Nationwide Children's Hospital

Attention-Deficit/Hyperactivity Disorder and Behavioral Inhibition: Visuospatial Working Memory Mediates Stop-signal Task Performance

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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).

The Stop-Signal Task (SST) - a modified go, no-go task - is the premiere measure used in clinic- and laboratory-based research to investigate BI in children. In a prototypical stop-signal paradigm, children are pre-trained to respond differentially to two go-stimuli (e.g., the letters X and O) using left and right response buttons, and withhold their response to the go-stimulus whenever it is followed by a stop-signal, typically an auditory tone presented within milliseconds following the go-stimuli (see Figure 1). 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: Stop-signal Reaction Time) 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 2.

A recent meta-analytic review (Alderson, Rapport, & Kofler, 2007) of the stop-signal task found that the primary measure of BI (reaction time to the stop-signal) reflects a more generalized deficit in attention/cognitive processing rather than behavioral inhibition. A second study (Alderson, Rapport, Sarver, & Kofler, 2008) corroborated the meta-analytic findings and suggested that performance on the stop-signal task is downstream of higher order cognitive processes, such as working memory. This finding contrasts extant BI models of inhibition (Barkley, 2006; Sonuga-Barke, 2002) and provide support to nascent models that suggests working memory, rather than BI, is a central core component of the disorder (Rapport, Chung, Shore, & Isaacs, 2001; Rapport, Kofler, Alderson, & Raiker, 2007).

Working memory research in children with ADHD has gained considerable momentum within the last few years with contradictory findings between meta-analytic reviews and more recent empirical studies concerning the hypothesized role of working memory deficits in ADHD. A recent study (Rapport, Alderson, Kofler, Sarver, Bolden, & Sims, in press) addressed methodological problems that may have contributed to discrepancies in earlier studies, and examined overall and specific phonological and visuospatial memory subsystem components based on Alan Baddeley's model of working memory. Results indicated that children with ADHD exhibited both phonological and visuospatial working memory deficits in each of the respective buffer/rehearsal loops, as well as the domain-general central executive.

The current study attempts to account for between-group SSRT variability, given recent meta-analytic and experimental findings that suggest SSRT does not reflect BI. Specifically, this study examines the role of working memory on BI in children with ADHD and typically developing children (TD). A conventional stop-signal task was administered as a measure of BI, while overall and specific phonological and visuospatial memory subsystem components, based on Baddeley's (2003) model, were assessed across 4 memory load conditions in 12 children with ADHD and 11 typically developing children (TD).

Figure 1. Stop-signal task.

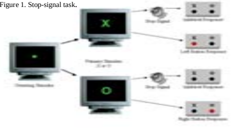


Figure 2. Graphical representation of stop-signal dependent measures

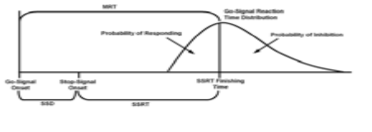
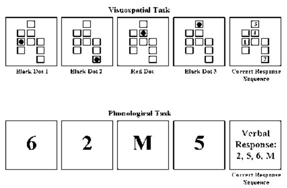


Figure 3. Visual Schematic of VS and PH Working Memory Tasks



METHODS

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 test-retest 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.

Table 1. Between-group effects with and without WM component covariates

	F	*p*
Between Group (ADHD, TD) Main Effects on BI Metrics		
SSRT	15.64	0.00
SSD	2.47	0.13
Phonological (PH) System covaried from SSRT		
PH Composite Score Analysis		
Between-group main effect	2.18	0.16
Covariate (PH composite score)	3.12	0.09
PH Buffer/Loop Analysis		
Between-group main effect	0.01	0.94
Covariate (PH buffer/loop)	10.57	0.00
Visuospatial (VS) System covaried from SSRT		
VS Composite Score Analysis		
Between-group main effect	0.25	0.62
Covariate (VS composite score)	4.63	0.04
VS Buffer/loop Analysis		
Between-group main effect	8.76	0.01
Covariate (VS composite score)	0.57	0.46
Central Executive (CE) covaried from SSRT		
Between-group main effect	0.12	0.73
Covariate (CE)	3.71	0.07

METHODS

Instruments

The stop-signal, VS, and PH tasks were 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. Children were seated approximately 0.66 meters from the computer monitor on all experimental tasks.

