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ADHD AND STOP-SIGNAL BEHAVIORAL INHIBITION: IS MEAN REACTION TIME CONTAMINATED BY EXPOSURE TO INTERMITTENT STOP-SIGNALS?

by

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Psychology in the College of Sciences at the University of Central Florida Orlando, Florida

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ABSTRACT

The current study investigates two recently identified threats to the construct validity of behavioral inhibition as a core deficit of attention-deficit/hyperactivity disorder (ADHD) based on the Stop-signal task: calculation of mean reaction time from go-trials presented adjacent to intermittent stop-trials, and non-reporting of the stop-signal delay metric. Children with ADHD (n=12) and typically developing children (TD) (n=11) were administered the standard stop-signal task and three variant stop-signal conditions. These included a No-Tone condition administered without the presentation of an auditory tone; an Ignore-Tone condition that presented a neutral (i.e., not associated with stopping) auditory tone; and a second Ignore-Tone condition that presented a neutral auditory tone after the tone had been previously paired with stopping. Children with ADHD exhibited significantly slower and more variable reaction times to go-stimuli, and slower stopsignal reaction times (SSRT) relative to TD controls. Stop-signal delay (SSD) was not significantly different between groups, and both groups' go-trial reaction times slowed following meaningful tones. Collectively, these findings corroborate recent meta-analyses and indicate that previous findings of stop-signal performance deficits in ADHD reflect slower and more variable responding to visually presented stimuli and concurrent processing of a second stimulus, rather than deficits of motor behavioral inhibition.

This work is dedicated to my mother and father, Fran and George Alderson.

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INTRODUCTION

Attention deficit/hyperactivity disorder (ADHD) is characterized by difficulties with attention, hyperactivity, and impulsivity, and occurs in an estimated 3% to 5% of school-age children (Barkley, 2006; Szatmari, 1992). Presence of the disorder conveys increased risk for several pejorative outcomes including long-term scholastic underachievement and interpersonal peer problems in affected children (for reviews, see Barkley, Fischer, Smallish, & Fletcher, 2006; Manuzza, Klein, Bessler, Malloy, & LaPadula, 1993).

Treatment and prevention of ADHD is dependent on a comprehensive understanding of its underlying mechanisms and core features. Current models suggest that a deficiency in behavioral inhibition - a covert process detectable through the observation of secondary behaviors - is a core feature of the disorder (Barkley, 2006; Sonuga-Barke, 2002). Anatomical structures such as the prefrontal and frontal cortices are hypothesized correlates of behavioral inhibition (Aman, Roberts, & Pennington, 1998), wherein motoric responses initiated in response to peripheral stimuli (e.g., visual or auditory) are overridden or terminated following commands from these areas. Involvement of the basal ganglia may serve to ensure proper execution of desired motor responses, and the dopaminergic and noradrenergic systems are probable candidates involved in behavioral inhibition at the neurotransmitter level (Rieger, Gauggel, & Burmeister, 2003).

Performance measures used to index the behavioral inhibition construct typically involve a dual-task paradigm in which children respond to a primary stimulus and withhold a response when presented with a secondary stimulus. Examples include the (a) Go-No-Go Task (Iaboni, Douglas, & Baker, 1995), (b) Change Task (Schachar, Tannock, Marriott, & Logan, 1995), (c) Stroop Color-Word Interference Test (Barkley, 1997), and

(d) Stop-signal Task (Logan, Cowan, & Davis, 1984). The Stop-signal task is considered the primary measure used in clinic- and laboratory-based research to investigate behavioral inhibition in children with ADHD, due to its unique ability to capture theoretically important cognitive processes by means of the stop-signal reaction time metric.

The conventional stop-signal task requires children to respond differentially to two distinct go-stimuli (e.g., the letters X and O) using left and right response buttons. On a predetermined number of trials (most often 25%) children are instructed to stop themselves from responding to a visually presented go-stimulus – the X or O - if it is followed by a specific signal such as an auditory tone. The onset asynchrony between the go-stimulus and stop-stimulus may be manipulated, providing a range of stop-signal delays. Contemporary stop-signal studies typically utilize dynamic stop-signal delays that increase or decrease after each stop-trial, depending on inhibitory success. Reaction times to the primary stimulus (i.e., MRT: Mean Reaction Time) are computed by measuring the latency between the presentation of the go-stimulus and the child's response. Stop-signal reaction time (SSRT) is the most commonly reported measure of stop-signal behavioral inhibition - it refers to the latency between the presentation of the stop-signal and the initiation of the stop process, and is typically calculated by subtracting the mean stopsignal delay from mean reaction time. According to Logan et al.'s (1984) race model of behavioral inhibition, response inhibition depends on whether the stop process can overtake the go-process when go- and stop-processes are activated in close temporal sequence (i.e., go-signal activation followed by stop-signal activation). A slow reaction time to a stop-stimulus (SSRT) decreases the probability that the stop-process will

overtake the go-process. The relationships among MRT, stop-signal delay, and SSRT are depicted graphically in Figure 1.

Extant research of behavioral inhibition using the Stop-signal task indicates that children with ADHD have slower and more variable choice reaction times (MRT) and stopping reaction times (SSRT) relative to typically developing children. These findings have been replicated in laboratories in Europe (Overtoom et al., 2002), Canada (Schachar, Mota, Logan, Tannock, & Klim, 2000), and the United States (Walcott & Landau, 2004) using samples of carefully diagnosed children with ADHD. Despite strong inter-study reliability, recent meta-analytic reviews identified problems with the calculation of MRT from go-trials presented adjacent to intermittent stop-trials, and nonreporting of the SSD metric that collectively threaten the construct validity of SSRT as a measure of behavioral inhibition (Alderson, Rapport, & Kofler, 2007; Lijffijt, Kenemans, Verbaten, & van Engeland, 2005). The meta-analysis of Alderson et al. (2007) served as a review for this study and is available in Appendix A.

The practice of calculating children's basic motor response speed (i.e., MRT) by averaging extracted non-stop trials (i.e., go-trials) presented before and after stop trials within an experimental block represents a potential methodological confound in past studies examining behavioral inhibition in ADHD by means of the Stop-signal paradigm. This methodology implies that children's MRT to the go-stimulus is uninfluenced by exposure to stop signals on previous trials or by the anticipation of stop-signals on future trials, and is contrary to the well-documented effects of intermittent tones on reaction time. For example, stimuli that momentarily capture the attention of a participant (i.e., singleton distracters) often exert a slowing effect on reaction time (Dalton & Lavie,

2004), even when the distractor is minimally associated with the task or target stimulus (Mason, Humphreys, & Kent, 2004; 2005). Studies of negative priming reveal a similar effect, wherein implicit memory of a stimulus previously associated with a meaningful stimulus creates a response conflict and slows reaction time on subsequent trials (Fox, 1995; May, Kane, & Hasher, 1995).

Two studies have directly examined the effects of intermittent stop-signals on reaction time to a go-stimulus. Schachar et al. (2004) reported that children with ADHD and typically developing children both slowed their go-response on trials following unsuccessful inhibition (referred to as error monitoring), although children with ADHD slowed significantly less relative to control children. Their estimate of error monitoring may have been inadvertently deflated, however, by including the same go-trial reaction time data (following unsuccessful inhibition) in the standard-task/error-monitoring contrast metrics. The second study examining intermittent stop-signal effects on reaction time also reported a slowing effect on MRT, and failed to find motor inhibition differences in children with ADHD after controlling for baseline reaction time (Rommelse et al., 2007). Their ten-option go-response, Stop-signal paradigm and use of visuospatial rather than traditionally used phonological text-based stimuli, however, may limit the generalization of their findings.

A second potential confound identified by both meta-analytic reviews involved the non-significant stop-signal delay effect size (Alderson et al., 2007; Lijffijt et al., 2005). These findings suggest that the between-group SSRT variability reported in past studies comparing children with ADHD to typically developing controls reflects baseline differences in MRT rather than true inhibitory deficits. The meta-analytic results,

however, were based on derived estimates that relied on unconventional effect size calculations (i.e., unstandardized mean gain scores or pooling pooled standard deviations) due to the non-reporting of stop-signal delays and associated standard deviations in the literature. No published, experimental study to date has directly examined and reported stop-signal delay differences between children with ADHD and typically developing children. In the current study, behavioral inhibition differences between children with ADHD and typically developing control children were examined directly based on the stop-signal delay metric.

The primary aim of the current study was to investigate whether distinctive types of intermittent auditory tones - meaningful (associated with stopping) and non-meaningful (not associated with stopping) – exert an overall or differential (between-group) effect on children's MRT and MRT variability. If meaningful tones significantly influence children's reaction time or MRT variability, past estimates of MRT based on extracted go-trial reaction times likely bias the overall calculation of behavioral inhibition deficits (i.e., the SSRT metric). This is because variability in SSRT is derived from three sources: (a) variability in stop-signal delay if MRT is held constant; (b) variability in MRT if stopsignal delay is held constant; and (c) variability in both MRT and stop-signal delay (SSD) based on Logan et al.'s (1997) formula (SSRT = MRT - SSD). The occurrence of a biased effect, if present, is expected to slow children's MRT relative to a non-meaningful tone or no-tone condition based on extant literature. This is also the first experimental study to directly compare stop-signal delay between children with ADHD and typically developing control children in the context of a conventional stop-signal paradigm. A nonsignificant or small stop-signal delay effect is expected based on the results of recent

meta-analytic findings (Alderson et al., 2007; Lijffijt et al., 2005), which would suggest that children with ADHD do not differ from typically developing children with respect to motor behavioral inhibition processes.

METHOD

Participants

The sample was comprised of twenty-three male children aged 8 to 12 years (M = 9.04, SD = 1.36), recruited by or referred to the Children's Learning Clinic–IV (CLC-IV) through community resources (e.g., pediatricians, community mental health clinics, school system personnel, self-referral). The CLC-IV is a research-practitioner training clinic known to the surrounding community for conducting developmental and clinical child research and providing *pro bono* comprehensive diagnostic and psychoeducational services. Its client base consists of children with suspected learning, behavioral or emotional problems, as well as typically developing children whose parents agreed to have them participate in developmental/clinical research studies. A psychoeducational evaluation was provided to the parents of all participants.

Two groups of children participated in the study: children with ADHD, and typically developing children (TD) without a psychological disorder. All parents and children gave their informed consent/assent to participate in the study, and IRB approval was obtained prior to the onset of data collection.

Group Assignment

All children and their parents participated in a detailed, semi-structured clinical interview using the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Aged Children (K-SADS). The K-SADS assesses current and past episodes of psychopathology in children and adolescents based on DSM-IV criteria. Its psychometric properties are well established, including interrater agreement of .93 to 1.00, and testretest reliability of .63 to 1.00 (Kaufman et al., 1997).

