-reward-only assessments.

Initial studies of delay-related impulsivity in ADHD (Solanto et al., 2001; Sonuga-Barke et al., 1992) used the Choice Delay Task, which involves making repeated choices between receiving 1 point (exchanged for 1 penny) after a 2 s delay and 2 points after a 30 s delay. Sonuga-Barke and colleagues (1992) found that overall delay (as reflected in session length), rather than pre-reward delay or reward size, produced impulsive responding in hyperactive children compared to controls. This finding has been replicated in subsequent studies (Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2008; Solanto et al., 2001; see review byWillcutt et al., 2008). In addition, Solanto et al. (2001) found that teacher ratings of hyperactivity and impulsivity predicted delay aversion. Furthermore, both children with and without ADHD showed a reliable increase in their preference for the delayed reward after receiving the reward halfway through the task, suggesting that reward salience may influence delay-related impulsivity.

Barkley and colleagues (2001) examined delay-related impulsivity among adolescents with and without ADHD using a traditional hypothetical discounting task (Green et al., 1994; Green, Myerson, Lichtman, Rosen, & Fry, 1996). The task involved a series of choices regarding hypothetical amounts of money available immediately or after some specified delay interval. ADHD participants exhibited greater delay discounting than did the control participants for $100 delayed rewards but not for $1000 delayed rewards. The authors interpreted the lack of group differences for the $1000 delayed rewards as a result of the reward context. Specifically, the $1000 choices always followed the $100 choices and most of the immediate amounts for the $1000 choices were larger than the delayed amount for $100 choices, which resulted in a general preference for the immediate reward. The results of this study raise important questions regarding task design issues including the selection of developmentally appropriate delay intervals and reward values to be used in delay discounting tasks.

Scheres and colleagues (Scheres et al., 2006; Scheres et al., 2008) have also examined the relationship between delay-related choice and ADHD. Scheres et al. (2006) found little evidence of greater preference for immediate rewards among children with and without ADHD using real-time discounting tasks, failing to support previous research in this area (Barkley et al., 2001; Solanto et al., 2001; Sonuga-Barke et al., 1992). Possible reasons for the null findings may be the possible inclusion of subthreshold children for control participants; the inclusion criteria of a *T*-score below 65 on ADHD-related scales is greater than 1 standard deviation above the mean and teacher ratings were not included. In addition, group differences may have been present if ADHD-subtype differences were considered (Scheres, 2009). More positive results were obtained in a subsequent study of undergraduate students selected to vary in self-reported ADHD symptoms (Scheres et al., 2008). Greater self-reported symptoms of hyperactivity/impulsivity were associated with steeper discounting on a real-time discounting task but not on a hypothetical discounting task. The authors interpret these findings as evidence that hyperactivity/impulsivity may be related to an inability or unwillingness to make choices for delayed options primarily when the delays and rewards are actually experienced by the participant (Scheres et al., 2008, p. 224). Consistent with this dimensional approach, others have observed a positive relationship between delay aversion and ADHD symptoms in pre-school children (Sonuga-Barke, Dalen, & Remington, 2003) and school-age children (Thorell, 2007) using a modified version of the Choice-Delay Task (c.f., Wahlstedt, 2008).

Given this emerging literature and the theoretical relevance of delay-related choice in etiological models of ADHD, an important next question is whether empirically supported treatments for ADHD reduce the tendency of children with ADHD to select smaller immediate rewards over larger delayed rewards. Stimulant medication is a leading intervention for the disorder (American Academy of Child and Adolescent Psychiatry, 2007; American Academy of Pediatrics, 2001) and is the focus of the present work. According to the dynamic developmental theory proposed by Sagvolden and colleagues (Sagvolden et al., 2005), dysregulated frontostriatal circuits and hypofunctioning dopamine systems are responsible for inattentive, hyperactive, and impulsive behaviors which characterize ADHD. Sagvolden also argues that stimulant medication, such as methylphenidate, may lengthen the delay-of-reinforcement gradient by increasing tonic dopamine levels (Sagvolden, Aase, Zeiner, & Berger, 1998). Furthermore, the delay aversion hypothesis has implicated catecholamine-modulated brain reward circuits and the importance of dopamine in particular (Sonuga-Barke et al., 2008; Willcutt et al., 2008) suggesting that stimulant medication may reduce delay-related impulsivity in children with ADHD.

The effect of stimulants on delay-related impulaisivty in ADHD has not been previously studied, but there are relevant animal and human studies. Interestingly, d-amphetamine

increases delay discounting in rats (Evenden & Ryan, 1996). However, both d-amphetamine and methylphenidate have been found to dose-dependently decrease delay discounting in rats reared in an isolated environment (considered to be more impulsive), whereas the opposite effect may be observed among rats reared in an enriched environment (Perry, Stairs, & Bardo, 2008). Based on these findings, the authors suggest that psychostimulants may decrease impulsive choices among high-impulsive individuals, whereas it may increase impulsive choices in low-impulsive individuals. The limited studies in humans have found that the administration of acute d-amphetamine (de Wit, Enggasser, & Richards, 2002) resulted in decreased delay discounting on a real-reward question based measure. Furthermore, methylphenidate reduced impulsive responding on a real-time discounting task among adult males with a history of criminal behavior (Pietras, Cherek, Lane, Tcheremissine, & Steinberg, 2003).

The current study

Building upon recent theoretical models of ADHD and growing evidence that ADHD is associated with delay-related impulsivity, the purpose of the current study was to examine the effects of stimulant medication on real-time and hypothetical delay discounting tasks among children with ADHD. To our knowledge, the present study is the first controlled investigation of the effects of stimulant medication on a delay discounting task among individuals with ADHD. We hypothesized that methylphenidate would reduce the preference for smaller immediate over larger delayed real-time rewards. To the extent that task differences emerged, medication effects were expected to be less likely for the hypothetical discounting task because hypothetical discounting measures tend to be less sensitive to state changes in impulsive responding (see Lane, Cherek, Pietras, & Tcheremissine, 2003; Reynolds & Schiffbauer, 2004). Two active doses of methylphenidate were administered, and we predicted a linear effect of methylphenidate on delay discounting, as seen in a variety of cognitive domains.

Method

Participants

Participants were 49 children between the ages of 9–12 years diagnosed with ADHD. Sample characteristics are listed in Table 1. Participants were recruited from the Center for Children and Families at the University at Buffalo as well as from the community through flyers placed in the offices of pediatricians. All participants were recruited to attend a week-long summer research program designed to examine the effects of stimulant medication on neurocognitive processes implicated in ADHD. Parents were offered modest monetary remuneration for their participation. Children were rewarded daily with toys and gift cards.

Exclusion criteria included (1) estimated Full Scale IQ below 80; (2) history of seizures or other neurological problems and/or medication to prevent seizures; (3) history of other medical problems for which psychostimulant treatment may involve considerable risk; (4) current use of psychotropic medications other than for ADHD (i.e., antipsychotics, mood stabilizers, antidepressants, and anxiolytics) (5) history or concurrent diagnosis of pervasive developmental disorder, schizophrenia or other psychotic disorders; (6) absence of functional impairment; or (7) vision or hearing problems that would make it difficult to complete the discounting tasks (or other tasks, data not reported).

Diagnostic Assessment

All participants had a DSM-IV (American Psychiatric Association, 2000) diagnosis of ADHD. The diagnostic assessment involved a structured computerized clinical interview with one or both parents (Diagnostic Interview Schedule for Children Version IV (DISC-

IV); Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). In addition, parents and teachers completed two standardized rating scales: the Disruptive Behavior Disorder (DBD) rating scale (Pelham, Fabiano, & Massetti, 2005; Pelham, Gnagy, Greenslade, & Milich, 1992) and the Impairment Rating Scale (Fabiano et al., 2006). The DBD measures all DSM-3R and –IV symptoms of ADHD, Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD), on a 0–3 Likert Scale. The DBD has been previously shown to have sound psychometric properties and has been used extensively in studies of children with ADHD (see Pelham et al., 2005; Pelham et al., 1992). The IRS, an eight item visual-analog scale that evaluates the child's problem level and need for treatment in several developmental domains (e.g., peer relationships, academic performance, classroom behavior), has adequate psychometric properties in ADHD and normative populations (see Fabiano et al., 2006).

In order to meet diagnostic criteria, children were required to exhibit six or more symptoms of inattention and/or six or more symptoms of hyperactivity/impulsivity according to the DISC and/or DBD rating scale based on reports from the parent and teacher[1]. In addition, cross-situational impairment had to be present according to the IRS and/or the DISC. Seventy-one percent of the children were diagnosed with ADHD-Combined Type (n = 29 boys, 6 girls), 23% were diagnosed with ADHD-Inattentive Subtype (n = 7 boys, 4 girls), and 6% were diagnosed with ADHD-Hyperactive/Impulsive Subtype (n = 3 boys). As expected, comorbidity with externalizing disorders was common, with 65% of the sample meeting criteria for Oppositional Defiant Disorder (ODD) and 22% of the sample meeting provisional criteria for Conduct Disorder (CD)[2].

Standardized measures of intellectual ability and academic achievement included the Vocabulary and Block Design subtests from the Wechsler Intelligence Scale for Children - Fourth Edition (WISC-IV; Kaplan, Fein, Kramer, Delis, & Morris, 2004) and the Reading, Mathematics, and Spelling subtests from the Woodcock-Johnson Test of Achievement (WJTA; Woodcock, McGrew, & Mather, 2001). Full Scale IQ was determined by prorating scores based on performance on the Vocabulary and Block Design subtests from the WISC-IV. As shown in table 1, the sample was generally in the average range on measures of IQ and achievement.

Setting

The Summer Research Camp was held from 7:30 am to 5pm Monday through Friday. On Monday through Thursday cohorts of 5 children completed a variety of computerized tasks, administered individually. In addition to the cognitive testing, children participated in three 30-minute academic periods to assess performance and behavior in the classroom. Recreational activities, meals, and snacks were intermingled with testing. Friday served as a make-up/fun day and consisted of indoor and outdoor games interspersed with piloting of additional lab tasks. Children earned points throughout the day for task participation and appropriate behavior. These points were exchanged for toys and gift cards at the end of each day. Task order was randomized between participants but remained consistent within a child across testing days. Data from the current analyses are limited to two of these tasks, the Experiential Discounting Task (EDT) and Hypothetical Discounting Task (HDT).