Twelve children met the following criteria and were included in the ADHD group: (1) an independent diagnosis by the CLC-IV's directing clinical psychologist using DSM-IV criteria for ADHD based on K-SADS interview with parent and child; (2) parent ratings of at least 2 SDs above the mean on the Attention Problems clinical syndrome scale of the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001), or exceeding the criterion score for the parent version of the ADHD-Combined subtype subscale of the Child Symptom Inventory (CSI; Gadow, Sprafkin, & Salisbury, 2004); and (3) teacher ratings of at least 2 SDs above the mean on the Attention Problems clinical syndrome scale of the Teacher Report Form (TRF; Achenbach & Rescorla, 2001), or exceeding the criterion score for the teacher version of the ADHD-Combined subtype subscale of the CSI (Gadow et al., 2004). The CSI requires parents and teachers to rate children's behavioral and emotional problems based on DSM-IV criteria using a 4-point Likert scale. The CBCL, TRF, and CSI are among the most widely used behavior rating scales for assessing psychopathology in children. Their psychometric properties are well established (Rapport, Kofler, Alderson, & Raiker, 2007). All children in the ADHD group met criteria for ADHD-Combined Type, and six were comorbid for Oppositional Defiant Disorder (ODD).

Eleven children met the following criteria and were included in the typically developing group: (1) no evidence of any clinical disorder based on parent and child K-SADS interview; (2) normal developmental history by maternal report; (3) maternal rating below 1.5 SDs on the clinical syndrome scales of the CBCL and TRF; and (4) parent and teacher ratings within the non-clinical range on all CSI subscales. Typically developing children were actively recruited through contact with neighborhood and community schools, family friends of referred children, and other community resources.

Children that presented with (a) gross neurological, sensory, or motor impairment, (b) history of a seizure disorder, (c) psychosis, or (d) Full Scale IQ score less than 85 were excluded from the study. None of the children were receiving medication during the study – seven of the children with ADHD had previously received trials of psychostimulant medication.

Instruments

The Stop-signal Task and administration instructions were acquired from Dr. Schachar's research group, and the experiment used task parameters described by Schachar et al. (2000). Go-stimuli were displayed for 1000 ms as uppercase letters X and O positioned in the center of a computer screen. X's and O's appeared with equal frequency throughout the experimental blocks. Each go-stimulus was preceded by a dot (i.e., fixation point) displayed in the center of the screen for 500 ms. The fixation point served as an indicator that a go-stimulus was about to appear. A 1000 Hz auditory tone (i.e., stop-stimulus), delivered through sound-deadening headphones, was generated by the computer and presented randomly on 25% of the experimental trials. Stop-signal delays were initially set at 250 ms, and dynamically adjusted + 50 ms contingent on children's performance on the previous trial. Successfully inhibited stop-trials were followed by a 50 ms increase in stop-signal delay, and unsuccessfully inhibited stop-trials were followed by a 50 ms decrease in stop-signal delay. The algorithm was designed to

approximate successful inhibition on 50% of the stop-trials. A two-button response box was utilized wherein the left and right buttons were used to respond to the letters X and O, respectively. All participants completed five consecutive experimental blocks of 32 trials (i.e., 24 go-trials, 8 stop-trials).

Three additional Stop-signal Task conditions were presented to examine the effect of stop-signals (i.e., auditory tones) on children's primary reaction time. All task parameters were identical to the previously outlined standard stop-signal condition with exceptions noted below.

A No-tone condition was administered without the presentation of an auditory tone. This condition was included to provide a measure of children's pure reaction time to the primary stimulus, uncontaminated by the influence of intermittent stop-signals or previous exposure to meaningful signals.

An Ignore-tone condition was administered to determine whether the intermittent presentation of a neutral (non-meaningful) auditory tone exerts an effect on children's reaction time to the go-stimulus, even though the tone has never been paired with stopping. This condition always preceded the standard stop-signal condition. Children were presented with an auditory tone, but instructed to ignore it.

An Ignore-tone-2 condition was administered to determine whether the intermittent presentation of a non-meaningful auditory tone exerts an effect on children's reaction time to the go-stimulus, when the tone has been previously paired with stopping. This condition was always administered after the standard stop-signal condition, and was identical to the standard task except that participants were told to ignore the stop-signal.

Procedures

Each participant's performance on the stop-signal task was assessed once per week on Saturdays over a 4-week period at the Children's Learning Clinic-IV. The stop-signal task was administered as part of a larger battery of laboratory-based tests that required the child's presence for approximately 2.5 hours per session. Breaks were scheduled between tasks to minimize the effects of fatigue. Each child was administered a total of four stopsignal task conditions: No-tone, Ignore-tone, Standard-tone, and Ignore-tone-2, across the four testing sessions (one each session, one week apart). The No-tone and Ignore-tone conditions were counterbalanced so that each was administered before the other with equal frequency. The No-tone and Ignore-tone conditions always preceded the Standardtone condition to allow for the measurement of reaction time in the absence of experience with a meaningful auditory tone. The Ignore-tone-2 condition was always administered during the fourth session, following the Standard-tone condition.

Children were seated approximately 0.66 meters from the computer monitor. Prior to the administration of each experimental condition, they were required to complete two practice blocks, each consisting of 32 trials. Children were provided the following instructions during the practice phase of the Standard-tone condition: *You are going to divide your time into two parts, practice time and test time. This is your control box. This is the X button, and this is the O button. Your job is to watch the computer screen. At first you will see a dot. It is important to look at the dot because when it disappears, you will see the letter X or O. If the letter is X, press the left button on your gamepad. If the letter is O, press the right button on the gamepad. As soon as you see the letter, push the matching button (i.e., X or O) as quickly as you can. Always use your thumbs to push the*

X and O buttons. Go as fast as you can without making mistakes. Every once and a while you will hear a beep through your headphones. When you hear the beep, I want you to stop yourself from pushing the button. Following these instructions, children were asked to explain the task. In the event that a child did not respond correctly, the instructions were read again until the child was able to orally communicate that they understood the directions. Prior to administration of each experimental phase, children were told that they were going to begin the test portion of the session and that it would be longer in duration relative to the practice session. They were also reminded to push the buttons as fast as possible and to always use their thumbs.

Instructions for the No-tone, Ignore-tone, and Ignore-tone-2 conditions were identical to those of the Standard-tone condition except for the explanation of the stop-signal tone. Specifically, the tone was not mentioned in the No-tone condition, and prior to the Ignore-tone and Ignore-tone-2 conditions, children were administered the following additional instructions: *Sometimes you will hear a beep. When you hear the beep I want you to ignore it.*

RESULTS

Preliminary analysis of power, potential outliers, and demographic variables were followed by a three-tier approach to examine the central experimental questions. SSRT and stop-signal delay for the standard task were examined initially to determine whether children with ADHD exhibit behavioral inhibition deficits relative to TD children. MRT differences in children with ADHD relative to typically developing children across the No-tone, Ignore-tone, Standard-tone, and Standard-tone-2 conditions were examined subsequently to determine (1) whether children with ADHD exhibit slower choice reaction times to the go-stimulus (MRT) relative to TD children, and (2) whether intermittent auditory tones – meaningful (associated with stopping) and non-meaningful (not associated with stopping) – exert an overall or differential (between-group) effect on children's MRT. A final set of analyses examined potential between-group differences in reaction time variability across the four experimental conditions to examine whether intermittent auditory tones – meaningful and non-meaningful – exert an overall or differential (between-group) effect on children's MRT variability.

Data Screening

Power Analyses

GPower software version 3.0.5 (Faul, Erdfelder, Lang, & Buchner, 2007) was used *a priori* to determine needed sample size for omnibus tests as recommended by Cohen (1992). A Hedges' *g* effect size of 0.63 was chosen based on the average magnitude of

SSRT differences between children with ADHD and TD children reported in a recent meta-analytic review (Alderson et al., 2007). Power was set to .80 (Cohen, 1992). For an SSRT Hedges' g effect size of 0.63, $\alpha = .05$, power $(1 - \beta) = .80$, and 2 groups, 22 total subjects are needed for a repeated measures ANOVA (conditions: Standard-tone, Ignoretone-2) to detect differences and reliably reject H₀. A repeated measures power analysis was computed based on the expectation that SSRT metrics would be available for both the Standard-tone and Ignore-tone-2 conditions (i.e., that children would inhibit responding to some ignore-tones following exposure to the Standard-tone task). A nearly identical procedure was used to estimate the needed sample size for MRT and MRT variability (SDRT), based on the average magnitude of MRT and SDRT differences between children with ADHD and TD children (Alderson et al., 2007). The correlation between task conditions was set moderately high (r = .75) because previous studies have assumed that MRT is unaffected by intermittent stop trials and would thus approximate MRT during an equivalent, simple choice reaction time task. For an MRT Hedges' g effect size of 0.45, $\alpha = .05$, power $(1 - \beta) = .80$, 2 groups, and 4 repetitions (i.e., No-tone, Ignore-tone, Standard-tone, and Ignore-tone-2 conditions), 14 total subjects are needed for a repeated measures ANOVA to detect differences and reliably reject H₀. For an SDRT Hedges' g effect size of 0.73, $\alpha = .05$, power $(1 - \beta) = .80$, 2 groups, and 4 repetitions (i.e., No-tone, Ignore-tone, Standard-tone, and Ignore-tone-2 conditions), 6 total subjects are needed for a repeated measures ANOVA to detect differences and reliably reject H_0 . A power analysis for SSD was not calculated due to non-significant effect sizes reported in previous meta-analytic reviews (Alderson et al., 2007; Lijjifft et al. 2005).

Outliers

Each of the dependent variables were screened for univariate outliers, defined as scores of greater than 3 standard deviations above or below the group mean. This procedure resulted in no outliers.

Preliminary Analyses

Demographic data are shown in Table 1. Sample ethnicity was mixed with 16 Caucasians (69%), 5 Hispanics (22%), and 2 African Americans (9%). All parent and teacher behavior ratings scale scores were significantly higher for the ADHD group relative to the TD group (see Table 1). Children with ADHD and typically developing children did not differ on age, F(1,21) = 2.34, p = .14, or measured intelligence based on WISC-III or WISC-IV Full Scale Scores (Wechsler, 1991; 2003), F(1,22) = 2.43, p =.13. A univariate ANOVA revealed that families of children with ADHD had lower average Hollingshead (1985) SES scores than TD children, F(1,21) = 6.31, p = .02. IQ, age, and SES were not significant covariates of any of the analyses reported below. We therefore report simple model results with no covariates. Means, SDs, and between-group contrasts are presented in Table 2.

Tier I: Behavioral Inhibition

SSRT and SSD were not calculated for the Ignore-tone-2 condition because the frequency of response inhibition during "stop-trials" in the Ignore-tone-2 condition was insufficient to provide a reliable estimate. With a sample size of 23, effect sizes of 1.098

or higher would be reliably detected by a between-group ANOVA. Sixty-four percent of reviewed studies reported an ES confidence interval that included or exceeded this value (Alderson et al., 2007). SSRT and stop-signal delay during the Standard-tone condition were analyzed using one-way ANOVAs with group (ADHD, TD) as the fixed factor. There was a significant main effect for group on SSRT, F(1, 22) = 15.64, p = 0.001. The main effect for SSD was not statistically significant, F(1, 22) = 2.47, p = .131 (see Table 2).