Experiential Discounting Task (EDT)—The EDT is a computerized, real-time discounting task during which participants experience chosen rewards at specified time delays throughout the assessment. Participants were seated at a desk equipped with a computer mouse, 43 cm (diagonal) CRT computer monitor linked to the PC running the

[1]Teacher reports were missing from 5 children. Analyses with these 5 children excluded yielded comparable results.
[2]Given the pejorative nature of a diagnosis of conduct disorder, we prefer to use the term provisional in the absence of additional diagnostic information.

task, a coin dispenser (Transact 2, Telequip, Salem, NH), and a transparent glass jar to put coins into from the coin dispenser during the task. Each participant completed four brief sessions, three of which involved choices between an adjusting and certain amount of money (initially, $0.15) that was delivered immediately or a standard amount of money ($0.30) that was delayed and probabilistic (35%). For the other session, there was no delay (0s) associated with the standard option. The reward of either option for this "no-delay" session was delivered immediately; however, the standard amount was still probabilistic as with the other sessions.

During the task, choice options were indicated by light bulbs on the computer monitor which "illuminated" when the participant could make a choice. On the right-hand side was the adjusting immediate amount, which adjusted in value according to participant choices. The delayed standard amount was on the left-hand side and was fixed. Except for the no-delay session described above, if a participant chose the standard reward, he or she was required to wait the specified delay of that session (7, 14, 28 s) to see if the money would be delivered, because this option was probabilistic. If the money was delivered, it could then be put into the "bank" by clicking on the image of a bank building that illuminated to indicate when the money was to be delivered. For each response that illuminated the bank, the appropriate amounts of coins were delivered from the coin dispenser.

All participants received the following standardized set of instructions along with a brief demonstration of making choices during the EDT.

> In this activity, you'll use the computer to make choices between different amounts of money you'd like to receive. There is no right or wrong way to do this activity you just get to choose whichever amount of money you prefer. At the end of the activity, you will trade in the money you receive for points that you can use in the points store. Every five cents you get are worth one point. Okay, now I am going to show you how you can make choices between getting different amounts of money. The amount of money on this side [point left] is larger and it will always be the same: 30 cents. The amount of money on this side [point right] is smaller: 15 cents and it will change. Here is how it works: you can choose to get 15 cents now by clicking on this light bulb or you can choose to get 30 cents later by clicking on this light bulb. If you choose 30 cents, you may or may not get the money and you have to wait a little while to see if the money goes into the bank. If you choose the smaller amount of money, 15 cents, you will definitely get it right away. When you get money, the bank will light up and you have to click on the bank to make the money come out of the coin dispenser.

After completing the demonstration, examiners started the first session, during which there was no delay (0 s) associated with the standard, probabilistic option. Therefore, for this session participants received the chosen money immediately for either choice option. Participants proceeded to make their choices until an indifference point was reached, which was defined by a participant choosing each option (i.e., immediate and delayed) three times within six consecutive choice trials. After an indifference point was established, or the delayed option was chosen 15 times (reflect minimal discounting, as the participant made choices almost exclusively for the delayed option), a message appeared indicating that that particular session was over. The participant then completed the remaining sessions (i.e., 7, 14, and 28 s) in a fixed ascending order. This approach is taken in some previous delay discounting studies (Barkley et al., 2001; Green et al., 1996) and was taken here particularly because large between-subjects order effects could compromise our broader goal of examining individual differences in treatment effects. After completion of all four sessions, participants exchanged the money that they earned for points. Typically, the task lasted for 20–30 minutes.

Hypothetical Discounting Task (HDT)—Hypothetical delay discounting was measured with a modified version of the task used by Barkley et al. (2001). Participants were presented with hypothetical choices between variable, immediate amounts of money versus a fixed amount of $100 at various delays. The hypothetical choices were printed on 8.5- × 11-in sheets of white paper organized in a binder with the variable, immediate amount on the left side of the sheet and the fixed, delayed amount on the right side. The experimenter informed participants that when they made their choices they should imagine that they would get the money, although they would not actually receive any money during the task. One choice trial was printed per page, and the experimenter would read aloud from the page, e.g., "Which one would you choose? (printed on top of page) $20 now (pointing to the box on left bottom) or $100 in 1 year (pointing to the box on right bottom)?"

Each participant was administered the five delays in the same ascending sequence (e.g., one day, one week, one month, six months, and one year) to maintain consistency across tasks. These delays were altered from the Barkley et al. (2001) task (1 month, 1 year, 5 years, or 10 years) since the participants in the current study were younger, on average, and shorter delays were thought to be more relevant for children ages 9–12. However, the immediate (1, 10, 20, 30, 40, 50, 60, 70, 80, 90, 95, and 100) and fixed ($100) reward amounts replicated Barkley's (2001) procedures. In contrast to the task reported by Barkley, the immediate choices within each delay were presented in one of five random orders, rather than in fixed ascending or descending order. The experimenter presented the participant with one sheet at a time and prompted the participant to consider their choice, point and then state their choice. Participants did not receive any of the money or points for the choices they made.

Medication Assessment

After an initial practice day, each child participated in a 3-day double-blind, placebo-controlled medication assessment. Active doses were long-acting MPH (Concerta®) with the nearest commercially available equivalents of 0.3 and 0.6 mg/kg TID immediate-release MPH. As Concerta® was designed to mimic TID MPH, the pharmacokinetic properties of the two agents are relatively similar (Amodio, Master, Yee, & Taylor, 2008), but Concerta® allowed us to test over the course of the entire day without the peaks and valleys that may be evident with repeated IR dosing.

Most (81%) participants were taking stimulant medication during the school year. In order to promote medication tolerability, sixteen out of 49 children were order restricted so that they received the low dose prior to receiving the high dose. These restrictions occurred with children who were naïve to stimulant medication or in cases where the high dose provided in the study was at least 2.5 times the child's current clinical dose.

Participants currently taking stimulant medication were asked to discontinue their medication at least 24 hours prior to the practice day. This period is sufficient given, for example, a mean half life for Concerta® of 3.6 hr and no change in the half life or other pharmacokinetics properties of the drug with repeated versus single dosing (Modi, Lindemulder, & Gupta, 2000). Participants taking Strattera completed a 1-week washout period prior to participating in the medication assessment.

Medication was administered when the child arrived in the morning, 90 minutes prior to the initial cognitive task. Two prior studies, including one by this group, have established that Concerta® reliably separates from placebo in this timeframe (Pelham et al., 2001; Swanson et al., 2003). Pelham et al. study also established that a 20% higher Concerta® dose produces comparable effects to a TID IR MPH dose over a 12 hour period (i.e., 18mg of Concerta=15mg of IR MPH dosed as 5mg TID). We used similar procedures as this study to calculate our matching doses of Concerta®. Doses ranges from 18 to 90 mg (dose was

capped at 90 mg for safety reasons). The mean low dose was 39 mg Concerta® (*SD* = 10) and the mean of the high dose was 73 mg Concerta® (*SD* = 16).

To maintain blinding, subjects were given the same number of opaque capsules per day regardless of actual MPH dose. Side effects were rated daily by camp counselors and parents using the Pittsburgh Side Effect Rating Scale, which inquires about common side effects seen with stimulants (rated none to severe) (Pelham et al., 1993). Blood pressure and heart rate were also assessed daily during times of peak medication effects. Medication was generally well-tolerated, and no child was withdrawn from the study.

Procedure

Children were brought in to the testing rooms and were reminded of the laboratory rules: 1) follow directions, 2) stay in your assigned area, 3) use material and possessions appropriately, and 4) try your best. Children could earn 100 points for following the rules and completing the tasks during the activity period, but were also informed that, following a single warning, they would lose 25 points per rule violation. Under these circumstances, appropriate behavior was well-maintained.

Data Reduction

EDT—As reported previously (Reynolds & Schiffbauer, 2004), the raw EDT data of each session were transformed according to the indifference value of the no-delay choice block. Again, there was no delay associated with the standard option for this block of choices; however, the “delayed” option had a .35 probability of resulting in money being delivered. Therefore, inter-individual variability across the no-delay sessions was thought to reflect individual differences in response to probabilistic outcomes, which was not of particular interest for the current study. To reduce inter-individual variability based on the probabilistic nature of the standard option, each participant’s data was normalized based on his or her indifference value for the no-delay session. This was accomplished by dividing the indifference values of the delay sessions (with delays of 7, 14, and 28s) by the indifference value of his or her no-delay session. By transforming the data in this manner, the indifference value for each participant’s no-delay session was converted to a value of 1 (with no variability between participants), and the indifference values of the remaining three delay sessions were converted to values less than 1. These transformed indifference values represent the proportional amount of discounting that occurred for each delay above and beyond that of the no-delay session. The transformed indifference values were used to compute the area under the curve (AUC) (Myerson, Green, & Warusawitharana, 2001), a common approach to analyzing discounting data (e.g., (e.g., Krishnan-Sarin et al., 2007; Reynolds, Penfold, & Patak, 2008) that eliminates some of the problems associated with measures based on a hyperbolic function. Smaller area values indicated greater discounting by delay and greater impulsivity.

HDT—Because each choice (i.e., each of 12 immediate values for each of the 6 delays) was made only once, a switch point was determined rather than an indifference point. The switch point was operationalized as the lowest immediate value that was chosen for a given delay[3]. This value was then divided by the largest possible immediate amount ($100) to standardize the values for each delay. As with the EDT, area under the curve was used to characterize these discounting data to maintain consistency across measures (see Myerson et al., 2001).

[3]The total number of immediate choices for each delay was also examined and the results were comparable for the two outcomes.

Data Analysis

Using placebo session data, correlation analyses were used to explore relationships between age and IQ and the discounting measures and also associations between the discounting assessments themselves. To examine the effects of stimulant medication on delay discounting, separate repeated measures ANOVAs were conducted for the two discounting procedures, with medication dose as a within-subjects factor. Rather than the omnibus two-df dose effect, we examined focused single-df orthogonal polynomial contrasts: placebo v. the average of the two active doses of MPH, and MPH dose (low v. high). The same approach was used to examine whether stimulant medication reduced probabilistic discounting on the EDT. Sex and subtype differences were tested in exploratory models since a steepened delay-of-reinforcement gradient may be related primarily to the hyperactive/impulsive symptoms of ADHD (Sagvolden et al., 2005). Effect sizes were computed as Cohen's d (Cohen, 1988).

Results

Preliminary analyses

Age was positively associated with area under the curve (i.e., less preference for the immediate reward) on the HDT in the placebo condition, $r = .34$, $p < .05$, but it was unrelated to delay-related choice on the EDT on placebo, $r = -.09$, $p > .56$. In contrast, IQ was positively correlated with area under the curve on the EDT in the placebo condition, $r = .30$, $p < .05$, but it was unrelated to delay discounting on the HDT, $r = .13$, $p > .38$. Neither age nor IQ was associated with the effect of medication (v. placebo) on the HDT or the EDT, rs< 0.20. Delay discounting on the EDT and HDT were uncorrelated in the placebo, low MPH, and high MPH conditions, $|r$s$|$<.12, ps > .40, supporting the plan to analyze the two tasks separately. Delay discounting was significantly and positively correlated across all dose conditions for the EDT (rs = .54 to .72, ps < .001). The HDT AUC exhibited marked stability across doses, with all three correlations above .80, rs = .83 to .95, ps < .001.