Tier II: Mean Reaction Time (MRT)

A group (ADHD, TD) by condition (No-tone, Ignore-tone, Standard-tone, Ignoretone-2) mixed-model ANOVA on mean reaction time (MRT) revealed significant main effects for group, F(1, 21) = 9.37, p = .006, and MRT condition, F(3, 63) = 11.14, p <.001. LSD post hoc analyses indicate that MRTs were faster in the No-tone, Ignore-Tone, and Ignore-tone-2 conditions relative to the Standard-tone condition (all p < .01), and none of the variant conditions were significantly different from each other (all p > .05). These findings, however, must be interpreted in the context of the significant overall group by MRT condition interaction, F(3, 63) = 3.03, p = .04. Three planned comparison mixed-model ANOVAs were conducted to explicate the interaction effect between group and condition, while only including the Standard task and one variant condition (i.e., Notone, Ignore-tone, or Ignore-tone-2) in each analysis. The comparisons analyses provide additional information about differential group changes in reaction time for each variant condition relative to the Standard-tone condition. The main effects for group and condition were significant in all analyses (all p < .05); however, the group by condition interaction was only significant for the Ignore-tone-2/Standard-tone analysis, F(1, 21) =6.70, p = .02. Figure 2a displays the ADHD and TD groups' MRT across conditions. Figures 2b-d show the effect of Ignore-tone, No-tone, and Ignore-tone-2 condition effects on MRT, relative to the Standard-tone condition.

Tier III: Mean Reaction Time Variability (SDRT)

A group (ADHD, TD) by condition (No-tone, Ignore-tone, Standard-tone, Ignoretone-2) mixed-model ANOVA on mean reaction time variability (SDRT) revealed a significant main effect for group, F(1, 21) = 21.80, p < .001, but not MRT condition F(3, 63) = 0.605, p = .61. The group by MRT condition interaction was not significant, F(3, 63) = 2.32, p = .08. Collectively, this finding indicates that the MRT of children with ADHD was significantly more variable relative to typically developing controls regardless of condition.

DISCUSSION

When go- and stop-processes are activated in close temporal sequence (i.e., go-signal activation followed by stop-signal activation), response inhibition depends on whether the stop process can overtake the go-process according to Logan et al.'s (1984) race model of behavioral inhibition. A slow reaction time to a stop-stimulus (SSRT) decreases the probability that the stop-process will overtake the go-process. Past investigations of the Stop-signal Task traditionally examine SSRT as the primary measure of behavioral inhibition, and suggest that the occurrence of slower SSRTs in children with ADHD relative to typically developing children provides evidence of motor inhibition deficits. Two recent meta-analytic reviews (Alderson et al., 2007; Lijffijt et al., 2005) reported significantly slower SSRTs in children with ADHD relative to typically developing controls, but attributed the finding to an underlying deficit of attention or cognitive processing, rather than deficient inhibitory control based on non-significant betweengroup differences in estimated stop-signal delay metrics. The current study directly examined stop-signal delay differences between ADHD-Combined Type and typically developing controls and found that differences in MRT, rather than stop-signal delay, accounted for SSRT variance. Collectively, these findings corroborate recent metaanalytic findings and do not support models of ADHD that predict behavioral inhibition deficits in children with ADHD.

The overall finding of slower and more variable responding to the go-stimulus across experimental conditions by children with ADHD is consistent with recent meta-analytic findings (Alderson et al., 2007; Lijffijt et al., 2005) and performance outcomes

commonly observed on a wide array of standardized tests, neurocognitive tasks, and experimental paradigms (for a review, see Barkley, 2006; Rapport, Chung, Shore, & Isaacs, 2001). Factors such as slower cognitive processing (Kalff et al., 2005), slower motor speed (van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005), deficient cognitive energetic resources (Sergeant et al., 1999), and deficient attentional processes (Lijffijt et al., 2005) have been offered as potential explanations for these differences. The possibility that slower motor speed alone accounts for the between-group differences in MRT can be partially addressed by comparing the between-group differences under the No-tone and Standard-tone experimental conditions. The mean reaction time of children with ADHD was consistently slower relative to TD children, even under the No-tone condition, and the magnitude of the between-group differences under the No-tone and Standard-tone conditions was nearly identical. This finding indicates that children with ADHD are slower processing and responding to even simple, dual-choice stimuli (i.e., respond to 'X' or 'O') relative to controls regardless of whether or not a tone is present.

Children's slower MRTs during the Standard-tone task relative to the variant conditions is also consistent with the negative priming literature. Implicit memory of the stop-stimulus is expected to create a response conflict (i.e., to respond or not respond) on subsequent trials, and slow reaction time to the go-stimulus due to additional cognitive processing demands (Logan, 1988; Neill & Valdes, 1992; Neill, Valdes, Terry, & Gorfein, 1992). The finding that exposure to intermittent auditory tones resulted in significantly slower MRTs only when the tones were meaningful (i.e., stop-signals) is consistent with a negative priming effect. MRTs estimated in traditional Stop-signal paradigms (i.e., mean reaction time of go-responses obtained from go-trials adjacent to

intermittent stop-trials) may therefore be downstream from more complex cognitive processing and executive functions that include working memory, self regulation, and internalization of speech. Additional research comparing single- and dual-choice stimuli is needed to disentangle the extent to which simple motor speed and cognitive processing demand deficits contribute to the consistently slowed response time in children with ADHD.

Accurate MRT estimations are critical to assessing behavioral inhibition differences between ADHD and typically developing children, given the role of MRT in the calculation of SSRT (i.e., SSRT = MRT - SSD). Previous stop-signal studies estimated children's MRT by averaging reaction times to the go-stimulus on go-trials presented before and after stop-trials – a methodological approach which assumes MRT is unaffected by potential carryover effects resulting from intermittent exposure to stopsignals. Children's performance on the Standard-tone Stop-signal Task was contrasted with three variant experimental conditions (No-tone, Ignore-tone, and Ignore-tone-2) to address this possibility. Simply hearing a tone not previously associated with responding, coupled with the instruction to ignore it, had no discernable effect on TD children or those with ADHD given the non-significant differences in each group's MRT between the No-tone and initial Ignore-tone conditions. This finding suggests that the mere presence of a non-meaningful auditory signal in the context of a stop-signal paradigm does not exert a singleton distractor effect by momentarily capturing children's attention and slowing their reaction time (Dalton & Lavie, 2004).

The question of whether a meaningful auditory tone exerts an overall or differential effect on children's mean reaction time was examined by comparing children's

performance under the Standard-tone to the variant tone conditions. Both groups of children showed slower MRT under the Standard-tone condition relative to the initial two variant conditions, which suggests that the current practice of estimating base differences in MRT by extracting go-trials from meaningful stop-trials is likely to inflate the SSRT estimate for all children (SSRT = MRT – SSD).

A serendipitous finding emerged when comparing between-group MRT differences in the Ignore-tone-2 and Standard-tone conditions. Typically developing children's MRTs reverted to levels comparable to their MRTs observed under the No-tone and initial Ignore-tone conditions. This finding indicates that (a) they were able to successfully ignore or suppress the previous association between hearing a tone and stopping, or (b) the association decayed sufficiently over the 7-day interval between assessment sessions. In contrast, the MRTs of children with ADHD remained slowed and comparable to their mean reaction time under the Standard-tone condition. At least two explanations may account for this finding. Children with ADHD may fail to invoke effective metacognitive processes necessary to suppress previously learned associations (e.g., by reminding themselves that the tone no longer has meaning or to simply block out the tone and focus on the X and O stimuli). Some support for this explanation is provided by past studies documenting deficient metacognition in children with ADHD relative to controls (for a review, see Barkley, 1997). An alternative explanation is that mechanisms responsible for allowing stimulus-response associations to fade and eventually decay are deficient in children with ADHD over this time interval – a finding consistent with past reports of excessive perseveration in ADHD (Houghton et al., 1999). Collectively, these findings provide fertile ground for investigating whether suppression and/or decay

deficiencies contribute to the well-documented executive functioning deficits associated with ADHD (Biederman, 2004; Klorman et al., 1999; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005).

The unique contribution of the current study was its systematic examination of MRT under meaningful and non-meaningful tone conditions, and direct examination of the stop-signal delay metric. Several caveats merit consideration despite these methodological refinements. Generalization of findings from highly controlled laboratory-based experimental investigations to the larger population of children with ADHD is always limited to some extent, and studies with relatively small sample sizes are vulnerable to Type II errors. The results of this study, however, were highly consistent with recent meta-analytic reviews that found significant MRT and SSRT differences, but not significant stop-signal delay differences. It is unlikely that the nonsignificant stop-signal delay finding is related to low power, given the large SSRT effect size (ES = 1.67) between children with ADHD and typically developing children. That is, because SSRT is derived from MRT and stop-signal delay, and between-group differences in SSRT were exceptionally large, increased power would only have allowed for the detection of very small magnitude stop-signal delay differences relative to very large SSRT differences. We were also unable to test a true covariate model (i.e., ANCOVA) due to the relatively small study sample size. Independent experimental replication with a larger sample and samples that include females, older children, and other ADHD subtypes is recommended.

Several of the children with ADHD met diagnostic criteria for ODD; however, the degree of comorbidity may be viewed as typical of the ADHD population based on recent

epidemiological findings (i.e., 59 %; Wilens et al., 2002), and a recent meta-analytic review reported that CD/ODD comorbidity did not significantly moderate ADHD children's mean reaction time, mean reaction time variability, or stop-signal reaction time (Lijffijt et al., 2005).

Finally, although the No-tone and Ignore-tone conditions were counterbalanced, the Standard-tone and Ignore-tone-2 conditions were always presented as the third and fourth experimental condition, respectively, to assure that children were not exposed to stopsignals prior to administration of the No-tone and Ignore-tone 2 conditions. Consequently, the possibility of an order effect cannot be entirely eliminated, but is unlikely given the pattern of results relative to the pattern normally expected for order effects involving reaction time data (i.e., order effects are typically associated with faster reaction times in later trials of experimental tasks). Overall, the MRTs in the last condition were not faster than the previous conditions, and were slower for the ADHD group.

The Stop-signal paradigm is currently the most commonly used and experimentally sophisticated measure of behavioral inhibition in child psychopathology research. Results gleaned from our study of ADHD and typically developing control children's stop-signal performance suggest that between-group differences in SSRT are not attributable to behavioral inhibition, but rather to slower processing of and responding to visually presented stimuli, and further slowed by having to process a second stimulus (tone) rather than behavioral inhibition. This finding highlights the need for methodological refinement in controlling for initial differences in children's MRTs, and challenges prevailing views concerning the central role of motor behavioral inhibition deficits in

ADHD. The inclusion of stop-signal delay metrics in future studies is warranted to ensure that between-group differences in SSRT reflect behavioral inhibition deficits rather than differences in children's MRT. Additionally, the use of separate go-trials in future stopsignal investigations is recommended to provide uncontaminated estimates of MRT. These findings have potentially important clinical implications, and may help explain the inefficacy of cognitive therapies that target symptoms related to impulsivity/behavioral inhibition deficits (Rapport et al., 2001).