MPH effects on probabilistic discounting

In the current sample of children with ADHD, probabilistic discounting, as reflected in the indifference values for the 0 s choice blocks, was not influenced by medication, MPH v. placebo and MPH dose Fs < 2.1, ps > .15, (0s-delay indifference Ms[SDs] = .24 [.07], .22 [.07], .23 [.07], for placebo, low-, and high-MPH, respectively), nor were they reliably associated with age, sex, or subtype, ps > .25.

MPH effects on delay discounting

Consistent with predictions, delay discounting on the EDT was reduced with the active MPH (AUC Ms = 0.48 and 0.49, for the low and high doses, respectively, *SD*s = 0.15) compared to placebo (AUC M = 0.44, *SD* = 0.16), F (1, 47) = 7.8, $p < .01$, an effect of moderate size, Cohen's d = .57[4] (see also Figure 1). Delay discounting on the EDT did not reliably differ between the two active doses of MPH, F <1.

In contrast to the results for the EDT, MPH appeared to have no effect on delay discounting on the HDT (*M* = 0.34, *SD* = 0.31 for all 3 conditions), MPH v. placebo and dose Fs <2.1, ps > .15 (see Figure 2). The effect of MPH v. placebo was not reliably correlated between the EDT and the HDT, $r = .18$, $p = .23$.

[4]A child (female, age 9, combined subtype) with outlying data (i.e., difference in area under the curve between placebo and active medication was 3 standard deviations below the mean) was excluded from all analyses. The pattern of statistical significance did not change when this child was included in the analyses, although the effect size was reduced to d=.43, p<.05.

Exploratory Analyses

Children meeting diagnostic criteria for the inattentive subtype did not discount less on placebo than children identified as hyperactive/impulsive or combined subtype on either the EDT or HDT, *F*s<1. In addition, delay discounting during the placebo condition was not influenced by sex, EDT, F (1, 47) = 1.7, $p > .20$; HDT, $F < 1$. Sex and subtype were included in the models examining the effect of MPH on delay discounting, but they did not influence the findings reported above. However, tests of both factors were limited by the small sample size for participants with the inattentive subtype (n=11) and female participants (n=9).

Discussion

The present study is the first to examine the impact of stimulant medication, an effective treatment for ADHD, on real-time and hypothetical delay discounting tasks among children with ADHD. Etiological models of ADHD have implicated motivational processes, such as delay aversion (Sonuga-Barke, 2002), steepened delay of reinforcement gradients (Sagvolden et al., 2005), and the related construct of delay discounting (e.g., Scheres et al., 2006; Scheres et al., 2008), particularly in relation to the hyperactive-impulsive symptoms of ADHD. Variability in the way in which these constructs are assessed has complicated our understanding of delay-related impulsivity and suggests that multi-method assessment may be the most informative approach. Thus, the current study included experiential and hypothetical delay discounting tasks to evaluate the effect of the stimulant methylphenidate on delay-related choice in a clinical population. The results of the current study suggest that methylphenidate acutely reduces delay-related impulsivity in children with ADHD, but only when the delays and rewards are actually experienced by the participant.

Consistent with our predictions, the EDT was sensitive to the effects of stimulant medication, whereas the hypothetical discounting task appeared to be insensitive to stimulant medication. This finding is consistent with the few studies that have been conducted to examine the effects of substances on various discounting measures. The EDT has been sensitive to state changes in impulsivity due to sleep deprivation (Reynolds & Schiffbauer, 2004) and consumption of alcohol (Reynolds, Richards, & de Wit, 2006). By contrast, hypothetical discounting measures are not typically influenced by manipulations of state impulsivity (e.g., Lane et al., 2003; Reynolds et al., 2006; Richards et al., 1999) but have demonstrated a relationship between individuals characterized as impulsive and an increased preference for smaller, immediate hypothetical rewards than larger, delayed hypothetical rewards (e.g., Alessi & Petry, 2003; Madden, Petry, Badger, & Bickel, 1997). Therefore, the decision to use experiential or hypothetical discounting tasks may depend on the particular research question given the apparent differential sensitivity of each type of task to particular experimental manipulations thought to influence impulsivity.

Although this study did not include typically developing children to examine whether children with ADHD exhibit greater delay-related impulsivity, previous research would suggest that both the EDT and HDT would discriminate between individuals with and without ADHD (e.g., Barkley et al., 2001). Future research should include a comparison group of typically developing children to evaluate whether children with ADHD engage in greater delay discounting using a variety of delay-related choice tasks, including the Choice-Delay Task and the EDT. Furthermore, it may be that individuals characterized as "impulsive" respond differently to factors considered to acutely influence impulsive responding than non-impulsive individuals. This would be consistent with the effects of psychostimulants on delay discounting in rats from differential rearing environments (Perry et al., 2008). Based on the animal work, stimulant medication may reduce delay discounting among individuals with ADHD but increase delay discounting in individuals without

ADHD. The inclusion of a control group would also enhance our understanding of whether stimulant medication reduces impulsive responding to a similar level that of typically developing children.

Though the effects of stimulant medication on real-time discounting are consistent with our predictions, this effect appears to be greatest during the final (28s) delay session (see Figure 1). This is the longest delay experienced by participants during the EDT, but it was also the last delay within a session, as delays were administered in a fixed, ascending order. Although this approach is not uncommon (e.g., Barkley et al., 2001;Green et al., 1996), it does confound delay length and time on task. That is, methylphenidate could be reducing a vigilance decrement or an increase in impulsivity with time on task, rather than discounting per se. Theoretical models of ADHD, such as the cognitive-energetic model (Sergeant, 2000) have postulated that inattentive and impulsive behaviors may increase as a function of time on task due to self-regulatory deficits in ADHD. Importantly, the hypothetical discounting task was also administered with a fixed, ascending delay order, and methylphenidate had no discernable effect on delay-related choice on this task. This finding might argue against the vigilance hypothesis. Instead, it seems more likely that methylphenidate reduced delay-related impulsivity when the rewards and delays are experienced by the participant. Nevertheless, it will be important for future research to vary the order in which delays are presented. Relatedly, the present data suggest that stimulant effects, and perhaps group differences, may interact with the delay period. Had we employed a maximum delay of 14 seconds, we may not have observed the beneficial effect of MPH. Future work should include longer delays (e.g., 1–5 minutes), to clarify how this process unfolds over a wider time frame in children with and without ADHD.

The finding that MPH reduced delay-related impulsivity is broadly consistent with Savolden's (e.g., 2005) dynamic developmental theory of ADHD and recent neuroimaging studies which reported decreased ventral striatal activation during reward anticipation among individuals with ADHD compared to healthy controls (Plichta et al., 2009; Scheres, Milham, Knutson, & Castellanos, 2007). The authors suggest that behavioral hyperresponsiveness to reward occurs to compensate for diminished activation of this region, as reflected in this neural hyporesponsiveness for anticipated reward. Similarly, stimulant medication may reduce delay-related impulsivity by increasing activation in dopamine-mediated brain regions such as the ventral striatum. However, the neurobiological underpinnings of the current findings remain speculative because MPH inhibits the reuptake of both dopamine and norepinephrine. It would be interesting to determine whether more specific dopaminergic, noradrenergic (e.g., atomoxetine, which is also FDA-approved for the treatment of ADHD), or even cholinergic (e.g., varenicline) agonists exert similar effects. This would speak both to the neurobiology and perhaps to the neuropsychological processes involved in delay discounting and would certainly be relevant to testing a corollary to Sagvolden's model. Interestingly, Sagvolden's theory is thought to be most relevant to the hyperactivity/impulsivity aspect of ADHD. One might expect that ADHD-Inattentive subtype would exhibit less delayed discounting or have a differential effect of stimulant medication on the process, as shown in previous studies (Scheres et al., 2008). Our exploratory tests of these hypotheses did not support these predictions. However, there were relatively few ADHD-Inattentive children in the present sample. Therefore, the tests were markedly underpowered and should be interpreted in that light.

The present data are also relevant to the dual-pathway model of ADHD (Sonuga-Barke, 2002, 2005; Sonuga-Barke et al., 2008), although the EDT employed here more closely resembles a delay discounting task than it does a delay aversion task that is the focus of Sonuga-Barke. Indeed, integrating the delay discounting literature with the studies of delay aversion among children with ADHD is challenging due to the methodological differences.

Conceptually, it is interesting to consider the different processes being measured with delay aversion tasks versus delay discounting tasks since several processes may be at play when an individual demonstrates a preference for smaller immediate over larger delayed rewards. Sonuga-Barke and colleagues (2008) postulate that delay-related choice is controlled by two components: the escape or avoidance of experiencing the negative affect associated with delay and the preference for immediacy linked to deficits in signaling delayed rewards. The delay discounting literature suggests that this behavioral preference reflects diminishing value of the reward as it becomes delayed, which may be a result of an aversion to delay (Cherek & Lane, 1999) or an impulsive drive for immediate reward. Thus, it is conceivable that these processes influence each other and may all be occurring when an individual makes an impulsive choice.

It has been suggested that these processes may be disentangled experimentally by examining the influence of post-reward delay (e.g., Marco et al., 2009; Sonuga-Barke et al., 2008). Delay aversion tasks require the participant to make repeated choices between two reward values available at two fixed delays and may vary the post-reward delay (i.e., amount of time between receiving a reward and presentation of the next choice). Sonuga-Barke and colleagues propose that comparing delay-related choice during conditions in which a post-reward delay is present versus absent may reveal which process is occurring. A recent study (Marco et al., 2009) did just that. ADHD children preferred the immediate reward moreso than controls under both conditions (albeit to a greater degree when no post-reward delay was present), supporting a dual component model in which both delay aversion and impulsive drive for immediate reward contribute to immediate reward preference. In contrast, delay discounting tasks used with humans systematically vary reward magnitude and the delays to receiving rewards but typically do not include a post-reward delay since this has been shown to eliminate the function of delay. As discussed by Lane et al. (2003), participants quickly learn that they will have to wait either before or after the choice and consistently choose the larger option. However, this may be a function of the type of rewards used and the time at which the participant is able to consume the reinforcer, which may be why animal studies include a post-reward delay and continue to see delay discounting (Lane et al., 2003).

Although the current study does not disentangle the components of delay-related impulsivity, it is clear that the broader construct of delay-related choice is important. There continues to be a need for improving our understanding of the overlapping and unique processes involved in delay-related impulsivity and its role in ADHD. It would be informative to include multiple measures of delay-related impulsivity in a single study to more fully understand the separate and overlapping aspects of these constructs in ADHD. Moreover, incorporating multi-method assessment such as neuroimaging studies (e.g., Plichta et al., 2009; Scheres et al., 2007) and behavioral observations during delay-related choice tasks will contribute to our understanding of the important components of delay-related impulsivity. The use of rewards which are immediately consumable, such as food or playing videogames, may also inform our understanding of delay-related impulsivity in ADHD.