Figure 1. A visual schematic portraying the relationship among mean reaction time (MRT), stop-signal delay (SSD), and stop-signal reaction time (SSRT) in the context of a traditional Stop-signal paradigm.



Figure 2a. MRTs of children with ADHD and typically developing children across stop signal tone conditions.



Figure 2b-c. Figures show MRTs of children with ADHD (triangles) and typically developing children (circles) as a function of (b) No-tone, (c) Ignore-tone, and (d) Ignore-tone-2 condition contrasts to the standard-tone condition. Vertical bars represent standard error.

Variable	ADHD		TD Children		
	$\overline{\mathbf{X}}$	SD	$\overline{\mathbf{X}}$	SD	F
Age	8.75	1.29	9.36	1.43	1.17
FSIQ	100.92	15.22	110.18	13.11	2.43
SES	43.46	12.25	52.50	7.57	6.13*
CBCL					
Attention Problems	78.50	10.53	55.64	7.06	36.68***
TRF					
Attention Problems	66.25	8.83	48.73	16.92	9.94**
CSI-Parent					
ADHD, Combined	77.75	9.92	48.73	11.11	9.29**
CSI-Teacher					
ADHD, Combined	63.08	11.05	49.50	9.57	43.83***

Table 1. Sample and demographic variables

* $p \le .05$, ** $p \le .01$, *** $p \le .001$

Note: CBCL = Child Behavior Checklist; CSI = Child Symptom Inventory –

symptom severity T-scores; FSIQ = Full Scale Intelligence; SES = Socioeconomic

Status; TD = Typically Developing Children; TRF = Teacher Report Form.
	ADHD (<i>n</i> = 12)		TD $(n = 11)$		Between-group	
	$\overline{\mathbf{X}}$	SD	$\overline{\mathbf{X}}$	SD	F	р
MRT ¹					9.37	0.006
MRT (NT)	680.01	172.68	517.74	66.22		
MRT (IT)	705.72	223.01	510.78	67.50		
MRT (ST)	836.07	286.80	669.70	149.35		
MRT (IT-2)	807.01	265.53	488.29	77.26		
SDRT	322.39	118.11	169.97	59.15	21.80	< 0.001
SSD	169.60	333.53	346.56	173.86	2.47	0.131
SSRT	666.48	259.19	323.14	130.08	15.64	0.001

Table 2. Stop-signal task dependent variables

Note. ADHD = Attention-Deficit/Hyperactivity Disorder; IT = Ignore-tone condition; IT-2 = Ignore-tone-2 condition; MRT = Mean Reaction Time; NT = No-tone condition; SDRT = Mean Reaction Time Variability (Standard Deviation of Reaction Time); SSD = Stop-signal Delay; SSRT = Stop-signal Reaction Time; ST = Standard-tone condition; TD = Typically Developing Children. ¹ MRT in the Standard-tone condition was significantly slower than MRTs in the No-tone, Ignore-tone, and Ignore-tone-2 conditions (p < .05), which did not differ from each other.

APPENDIX A: META-ANALYTIC REVIEW OF THE STOP-SIGNAL TASK

Attention-Deficit/Hyperactivity Disorder and Behavioral Inhibition: A Meta-Analytic Review of the Stop-Signal Paradigm

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RUNNING HEAD: ADHD STOP-SIGNAL META-ANALYSIS

Abstract

Deficient behavioral inhibition (BI) processes are considered a core feature of Attention-deficit/hyperactivity disorder (ADHD). This meta-analytic review is the first to examine the potential influence of a wide range of subject and task variable moderator effects on BI processes – assessed by the stop-signal paradigm – in children with ADHD relative to typically developing children. Results revealed significantly slower mean reaction time (MRT), greater reaction time variability (SDMRT), and slower stop-signal reaction time (SSRT) in children with ADHD relative to controls. The non-significant between-group stop-signal delay (SSD) metric, however, suggests that stop-signal reaction time differences reflect a more generalized deficit in attention/cognitive processing rather than behavioral inhibition. Several subject and task variables served as significant moderators for children's mean reaction time.

Attention-Deficit/Hyperactivity Disorder and Stop-Signal Behavioral Inhibition: A Meta-Analytic Review of the Stop-Signal Paradigm

Theories of attention-deficit/hyperactivity disorder (ADHD) evolved from implied brain damage (Strauss & Lehtinen, 1947) and dysfunction (Dolphin & Cruickshank, 1951; Strauss & Kephardt, 1955) to single construct theories of sustained attention (Douglas, 1972), arousal/activation regulation (Sergeant, Oosterlaan, & van der Meere, 1999), working memory (Rapport, Chung, Shore, & Isaacs, 2001), delay aversion (Sonuga-Barke, 2002), and behavioral inhibition (Barkley, 1997). Castellanos and Tannock (2002) provide a comprehensive review of these models and their underlying psychological/neurobiological constructs and aetiological factors.

Behavioral inhibition (BI) has garnered particular interest in recent years as a psychological construct used to describe a cognitive process that (a) sub-serves behavioral regulation and executive function (Barkley, 1997), and (b) underlies the ability to withhold or stop an on-going response (Schachar, Mota, Logan, Tannock, & Klim, 2000). This latter process, its assumptions and underlying metrics, and moderators of BI function in children with ADHD relative to normal controls, serve as the focus for the current meta-analytic review.

Current models of behavioral inhibition are derived largely from Gray's (1982) theory of brain-behavior processes wherein an underactive behavioral inhibition system fails to provide sufficient anxiety and fearfulness, resulting in the initiation or continuation of unwanted behavior (Quay, 1997). This inability to withhold or stop an on-going response is central to current theoretical models of ADHD, and may represent the primary component underlying executive functions such as working

memory, self-regulation, internalization of speech, and reconstitution (for a review, see Barkley, 1997). Performance measures used to index the BI construct traditionally involve a dual-task paradigm wherein participants respond to a primary stimulus and withhold a response when presented with a secondary stimulus. Examples of common BI measures include the (a) Go-No-Go task (Iaboni, Douglas, & Baker, 1995), (b) Change Task (Schachar, Tannock, Marriott, & Logan, 1995), (c) Stroop Color-Word Interference Test (Barkley, 1997), and (d) Stop-Signal Task (Logan, Cowan, & Davis, 1984). The stop-signal task (Logan, Cowan, & Davis, 1984) is the premier paradigm used to study children's ability to suppress prepotent and ongoing responses (i.e., inhibitory motor control).

The Stop-Signal Task

Investigations using the stop-signal task reveal that children with ADHD tend to have longer stop-signal reaction times relative to normal controls (Oosterlaan, Logan, & Sergeant, 1998) – a finding consistent with current theoretical models of ADHD that emphasize the importance of an individual's ability to stop an ongoing response and inhibit responding to pre-potent stimuli (Barkley, 1997). Its widespread adoption as a measure of behavioral inhibition is due to its unique ability to capture theoretically important cognitive processes by means of the stop-signal reaction time (SSRT) metric.

In a prototypical stop-signal paradigm, children are pre-trained to respond differentially to two stimuli (e.g., the letters X and O) using left and right response buttons. The average of these responses reflects the time required to receive the visual input, encode it, and emit a pre-trained motor response, referred to as mean reaction

time (MRT). After practice training, children are instructed to withhold their response to the go-signal whenever it is followed by a stop-signal, typically an auditory tone presented within milliseconds following the go-signal. The ability to withhold or stop an activated motor response is reflected by the stop-signal delay (SSD) metric – the measured time interval between the presentations of the go- and stop-signals. For example, if two groups of children emit similar mean reaction times in response to visual stimuli, then differences in behavioral inhibition (SSRT: stop-signal reaction time) are assumed to be due to between-group differences in SSD based on the recommended formula (SSRT = MRT-SSD). That is, one of the two groups required a longer time interval (SSD) between the go- and stop-signals to inhibit their activated motor response when signaled to do so.

The theoretical underpinnings of the stop-signal paradigm are grounded in Logan's (1981) pioneering work in the field. A go- and stop-process are hypothesized to operate independently of one another to enable and prevent the occurrence of controlled motor responses, respectively. When both processes are activated in close temporal sequence (i.e., go-signal activation followed by stop-signal activation), response execution depends on whether the stop process can overtake the go-process. Stop-signal reaction time (SSRT) – the primary measure of behavioral inhibition – thus reflects the relative speed of the stop process relative to the go-process, and is estimated by subtracting the time interval difference between the presentations of the go- and stop-stimuli (SSD) from the time required to process and emit a controlled motor response (MRT). This point becomes central to behavioral inhibition deficiencies ascribed to ADHD in the literature; between-group differences in BI

functioning must be present after accounting for initial differences in simple reaction time.

Early versions of the stop-signal paradigm examined the probability of inhibiting using a range of fixed stop-signal delays – children completed blocks of trials with each block having a different SSD. Two limitations of the paradigm were subsequently recognized. The primary metric for estimating behavior inhibition (SSRT) required a complex, multi-step process. Calculating SSRT initially involved estimating the probability of inhibiting a motor response following a stop signal (a response rate value between 0 and 1), rank-ordering the distribution of MRTs, and determining the nth MRT (i.e., MRT percentile rank corresponding to response rate). SSD was subsequently subtracted from MRT_{nth} (i.e., $MRT_{nth} - SSD = SSRT$), and the calculation was repeated for each fixed SSD to obtain an overall mean value. Investigators also realized that children frequently adopted an overly cautious response bias by intentionally delaying their go-stimulus response (slowed MRT) in anticipation of a stop-signal (Logan, Schachar, & Tannock, 1997). A dynamic tracking version of the stop-signal paradigm was developed to address these concerns, wherein the SSD was programmed to change following each trial based on a child's performance. Specifically, successful and unsuccessful inhibition of a motor response following the stop-signal causes the ensuing preprogrammed go/stop-signal interval to be shortened or lengthened by 50 msec, respectively. This modification has the desired effect of engendering a successful inhibition response rate of approximately 50% in all children, such that between-group differences in SSRT reflect differences in SSD rather than differential success rates, after MRT differences

are factored out of the equation (Logan et al., 1997). Stated differently, any variability in SSRT is derived from three sources: (a) variability in SSD if MRT is held constant; (b) variability in MRT if SSD is held constant; or (c) variability in both MRT and SSD based on Logan et al.'s (1997) formula. Specific implications for interpreting meta-analytic review findings are that a slow SSRT, coupled with a slow MRT in ADHD, indicates an inhibitory deficit in children with ADHD only if their SSD is also shorter relative to the control group SSD. An equivalent or longer SSD would suggest that children with ADHD exhibit equal or greater success at inhibiting their responses, relative to control children. The relationships among the go-stimulus, SSD, and SSRT are depicted graphically in Figure 1.

Insert Figure 1 about here

Meta-Analysis

The original meta-analytic review (Oosterlaan et al., 1998) of stop-signal performance in children with ADHD was based on eight studies published between 1990 and 1997. Participants were males between 6 and 12 years of age, and included normal controls, and children with single (i.e., ADHD, Conduct Disorder) and comorbid disorders (i.e., ADHD + Conduct Disorder, ADHD + Oppositional Defiant Disorder). Children with ADHD and those with CD exhibited slower go and stop processes, and reduced ability to successfully inhibit relative to normal controls when measured with the stop-signal task, go, no-go task, and change task. The potential role of moderator variables on children's performance was not quantified in the review.