Beyond the domain of delay-related impulsivity, it is important to consider the broader network of processes that may moderate group differences and medication effects. In the present study, the association between hypothetical delay discounting in the placebo condition and age (i.e., older children tended to discount less) is consistent with prior research (Green et al., 1996; Scheres et al., 2006), providing support for the construct validity of this task. Interestingly, age was unrelated to experiential discounting in the placebo condition. Instead, estimated IQ was associated with discounting on the EDT but not on the HDT. Specifically, individuals with higher estimated IQ engaged in less delay

discounting on the EDT. This finding replicates other recent reports of an inverse relationship between IQ and delay discounting (de Wit, Flory, Acheson, McCloskey, & Manuck, 2007; Marco et al., 2009). One possibility may be that more intelligent children have enhanced executive function, given the association between executive function measures and IQ, which might allow them to consider the consequences of their choices and modulate impulsive responding more adaptively. Alternatively, it has been suggested that IQ may serve as a proxy for socio-economic status, which may directly influence delay-related choice (Marco et al., 2009).

In summary, this study is the first to demonstrate stimulant effects on a delay discounting task among children with ADHD. Methylphenidate, an effective pharmacological treatment for ADHD, reduced the preference for smaller immediate rewards over larger delayed rewards when the delays and rewards are actually experienced by the child. This effect is broadly consistent with recent models of ADHD and raises the possibility that stimulant medication improves real-world behavior of children with ADHD by altering delay-related impulsivity (c.f., Solanto et al., 2001).

Acknowledgments

We thank Sarah Spencer for assistance with task development and data collection, and Rebecca Ashare and Michael Strand for comments on the manuscript. In addition, we thank Rosemary Tannock for comments on the design of the study, Lisa Burrows-McLean for developing the recruitment process, and Louise Cooper for preparing the medication. Finally, thank you to all of the families that participated in the Summer Research Camp. This research was supported by grant MH069434 from the National Institute of Mental Health.

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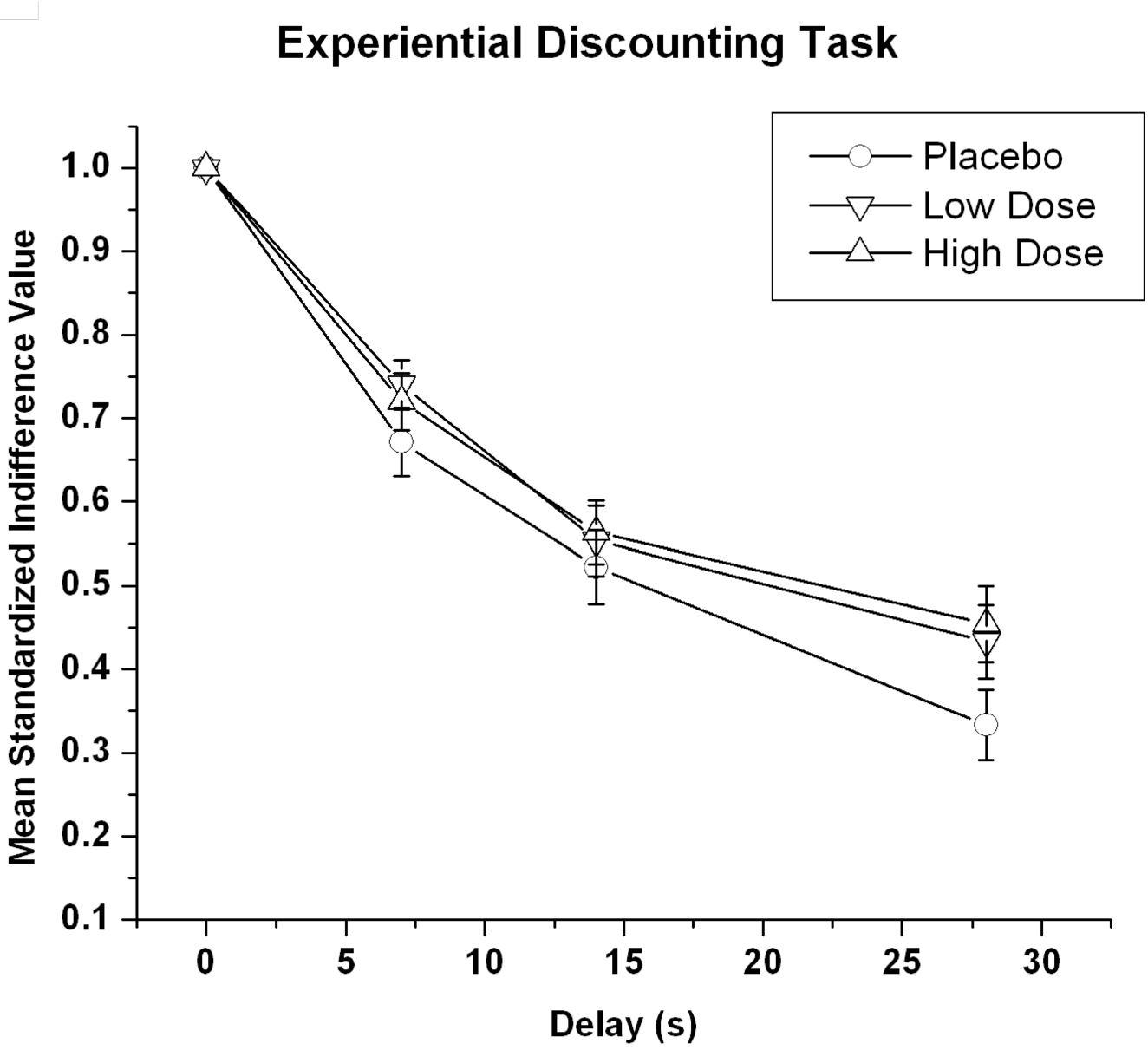

Figure 1.
Effect of Methylphenidate on the Experiential Discounting Task (EDT). Points show mean indifference values as a function of delay.