A second meta-analytic review (Lijffijt, Kenemans, Verbaten, & van Engeland, 2005) examined mean reaction time (MRT), stop-signal reaction time (SSRT), mean reaction time variability (SDRT), and five potential moderators of these indices (child-adult status, stop signal method, IQ, comorbidity with ODD/CD, and ADHD subtype) in twenty-nine studies (17 child, 1 adolescent, 6 adult, and 5 mixed child-adolescent) published since the Oosterlaan et al. (1998) meta-analytic review. Child-adult status was the only significant moderator of between-group effect size differences in mean reaction time (0.29), mean reaction time variability (0.65), and stop signal reaction time (0.58). The authors concluded that the longer response times (MRT) and more lapses of attention (SDRT) in children with ADHD, coupled with a non-significant SSRT-MRT difference score, were consistent with a general inattention rather than behavioral inhibition model of ADHD.

The conclusions reached by Lijffijt et al. (2005) may be premature for several reasons. Including fixed and dynamically changing stop signal delay studies to examine between-group differences in SSRT poses a serious threat to the metric's validity. Fixed stop signals have no associated within- or between-subject variability, and their inclusion with dynamically changing stop signal studies is likely to artificially deflate between-group differences in SSRT effect size estimates. Age alone emerged as a significant moderator for between-group differences for all three BI matrices; however, this finding, based on a child-adult dichotomy rather than distinct child age groupings, may suppress between-group SSRT effect size estimates

given the slower and more variable reaction times observed in younger children (Barkley, 2005; Rapport et al., 2001). Their MRT-SSRT difference score – based on pooling pooled standard deviation scores – inaccurately reflects the magnitude of between-group BI differences. Finally, the high within-group variability for study effects reported by the authors indicates that a considerable proportion of unexplained error may be due to uncontrolled sources not considered in either of the earlier reviews. Examination of additional potential moderating variables is warranted to address this issue.

Goals of the Present Meta-Analysis

The present meta-analytic review examines behavioral inhibition in children using the traditional stop-signal paradigm (i.e., two-choice primary task and discrete stopsignal). The unique contribution of the current review is its systematic examination of sample (age, diagnostic selection procedures) and task variable (type of go- and stopstimuli, task trials, target frequency) moderator effects on children's stop-signal BI performance either not quantified in previous reviews, or analyzed based on a limited number of studies. Moderating variables warrant scrutiny because of their potential to change the nature of dependent-independent variable relationships, with implications for theory development, refinement, and refutation (Holmbeck, 1997). A total of 24 studies were included to accomplish this goal, including four studies published since the original meta-analysis but omitted from the Lijffijt et al. (2005) review (Konrad, Gauggel, Manz, & Scholl, 2000b; McInerney & Kerns, 2003; Schachar et al., 2004; Walcott & Landau, 2004), and eight studies included in the original meta-analytic

paper (Oosterlaan et al., 1998) but omitted from Lijffijt et al.'s review $(2005)^1$. The present review also provides a more rigorous analysis of between-group stop-signal delay differences in children. This metric could not be examined and statistically analyzed until 1999 – following the development of the dynamic tracking stop-signal paradigm – but provides a critical index for assessing between-group differences in stop-signal behavioral inhibition. Failure of the stop-signal delay (SSD) index to account for significant between-group variability in SSRT indicates that betweengroup study differences are more likely due to pre-exiting differences in MRT that reflect inefficient cognitive processing and/or inattention rather than inhibitory control differences (Castellanos & Tannock, 2002; Overtoom et al., 2002; Rapport et al., 2001). Larger mean reaction time variability (SDRT) in children with ADHD, which reflect more lapses of attention, may be explained by a general attention deficit consistent with an emerging endophenotypic model (Castellanos, 2002), a deficit of interference control (Nigg, 2001), or a ubiquitous characteristic of ADHD. Inhibitory deficits, however, should be reflected by a disproportionately longer SSRT relative to MRT.

Moderators and Coding of Moderators

Age. The influence of children's age on BI performance indices was not examined in either the initial (Oosterlaan et al., 1998) or more recent (Lijffijt et al., 2005) meta-

¹ Updated meta-analytic reviews frequently exclude studies that were recently reviewed based on a confirmatory approach (i.e., to determine whether ES differences of similar magnitude emerge based on the more recent and different series of studies). The current review includes all published studies to enable a broader moderator analysis and to confirm the SSD effect reported by Lijffijt et al. (2005) after controlling for methodological limitations.

analytic review. It merits scrutiny, however, due to the well-documented developmental changes observed in children across a wide array of cognitive and motor tasks (Bedard et al., 2002; Nigg, 1999; Williams, Ponesse, Schachar, Logan, & Tannock, 1999). A significant age moderator effect would converge with the finding of Lijffijt and colleagues (i.e., children are slower and more variable relative to adults), and may indicate that between-group differences in BI are underestimated when study samples include older children, or that underlying mechanisms or processes related to BI improve with development.

The mean of the ADHD and normal control samples were averaged to create an overall combined age mean for each study (the mean age difference between the ADHD and normal control samples was approximately four months) and subsequently divided into two categories: young (7 years-0 months to 9 years-11 months), and old (age 10 years-0 months to 12 years-11 months). Three studies reported a range of values and were excluded from the age effects analysis. Table 1 provides a summary of reviewed studies.

Diagnostic Procedures. The current meta-analysis is the first to examine whether differences in group assignment criteria moderate effect size estimates for traditional stop-signal dependent measures. Assignment to groups has varied from exclusive reliance on narrow-band rating scales to comprehensive diagnostic evaluations involving extensive history taking, semi-structured clinical interview, and standardized rating scale scores. Diagnostic assignment based exclusively on rating scale cutoff scores appears to be the least face valid method of grouping, considering the myriad disorders and conditions featuring attention and behavioral problems as

core or secondary features (American Psychiatric Association, 2000). Moreover, significant variability in symptom endorsement on structured and semi-structured clinical interviews is not accounted for by rating scale endorsements (McGrath et al., 2004); and none of the current scales or inventories obtain critical diagnostic information concerning symptom onset and course.

Diagnostic assignment based on single sources of information (e.g., rating scales) is likely to increase group membership heterogeneity and suppress BI effect size estimates by including non-ADHD children in the ADHD group. This is particularly salient owing to the high inter- and intra-day variability observed in children with ADHD across settings (Castellanos et al., 2005), and the moderate specificity of most rating scales (Rapport, Timko, & Wolfe, 2006).

Two groupings of diagnostic criteria were formed. The first included studies that employed a comprehensive diagnostic procedure (i.e., a semi-structured or structured clinical interview complemented by teacher/parent questionnaires). The second included studies that relied exclusively on questionnaires or professional opinion (e.g., pediatric evaluation) to determine diagnostic standing.

Stop-Signal Stimuli Modality. Stop-signal studies traditionally use either phonological/text-based *go* stimuli (e.g., "X" and "O") coupled with an auditory tone as the stop-signal, or visual-spatial go and stop-signal stimuli (e.g., Rubia, Oosterlaan, Sergeant, Brandeis, & Leeuwn, 1998). Past investigations (Logan 1994; Logan & Cowan, 1984) examining BI performance on the stop-signal task found minimal performance differences when go- and stop-signal stimuli were modality specific (i.e., both phonological or both visual-spatial), but neither same nor different stimulus

modality influences on stop signal performance were analyzed in previous reviews (Lijffijt et al., 2005; Oosterlann et al., 1998). Stimulus modality may prove to be a particularly robust moderator of between-group BI differences, owing to the distinctiveness of the phonological and visual-spatial working memory systems (Baddeley, 1996; Michas & Henry, 1994; Pickering, Gathercole, & Peaker, 1998; Smith, Jonides, & Koeppe, 1996), and larger deficits in visual-spatial relative to phonological processing observed in ADHD (Martinussen, Rhonda, Hayden, Hogg-Johnson, & Tannock, 2005).

Text based (e.g., letters) and non-text based (e.g., auditory tones) go-stimuli were assigned to a phonological and visual-spatial grouping, respectively. Stop-stimulus modality was not examined in the analysis because nearly all studies (92%) used an auditory tone stop-signal.

Stop-Signal Delay (SSD). The change in stop-signal delay (SSD) methodology – initially incorporating pre-determined delay parameters, and later, a tracking algorithm (Schachar & Logan, 1990) – warrants scrutiny to examine whether variation among study results are partly accounted for by this uncontrolled source. The newer methodology is expected to reflect more precise and hence larger betweengroup ES estimates owing to its intra-individual adjustment features and control for instructional demands (Logan et al., 1997). For example, Schachar et al. (2004) found that typically developing children artificially slowed their MRT following unsuccessful stop-trials to a greater extent relative to children with ADHD, which resulted in smaller between-group BI differences. This effect is expected to be larger in studies that fail to control for artificial MRT slowing (i.e., fixed SSD studies). The

inclusion of SSD as a moderator also addresses whether results can be generalized across studies using the SSD fixed and dynamic methodologies.

Studies using predetermined, stop-signal delays across experimental blocks were assigned to a fixed category. Those in which stop-signal delay changed dynamically based on the child's response were assigned to a tracking category.

Trials. The number of pre-programmed trials used in stop-signal paradigms is highly inconsistent across studies, ranging from 192 to 432 experimental trials in the Oosterlann et al. (1998) meta-analytic review, and 96 to 1,920 (i.e., approximately 5.6 to 112 minutes) in more recent studies. Differences in trials indicate that task duration ranges from a few minutes to nearly 45 minutes depending on programmed experimental parameters¹. The breadth of this parameter in published studies obscures interpretations concerning the causal nature of performance differences; specifically whether they reflect deficient BI, an inability to sustain attention (Douglas, 1999; Hooks, Milich, & Lorch, 1994; Lijffijt et al., 2005), or elements of both processes.

The total number of experimental trials was analyzed as an indication of task duration due to the infrequent reporting of time data (only 8 of 24 studies included task duration data in time units). Total number of experimental trials was analyzed as a grouping variable using three categories: (1) low (< 200 trials), medium (200 to 300 trials), and high (> 300 trials).

Stop-Signal Target Density. Target density refers to the proportion of trials within an experimental block that are stop-trials, and is typically reported as a percentage (i.e., percent of stop trials out of total experimental trials). Children's accuracy and reaction time show significant changes due to target density manipulations and the

differential demands they place on working memory (Denney, Rapport, & Chung, 2005; Losier, McGrath, & Klein, 1996). A significant target density moderator effect would indicate that other factors, such as increased demand on the central executive system for switching between stimuli or between phonological and visuospatial working memory subsystems (Baddeley, 1996), influence BI effects.

Stop-signal target density was examined as a grouping variable using two categories based on the median split of the target densities reported across reviewed studies (median = 25, mean = 27.75): low ($\leq 25\%$) and high (> 25%).

Method

Literature Searches

Searches of the stop-signal behavioral inhibition literature were conducted using the databases PSYCINFO, ERIC, MEDLINE, PsychARTICLES, and Social Science Citation Index. The following headings were used within each database: Attention, ADD, ADHD, Hyper*, behavioral inhibition, stop-signal, stop task, go-no-go, and inhib*. An asterisk following a root word instructs search engines to look for any derivative of the word that is followed by the asterisk (e.g., inhibit, inhibits, inhibited, inhibition). Articles located by the search engines were scrutinized for additional references relevant to the review using front- and back-search methodology until no additional references relevant to stop-signal behavioral inhibition were located.

Inclusion Criteria

All studies included in the review compared the performance of children (age 7 years to 12 years) with ADHD to normal controls on the stop-signal task. This age range was selected based on the well-documented developmental differences in

cognitive strategies and processes observed in children relative to adolescents and adults (Lijffijt et al., 2005; Williams et al., 1999). Five additional inclusion criteria required that: (a) the primary task be a dichotomous two-choice reaction time task; (b) the inhibition response be initiated by a visual or auditory stop-signal; (c) responses to the stop-signal be measured by means of simple reaction time (i.e., change tasks were excluded); (d) participants be medication-free during the experiment; (e) participants not receive performance feedback – a condition occasionally included to examine between-group motivation differences; and (f) experimental conditions that included clearly defined comorbid disorders (e.g., ADHD and anxiety disorder)². Seventeen studies were excluded from the meta-analysis using these criteria³.

Studies that report multiple effect sizes from the same sample risk threats to statistical independence (Lipsey & Wilson, 2001). Among the studies reviewed for the current meta-analysis, multiple conditions and/or experiments were reported in five studies, and these additional conditions and separate experimental conditions were omitted from the review⁴.

Three stop-signal studies required special consideration. One reported two experiments that included independent samples (Pliszka, Borcherding, Spratley, Leon, & Irick, 1997). Both experiments were included in the current meta-analysis. SSRT was calculated using the subtraction and integration method in one study (Scheres, Oosterlaan, & Sergeant, 2001), and only the subtraction method was included in the review based on a coin toss. Finally, performance data for two SSDs were reported in one study (Overtoom et al., 2002), and only one set of data was used

for the review to avoid inflating effect sizes by over representing a particular sample (Lorber, 2004). Collectively, 25 stop-signal studies (59% of all stop-signal studies) were included in the final sample for analyses.

Effect Size Estimation

Effect size (ES) estimates were computed using Comprehensive Meta-Analysis software. They reflect the magnitude of difference between children with ADHD and typically developing children. Positive and negative ESs indicate higher and lower scores for the ADHD group relative to the control group (longer MRT and SSRT, larger SDRT), respectively. Hedges's *g* (1982) effect sizes were used for MRT, SDRT, and SSRT to correct for the upward bias of studies with small sample size (Lipsey & Wilson, 2001). The MRT-SSRT ES was computed using an unstandardized mean gain score. Effect sizes are classified as small (ES \leq 0.30), medium (0.30 < ES < 0.67), or large (ES \geq 0.67), whereas an ES of zero indicates no difference between means (Lipsey & Wilson, 2001). Unless otherwise specified, all ESs were computed using means, standard deviations, and sample size.

Effect Size Calculation Exceptions and Exclusions

MRT. One study (McInerney & Kerns, 2003) reported a non-significant difference between ADHD and normal controls on MRT, but did not report a specific *p*-value. This study was assigned an effect size value of zero to avoid inflating effect size estimates and reduce the likelihood of Type I error (Rosenthal, 1995). Three additional studies (Aman, Roberts, & Pennington, 1998; Plizska et al., 1997, Exp. 2; Walcott & Landau, 2004) did not report sufficient data to compute effect size estimates of MRT, and were excluded from this analysis.

MRT Variability (SDRT). Effect size estimates for three studies (McInerney & Kerns, 2003; Nigg, 1999; Stevens, Quittner, Zuckerman, & Moore, 2002) were

computed using a reported p-value and sample size. Eleven additional studies provided insufficient data to compute MRT variability (SDRT) effect size estimates and were excluded from this analysis⁵.

SSRT. One study's effect size was estimated based on the reported means, sample size, and *p*-value (Stevens et al., 2002). Two studies (Aman et al., 1998; Daugherty, Quay, & Ramos, 1993) provided insufficient data to compute an effect size for SSRT, and were excluded from this analysis.

Stop-Signal Delay (SSD). The SSD analysis included only newer tracking stopsignal studies owing to the lack of variation associated with earlier fixed stop-signal studies. A SSD between-group effect size was computed for eight tracking studies as an unstandardized mean gain with corresponding confidence intervals (Lipsey & Wilson, 2001). This approach was followed because none of the studies reported SSD means or standard deviations. SSD was algebraically solved using the functional equivalent of Logan's (Logan et al., 1997) formula: MRT – SSD = SSRT.

Data Analysis

Homogeneity analyses. A *Q*-test was performed on each outcome variable (i.e., MRT, SDRT, SSRT, and SSD) to examine the distribution of effect sizes from the included studies. A significant *Q* rejects the assumption of homogeneity and supports the examination of potential moderator effects (Lipsey & Wilson, 2001).

Moderator analyses. A fixed effects weighted regression approach using SPSS for Windows 12.0 was adopted to provide a measure of overall fit (Q_R), as well as an error/residual term (Q_E)⁶. A significant Q_R indicates that the model accounts for significant variability among effect sizes. A significant Q_E indicates that the residual

variance is greater than what is expected from random study-level sampling error. Both statistics are distributed as chi-square. Corrected *B*-weight standard error for each moderator was then tested against the *z*-distribution (Lipsey & Wilson, 2001).

Results

Overall Effect Size Summary

Twenty-two studies provided sufficient information to compute effect sizes for mean reaction time (MRT). The mean effect size of MRT between ADHD and typically developing children was 0.45 (95% confidence interval = 0.33 to 0.56), and indicates that children with ADHD have moderately slower MRT's relative to normal controls. The distribution of effect sizes was heterogeneous, Q(20) = 42.42, p < .01, ranging from -0.41 to 1.24. All effect sizes fell within two standard deviations of the mean effect size for MRT, suggesting the heterogeneity was not due to outliers. A *Fail-safe N* analysis (Rosenthal, 1995) indicated that an unlikely 339 studies would be needed to reduce the confidence interval of the effect size to include zero (i.e., result in no significant differences in MRT between ADHD and typically developing children).

Twelve studies provided sufficient information to compute effect sizes for MRT variability (SDRT). The mean effect size of SDRT between ADHD and typically developing children was 0.73 (95% confidence interval = 0.59 to 0.87), and indicates that children with ADHD have more variable MRT's relative to normal controls. The distribution of effect sizes was heterogeneous, Q(11) = 22.22, p = .02, ranging from 0.39 to 1.37. All effect sizes fell within two standard deviations of the mean effect size for SDRT, suggesting the heterogeneity was not due to outliers. The *Fail-safe N*

analysis indicated that 343 studies would be needed to reduce the confidence interval of the effect size to include zero (i.e., result in no significant between-group differences).

Twenty-two studies provided sufficient information to compute effect sizes for Stop-Signal Reaction Time (SSRT). The mean medium effect size of SSRT between ADHD and typically developing children was 0.63 (95% confidence interval = 0.52 to 0.74), and indicates that children with ADHD are on average 0.63 standard deviations slower reacting to stop signals compared to normal controls. The distribution of effect sizes was homogeneous, Q (21) = 32.33, p >.05 (range = 0.23 to 1.33), and all effect sizes fell within two standard deviations of the mean effect size for SSRT. The *Fail-safe N* analysis indicated that 741 studies would be needed to reduce the confidence interval of the effect size to include zero. The non-significant Q-statistic indicates that the amount of between-study variance can be attributed to random, study-level error variance, and does not support analysis of potential SSRT moderator effects.

Eight studies provided sufficient information to compute effect sizes for stopsignal delay (SSD). The mean effect size of -0.025 (95% confidence interval = -0.207 to 0.157) indicates that children with ADHD do not differ significantly in SSD relative to typically developing children. A Fail-safe N analysis was not performed because the obtained confidence interval includes zero.

Moderator Variables

Mean Reaction Time (MRT). The results of the weighted regression analysis indicate that the model explains a significant proportion of the variability across the

MRT effect sizes, $Q_R = 180.77$, df = 6, p < .001, and accounts for 41% of the variability. The moderators age (z = -2.78, p = .003), diagnostic evaluation (z = -2.40, p = .008), delay schedule (z = 7.78, p < .001), total experimental trials (z = 2.88, p = .002), and go-stimulus modality (z = 4.30, p < .001) were significant predictors of effect size variability across studies.

Younger children, the use of rating scales rather than comprehensive diagnostic procedures, newer stop-signal paradigms that dynamically alter the stop-signal delay interval based on children's ability to inhibit a response, a greater number of experimental trials, and visuospatial rather than phonological go-stimuli, were associated with large effect sizes. Stop-signal target density was not a significant predictor of MRT. A significant sum-of-squares residual ($Q_E = 117.31$, df = 12, p < .001) was obtained, indicating that there is residual variance in the model beyond subject-level sampling error even after including the six moderator variables (see Table 2). This indicates that there may be additional moderators other than those considered in this review that affect children's MRT.

Insert Table 2 about here

Mean Reaction Time Variability (SDRT). The regression analysis indicates that the model does not explain significant variability across the SDRT effect sizes, $Q_R = 0.03$, df = 6, p > .05. This finding indicates that moderator effects cannot explain the heterogeneous distribution of effect sizes. Table 2 displays a summary of the data for SDRT.

Stop-Signal Reaction Time (SSRT). A regression analysis of potential moderator effects on SSRT was not performed due to the non-significant Q-statistic, which indicated that between-study variance is attributable to random, study-level error variance. Examination of moderator effects could potentially be justified a priori based on past findings; however, the non-significant Q-statistic, coupled with the non-significant overall effect size for SSD (ES = -0.025), indicates that any residual variability in SSRT likely reflects systematic variability associated with MRT coupled with measurement and random error (SSRT=MRT-SSD).

Stop-Signal Delay (SSD)

A regression analysis to examine moderator effects on SSD was not conducted due to the non-significant overall effect size for the variable.

Discussion

The current study updates past (Oosterlaan et al., 1998) and recent (Lijffijt et al., 2005) meta-analytic reviews, and provides a unique examination of task and subject variable moderator effects for traditionally employed stop-signal performance indices. Our results corroborate those reported in previous meta-analytic reviews (Lijffijt et al., 2005; Oosterlaan et al., 1998) in finding that children with ADHD exhibit slower and more variable reaction times to primary task stimuli (i.e., go-stimuli). The effect size estimates for these variables are remarkably consistent across reviews (i.e., MRT ES = 0.49, 0.52, 0.45; SDRT ES = 0.73, 0.72, 0.72 for the Oosterlaan et al., 1998, Lijffijt et al., 2005, and current study, respectively), despite the inclusion of 16 and 12 studies not considered in the past two reviews, respectively. The slower and more variable reaction times in children with ADHD is

not unexpected, as these performance outcomes are commonly observed on a wide array of standardized tests, neurocognitive tasks, and experimental paradigms (for a review, see Barkley, 2005; Rapport et al., 2001). The differences have been attributed to slower cognitive processing (Kalff et al., 2005), slower motor speed (van Meel, Oosterlaan, Heslenfeld, & Sergeant, 2005), deficient cognitive energetic resources (Sergeant et al., 1999), and deficient attentional processes (Lijffijt et al., 2005). The increased ADHD-related variability has also been proposed recently as a potential endophenotype of ADHD related to catecholaminergic deficiencies, and consequently tertiary symptoms such as processing/attentional deficits and careless errors (Castellanos et al., 2005).