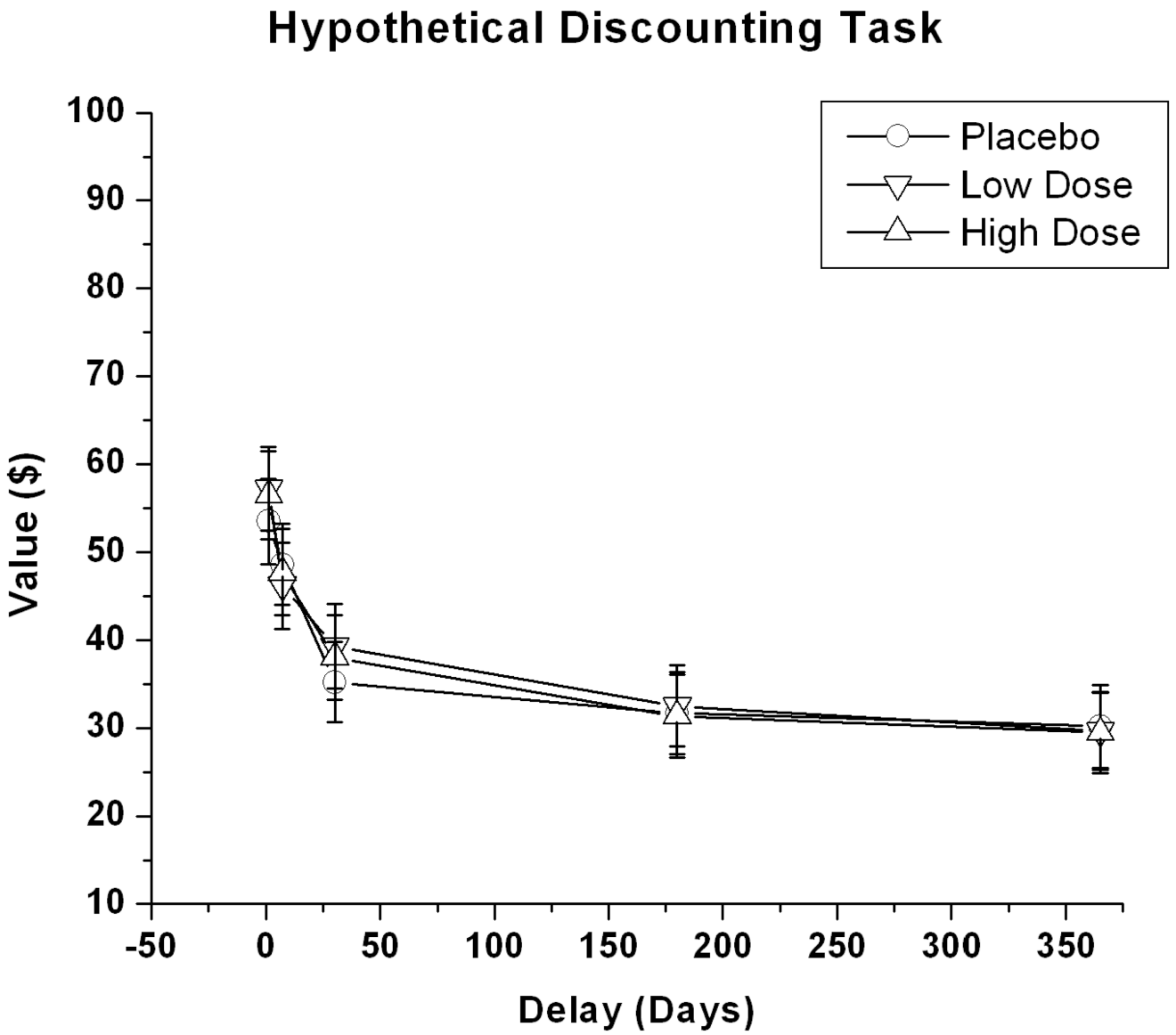

Figure 2.
Effect of Methylphenidate on the Hypothetical Discounting Task (HDT). Points show mean indifference values as a function of delay.

Table 1

Participant characteristics.

Demographics	
Age, mean (SD)	10.5 (1.1)
Gender %(male:female)	80:20
WISC Full Scale IQ, mean (SD)	104 (14)
Ethnicity, % (white:black:other)	76:14:10
WJ Test of Achievement, mean (SD)	
Letter-Word Identification	104 (10)
Calculation	106 (13)
Spelling	105 (13)
DBD rating scale*	
Hyp/Imp, mean (SD)	
Parent report	14.1 (5.9)
Teacher report	11.6 (7.5)
Inattentive, mean (SD)	
Parent report	17.0 (5.6)
Teacher report	13.7 (6.7)

**Note*. These values represent the total score of the items within each subtype domain on the DBD rating scale (range of 0–27).