Other factors may also contribute to the slower and more variable mean reaction times observed in ADHD. All reviewed stop-signal studies calculated children's mean reaction times to the go-stimulus (MRT) by selecting out non-stop trials within the experimental task, rather than obtaining a measure of pure motor speed uninfluenced by intermittent signals to withhold responding. Implicit to this methodology are the underlying assumptions that children's motor speed is uninfluenced by intermittent stop signals, and that children with ADHD and normal controls are similarly affected by intermittent exposure to stop signals. Previous research with adults shows that their primary reaction time is slower following successful and unsuccessful stop-trials relative to control trials (Rieger & Gauggel, 1999). Moreover, Schachar et al. (2004) found that children with ADHD differentially slow their MRT following unsuccessful stop-trials relative to typically developing children. Children with ADHD also performed more poorly under

intermittent relative to continuous schedules of reinforcement (Douglas & Parry, 1983).

Collectively, the possibility that intermittent cues contribute to between-group differences in MRT, and indirectly to SSRT based on conventional formula (SSRT=MRT-SSD), becomes an important consideration for future stop-signal investigations. The specific contributions of SSD and MRT to SSRT are central for quantifying the construct, and future studies may need to include uncontaminated experimental sessions for estimating children's motor reaction time independent of intermittent stop-signals.

The moderate effect size for stop-signal reaction time (SSRT) is consistent with extant literature and previous meta-analytic reviews. For example, Oosterlaan et al. (1998) and Lijffijt et al. (2005) reported SSRT effect sizes of 0.64 and 0.58, respectively, compared to an ES of 0.63 in the current review. Oosterlaan et al. (1998) interpreted their finding as evidence of deficient inhibitory control in children with ADHD relative to normal controls, but did not dissect the SSRT metric to determine the extent to which it reflected mean reaction time (MRT) relative to stopping speed differences (SSD) in ADHD. Lijffift et al. (2005) examined SSRT – MRT betweengroup differences (i.e., SSD) to determine whether the SSRT effect size metric disproportionately reflected initial reaction time rather than inhibitory differences in ADHD. They reported a non-significant SSD ES (-0.22), coupled with a large MRT variability effect size, and concluded that the results reflected an underlying attention deficit rather than deficient inhibitory control. Several factors, however, may have biased the Lijffift et al. (2005) SSD estimate. These include pooling, pooled standard

deviation scores, including studies that reflect motivational (i.e., reinforcement conditions) rather than inhibitory processes, and including fixed SSD with dynamic SSD tracking studies, the former of which has no associated variance and may deflate the estimate. These methodological issues were addressed in the current analyses, but did not alter the outcome. Our findings of a negative and non-significant betweengroup SSD effect size (-0.025) corroborates the Lijffift et al. (2005) results, and indicates that the moderate SSRT effect size estimate reflects differences in children's mean reaction time (MRT) to go-stimuli rather than between-group differences in stopping speed.

The impact of this finding transcends stop-signal research and raises important concerns regarding the central role of behavioral inhibition in extant models of ADHD. It is noted, however, that these findings only pertain to executive-motor inhibition, while interference control and cognitive inhibition (Nigg, 2001) were not addressed by the current review. Examination of other candidate endophenotypes such as working memory and response variability warrants further scrutiny, and may reveal that performance on the stop-signal task reflects processing that is downstream from other core deficits.

Moderator effects

Several variables served as significant moderators for mean reaction time differences between children with ADHD and typically developing children, and these findings were relatively consistent with extant literature. For example, the finding that younger children are associated with larger MRT ES estimates are consistent with lifespan and developmental studies (Bedard et al., 2002; Williams et

al., 1999). Delayed motor development is commonly reported in children with ADHD, as is poorer motor coordination (Diamond, 2000) and slower motor speed (Barkley, 2005). The results do not appear to reflect improvements of inhibitory control given the non-significant SSD ES.

The larger effect size favoring rating scales rather than comprehensive clinical diagnostic evaluation procedures appears incongruous without considering the influence of performance variability on the ES statistical formula. Comprehensive diagnostics typically increase sensitivity and specificity for diagnostic grouping (i.e., higher rate of true positives and fewer false positives). Extant reviews have consistently revealed that children with ADHD are more variable as a group on speeded and neurocognitive tasks (Barkley, 2005; Losier et al., 1996). Furthermore, direct comparisons of children with ADHD relative to children selected based on high rating scale scores (i.e., children with clinical disorders other than ADHD) reveal that children with ADHD exhibit significantly more variable performance on speeded motor tasks (Roberts, 1990). Thus, identifying more true positives (i.e., children with ADHD) is likely to lower the effect size estimates for most speeded performance indices because it inflates the ES denominator ($sd_{ADHD} + sd_{Control}/2$). That is, although within-group diagnostic heterogeneity decreases with comprehensive diagnostic methodologies, within-group performance variability increases, consequently reducing the overall effect size magnitude.

Studies that adjusted SSD following each trial (i.e., \pm 50 msec based on the previous trial's outcome) were associated with larger MRT effect sizes relative to studies that changed SSD following a specified number of trials. Continuously

adjusting the stop signal, such that children's probability of inhibiting approximates .50, may function to minimize the tendency of typically developing children (relative to ADHD) to slow their motor response following unsuccessful stop-trials as reported in previous studies (Schachar et al., 2004). The non-significant difference between ADHD and normal control stop-signal delay (SSD) ES estimates highlighted earlier, suggests that this effect probably reflects initial between-group differences in mean reaction time that are detected more accurately by the dynamic task. The finding also suggests that results cannot be generalized across studies using the SSD fixed and dynamic methodologies.

Larger between-group differences for MRT were also associated with greater numbers of experimental trials. This finding may reflect a greater fall-off in performance in children with ADHD over time, however, the potential interaction effect between group and performance over time could not be directly examined. A more likely explanation for the effect is that it represents the greater reliability of results associated with incorporating a larger number of trials – a common finding in the experimental literature (cf. Band, van der Molen, & Logan, 2003).

Go-stimulus modality was the second strongest predictor of MRT effect size variability. This finding reflects the larger between-group differences in mean reaction time required for processing visual-spatial relative to phonological gostimuli, and is consistent with recent findings of more pronounced deficits in visualspatial processing in ADHD relative to typically developing children (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005).

Limitations

Children with clinical disorders other than ADHD and comorbid ADHD samples were intentionally excluded from the current review for three reasons. Only a handful of stop-signal studies included separate samples of carefully diagnosed psychopathological control children (n=10), or children with comorbid disorders (n=6). Meta-analytic findings based on such small samples may be highly unstable and thus unreliable (Rosenthal, 1995). Moreover, Lijffijt et al. (2005) included comorbidity in their meta-analytic moderator analysis – despite the small number of samples available – and reported that it was not a significant moderator of children's mean reaction time, mean reaction time variability, or stop-signal reaction time. Finally, confirmation of a behavioral inhibition deficit in ADHD would clearly warrant comparison with appropriate psychiatric controls to ascertain whether the deficit is diagnosis-specific rather than a nonspecific effect of psychiatric diagnosis in general. Our results, coupled with the earlier Lijffijt et al. (2005) review, however, suggest a more generalized attentional or cognitive processing deficit in ADHD, and these deficiencies clearly warrant scrutiny in future investigations to determine whether they are pathognomic of ADHD.

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*Studies preceded by an asterisk were included in the meta-analysis

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Footnotes

¹ Task duration could not be estimated directly owing to insufficient details reported by the studies.

² Relatively few studies included children with comorbid disorders or other ADHD subytypes, and Lijffijt et al. (2005) reported that co-morbidity with ODD/CDD was not a significant moderator for any of the three BI metrics.

³A listing of excluded studies is available from the author [Aaron, Dowson, Sahakian, & Robbins, 2003; Bedard et al., 2003; Bekker et al., 2004; Epstein, Johnson, Varia, & Conners, 2001; Geurts, H. M., Verte, S., Oosterlaan, J., Roeyers, H., & Sergeant, J. A., 2004; Jennings, Van der Molen, Pelham, Debski, & Hoza, 1997; Murphy, 2002; Oosterlaan & Sergeant, 1998; Ossmann, & Mulligan, 2003; Rubia, Taylor, Smith, Oksannen, Overmeyer, & Newman, 2001; Rucklidge, & Tannock, R, 2002; Schachar & Tannock, 1995; Schachar, Tannock, Marriot, & Logan, 1995; Slusarek, Velling, Bunk, & Eggers, 2001; Willcutt et al. 2001; Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2004; Wodushek, & Neumann, 2003]. ⁴ Study details available from author. [One study included a second experiment that examined stop-signal performance in adults (Schachar & Logan, 1990). Stop-signal performance for both medicated and unmedicated children were reported in one study (Aman, Roberts, & Pennington, 1998), and only the unmedicated participant results were included in the review. One study included a second condition with unconventional stop-signal delays (Rubia, et al., 1998). Another study reported three additional conditions that examined the effects of reinforcement and repetition (Konrad, Gauggel, Manz, & Scholl, 2000). Finally, emotional regulation was

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examined by means of a separate experimental condition in one study (Walcott & Landau, 2004)].

⁵ Excluded studies available from author. [Aman et al., 1998; Daugherty et al., 1993;

Konrad et al., 2000; Konrad et al., 2000b; Manassis, Tannock, & Barbosa, 2000;

Overtoom et al., 2002; Pliszka et al., 1997, Exp. 1; Pliszka et al., 1997, Exp. 2;

Schachar et al., 2004; Solanto et al., 2001; and Walcott & Landau, 2004]

⁶ The $Q_{\rm B}$ and $Q_{\rm W}$ analog to ANOVA technique reported in many meta-analytic reviews was not used for primary analyses because it inflates Type I error when used with moderator variables – see Lipsey & Wilson, 2001, for details.

Figure Caption

Figure 1. Relationship of mean reaction time (MRT), stop-signal delay (SSD), and stop-signal reaction time (SSRT).



Citation	N	Mean Ages (SD)	Diagnostic Criteria	IQ	Total Task Time	Trials per Block	Blks	Total Trials	Go- Stim.	Stop- Stim.	SSD	TD	BC	Results
Schachar & Logan (1990) Ex. 2	13 ADHD 10 NC	9.3 (1.8) 10 (1.2)	Semistructured interview + Rating Scales	Yes	35-45	48	9	432	РН	РН	FX	25	No	MRT: ADHD = NC SDRT: ADHD > NC SSRT: ADHD > NC Errors: ADHD > NC
Daugherty et al. (1993)	9 ADD 15 NC	11.2 (0.9) 11.2 (1.1)	Rating Scales	No	NR	48	9	432	РН	РН	FX	25	No	MRT: ADD > NC SDRT: ADD > NC SSRT: ADD < NC Errors: ADD < NC
Oosterlaan & Sergeant (1996)	15 ADHD 17 NC	9.3 (2.1) 8.7 (1.9	Rating Scales	No	NR	64	4	256	VS	РН	FX	25	No	MRT: ADHD > NC * SDRT: ADHD > NC *** SSRT: ADHD > NC * Errors: ADHD > NC
Pliszka et al. (1997) Ex 1	14 ADHD 13 NC	7.2 (1.2) 7.5 (0.9)	Structured interview + Rating Scales	No	NR	48	9	432	VS	РН	FX	25	No	MRT: ADHD > NC ** SDRT: ADHD > NC * SSRT: ADHD > NC ** Errors: ADHD > NC ***
Pliszka et al. (1997) Ex 2	25 ADHD 31 NC	6 - 12 6 - 12	Standard Interview + Rating Scales	No	NR	48	9	432	VS	РН	FX	25	No	MRT: NR SDRT: NR SSRT: ADHD > NC ** Errors: NR
Aman et al. (1998)	22 ADHD 22 NC	12.1 (1.2) 12.1 (1.2)	Structured Interview + Rating Scales	Yes	10	48	4	192	РН	РН	FX	33	No	MRT: NR SDRT: NR SSRT: NR Errors: NR
Brandeis et al. (1998)	11 ADHD 11 NC	10.9 (NR) 11.2 (NR)	Rating Scales	Yes	NR	40	8	320	VS	VS	FX	50	No	MRT: ADHD > NC SDRT: NR SSRT: NR Errors: NR

Table 1. Stop-Signal Studies of Between-Group Comparisons of ADHD and Normal Control Children

Rubia et al. (1998)	11 ADHD 11 NC	9.0 9.4	Rating Scales	Yes	15	60	4	240	VS	VS	FX	33	No	MRT: ADHD > NC SDRT: ADHD > NC ** SSRT: ADHD > NC * Errors: ADHD > NC **
Nigg (1999)	25 ADHD 25 NC	9.6 (1.8) 10.1 (1.3)	Structured Interview + Rating Scales	Yes	20	64	4	256	РН	РН	TK	25	No	MRT: ADHD > NC *** SDRT: ADHD > NC ** SSRT: ADHD > NC *** Errors: ADHD < NC *
Konrad et al. (2000)	10 ADHD 10 NC	10.7 (1.3) 10.2 (1.1)	Semistructured Interview + Rating Scales	Yes	NR	40	8	320	VS	РН	ТК	25	No	MRT: ADHD > NC SDRT: NR SSRT: ADHD > NC*** Errors: NR
Konrad et al. (2000b)	31 ADHD 26 NC	10.5 (1.6) 10.2 (1.2)	Semi-structured interview + Rating Scales	Yes	NR	40	8	320	VS	РН	ТК	25	No	MRT: ADHD > NC SDRT: ADHD < NC SSRT: ADHD > NC *** Errors: NR
Manassis et al. (2000)	15 ADHD 16 NC	8-12 8-12	Structured interview + Rating Scales	No	NR	NR	NR	NR	РН	РН	TK	25	No	MRT: ADHD > NC SDRT: ADHD > NC * SSRT: ADHD > NC Errors: NR
Pliszka et al. (2000)	10 ADHD 10 NC	11.0 (1.2) 11.3 (0.9	Structured interview + Rating Scales	No	30	192	10	1920	РН	РН	FX	25	No	MRT: ADHD < NC SDRT: ADHD > NC ** SSRT: ADHD > NC Errors: ADHD > NC **
Purvis & Tannock (2000)	17 ADHD 17 NC	9.1 (1.1) 9.5 (1.3)	Semistructured Interview + Rating Scales	Yes	NR	NR	NR	256	РН	РН	TK	25	No	MRT: ADHD > NC * SDRT: ADHD > NC *** SSRT: ADHD > NC Errors: ADHD > NC
Schachar et al. (2000)	72 ADHD 33 NC	9.0 (1.4) 9.3 (1.5)	Semistructured interview + Rating Scales	Yes	NR	32	8	256	РН	PH	TK	25	No	MRT: ADHD > NC * SDRT: ADHD > NC SSRT: ADHD > NC ** Errors: NR

Kuntsi et al. (2001)	49 Hyper. 118 NC	8.8 (1.2) 9.0 (1.4)	Rating Scales	Yes	NR	64	4	256	VS	PH	FX	25	No	MRT: Hyp > NC ** SDRT: Hyp > NC *** SSRT: Hyp > NC Errors: Hyp > NC *
Scheres et al. (2001)	24 ADHD 41 NC	10.1 (1.5) 10.2 (1.6)	Rating Scales	Yes	NR	32	6	192	VS	РН	ТК	25	No	MRT: ADHD > NC SDRT: ADHD > NC SSRT: ADHD > NC Errors: ADHD > NC
Solanto et al. (2001)	77 ADHD 29 NC	8.5 (0.9) 8.7 (0.9)	Structured interview + Rating Scales	Yes	30	48	4	192	PH	РН	FX	33	No	MRT: ADHD < NC SDRT: NR SSRT: ADHD > NC *** Errors: ADHD > NC
Nigg et al. (2002)	46 ADHD 41 NC	9.6 (1.5) 10.1 (1.0)	Structured Interview + Rating Scales	Yes	20	64	4	256	РН	РН	ТК	25	No	MRT: ADHD > NC SDRT: NR SSRT: ADHD > NC Errors: NR
Overtoom et al. (2002)	16 ADHD 16 NC	10.4 (1.4) 10.3 (1.5)	Structured interview + Rating Scales	Yes	48	117	8	936	VS	РН	FX	40	Yes	MRT: ADHD > NC * SDRT: NR SSRT: (Overall) ADHD > NC ** (SOA 125) ADHD > NC * (SOA 200) ADHD > NC * Errors: ADHD > NC **
Stevens et al. (2002)	76 ADHD 76 NC	10.0 (1.6) 9.9 (1.6)	Rating Scales	No	7	40	4	160	PH	РН	ТК	25	No	MRT: ADHD < NC SDRT: ADHD > NC** SSRT: ADHD > NC* Errors: NR
Dimoska et al. (2003)	13 ADHD 13 NC	9.8 (1.5) 9.8 (1.1)	Rating Scales	Yes	NR	120	2	240	РН	РН	ТК	33	No	MRT: ADHD > NC * SDRT: ADHD > NC ** SSRT: ADHD > NC * Errors: ADHD > NC **

McInerney & Kerns (2003)	30 ADHD 30 NC	10 10	Structured interview + Rating Scales	Yes	NR	NR	NR	128	РН	РН	ΤK	25	No	MRT: ADHD = NC SDRT: ADHD > NC *** SSRT: ADHD > NC ** Errors: ADHD > NC**
Walcott & Landau (2004)	26 ADHD 23 NC	6-11 6-11	Rating Scales	No	NR	64	4	256	РН	РН	TK	NR	No	MRT: NR SDRT: NR SSRT: ADHD > NC *** Errors: NR
Schachar et al. (2004)	151 ADHD 41 NC	8.7 (1.7) 9.0 (1.8)	Semistructured interview + Rating Scales	Yes	NR	24	4	96	РН	РН	ТК	25	No	MRT: ADHD > NC * SDRT: NR SSRT: ADHD > NC ** Errors: ADHD < NC

	MRT					SDR	T		SSRT					
	Q	df	р		Q	df	р		Q	df	р			
Regression	180.8	6	< .001		0.03	6	n.s.		173.9	6	< .001			
Residual	117.3	12	< .001		0.01	4	n.s.		70.16	10	< .001			
R^2	0.61				0.79				0.71					
Adjusted R^2	0.41				0.49				0.54					
Constant	-0.14				0.53				-0.09					
Moderator Variables	В	SEB	Z	р	В	SEB	z	р	В	SEB	Z	р		
Age	-0.14	0.05	-2.78	0.003	0.2	3.14	0.06	n.s.	0.03	0.08	0.31	n.s.		
Diagnostic Evaluation	-0.16	0.07	-2.4	0.008	-0.22	6.56	-0.0	n.s.	0.25	0.08	2.94	0.002		
Go-Stimulus Modality	0.3	0.07	4.3	< .001	0.23	11.24	0.02	n.s.	0.09	0.11	0.84	n.s.		
Stop-Signal Delay	0.46	0.06	7.78	< .001	0.24	10.54	0.02	n.s.	0.23	0.08	3.1	<.001		
Target Density	-0.01	0.07	-0.21	n.s.	0.19	4.28	0.05	n.s.	0.44	0.08	5.49	< .001		
Total Experimental Trials	0.08	0.03	2.88	0.002	0.17	8.4	0.02	n.s.	0.17	0.04	4.84	< .001		

Table 2. Weighted Regression Model and Moderating Variables for MRT, SDRT, and SSRT

Note. B = regression coefficients; df = degrees of freedom; MRT = Mean Reaction Time; SDRT = Mean Reaction Time Variability; SEB = standard error of the regression coefficients; SSRT = Stop-Signal Reaction Time; Q = chi-square value; R^2 = variance accounted for by the model; and z = z-value.

APPENDIX B: IRB APPROVAL DOCUMENT

Fax 407

BW:jm



Office of Research & Commercialization

April 24, 2006

Mark Rapport, Ph.D. University of Central Florida Department of Psychology PH 409J Orlando, FL 32816-1390

Dear Dr. Rapport:

With reference to your protocol #06-3452 entitled, "Attention Deficit/Hyperactivity Disorder (ADHD): The Role of Working Memory as a Core Deficit," I am enclosing for your records the approved, expedited document of the UCF IRB Protocol Submission Form you had submitted to our office. This study was approved on 4/20/06. The expiration date will be 4/19/07. Should there be a need to extend this study, a Continuing Review form must be submitted to the IRB Office for review by the Chairman or full IRB at least one month prior to the expiration date. This is the responsibility of the investigator. Please notify the IRB office when you have completed this research study.

Please be advised that this approval is given for one year. Should there be any addendums or administrative changes to the already approved protocol, they must also be submitted to the Board through use of the Addendum/Modification Request form. Changes should not be initiated until written IRB approval is received. Adverse events and unanticipated problems should be reported to the IRB as they occur.

Should you have any questions, please do not hesitate to call me at 407-823-2901.

Please accept our best wishes for the success of your endeavors.

Cordially,

Barbara Word

Barbara Ward, CIM UCF IRB Coordinator (FWA00000351 Exp. 5/13/07, IRB00001138)

Copies: IRB File

BW:jm

12201 Research Parkway • Suite 501 • Orlando, FL 32826-3246 • 407-823-3778 • Fax 407-823-3299 .nt Equal Opportunity and Atlimative Action Institution

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