*Stop-Signal Task***.** The stop-signal task and administration instructions utilize identical task parameters of those described in Schachar et al. (2000). Go-stimuli are displayed for 1000 ms as uppercase letters X and O positioned in the center of a computer screen. X's and O's appear with equal frequency throughout the experimental blocks. Each go-stimulus is preceded by a dot (i.e., fixation point) displayed in the center of the screen for 500 ms. The fixation point serves as an indicator that a go-stimulus is about to appear. A 1000 Hz auditory tone (i.e., stop-stimulus), delivered through sound-deadening headphones, is generated by the computer and presented randomly on 25% of the experimental trials. Stop-signal delays (SSD) are initially set at 250 ms, but dynamically adjusted ± 50 ms contingent on a participant's performance on the previous trial. Successfully inhibited stop-trials are followed by a 50 ms increase in SSD, and unsuccessfully inhibited stop-trials are followed by a 50 ms decrease in SSD. The algorithm is designed to approximate successful inhibition on 50% of the stop-trials. A two-button response box is used wherein the left button is used to respond to the letter X, and the right button is used to respond to the letter O. All participants completed two practice blocks and five consecutive experimental blocks of 32 trials (i.e., 24 go-trials, 8 stop-trials). The stop-signal task is presented graphically in Figure 2.

Visuospatial (VS) working memory task. Children were shown nine identical 3.2 cm squares arranged in three vertical Columns on a computer monitor. The Columns were offset from a standard 3x3 grid to minimize the likelihood of phonological coding of the stimuli (e.g., by equating the squares to numbers on a telephone pad). A series of 2.5 cm diameter dots (3, 4, 5, or 6) were presented sequentially in one of the nine squares during each trial, such that no two dots appeared in the same square on a given trial. All but one dot presented within the squares was black – the exception being a red dot that was counterbalanced across trials to appear an equal number of times in each of the nine squares, but never presented as the first or last stimulus in the sequence to minimize potential primacy and recency effects. Each dot was displayed for 800 ms followed by a 200 ms interstimulus interval. A green light appeared at the conclusion of each 3, 4, 5, and 6 stimulus sequence. Children were instructed to indicate the serial position of black dots in the order presented by pressing the corresponding squares on a computer keyboard (see Figure 3), and to indicate the position of the red dot last. The last response was followed by an intertrial interval of 1000 ms and an auditory chime that signaled the onset of a new trial.

Phonological (PH) working memory task. The PH working memory task is similar to the Letter-Number Sequencing subtest on the WISC-IV (Wechsler, 2003), and assesses phonological working memory based on Baddeley's (2003) model. Children were presented a series of jumbled numbers and a capital letter on a computer monitor. Each number and letter (4 cm height) appeared on the screen for 800 ms, followed by a 200 ms interstimulus interval. The letter never appeared in the first or last position of the sequence to minimize potential primacy and recency effects, and was counterbalanced across trials to appear an equal number of times in the other serial positions (i.e., position 2, 3, 4, or 5). Children were instructed to recall the numbers in order from smallest to largest, and to say the letter last (e.g., 4 H 6 2 is correctly recalled as 2 4 6 H). Two trained research assistants, shielded from the participant's view, independently recorded oral responses (interrater reliability = 95.6% agreement). The PH task was presented in four counterbalanced set size blocks (i.e., 3, 4, 5, or 6 stimuli), with each set size consisting of 24 trials. The VS and PH tasks were each presented in four counterbalanced set size blocks (i.e., 3, 4, 5, or 6 stimuli), with each set size consisting of 24 trials. Children were administered a five trial practice block consisting of 3 stimuli immediately prior to the set size 3 experimental conditions until achieving a minimum of 80% correct. A practice block of four stimuli was used for experimental conditions with set sizes of 4, 5, and 6 stimuli. Children who failed to obtain a minimum of 80% correct across the five practice trials of 4 stimuli were re-administered the 3 stimuli practice trials, followed by another administration of the 4 stimuli practice trials, until achieving the 80% correct criteria.

VS and PH dependent variables. The number of stimuli correct for each of the four stimulus set size blocks (3, 4, 5, 6) served as the primary dependent variable for assessing children's overall VS and PH working memory performance (i.e., combined functioning of the central executive and buffer/rehearsal loop). Composite VS and PH scores were computed by averaging each child's score across set sizes to address questions concerning overall working memory differences among groups. The VS buffer/loop was estimated based on the preceding statistical/methodological rationale using the following procedures. PH composite scores were covaried from VS composite scores at each set size to remove common variance associated with the domain-general central executive. These four VS buffer/loop scores were then averaged to provide an overall estimate of the contribution of the VS buffer/loop to performance on the VS task independent of shared CE influences (see Figure 1 inset). Similarly, VS composite scores were covaried from PH composite scores at each set size to remove common variance associated with the domain-general central executive. These four PH buffer/loop scores were then averaged to provide an overall estimate of the contribution of the PH buffer/loop to performance on the PH task independent of shared CE influences. Finally, Two unstandardized predicted scores were computed by regressing VS scores onto PH scores at each set size, and PH scores onto VS scores at each set size, then averaging these scores to provide an estimate of CE functioning (i.e., shared variance between VS and PH scores) based on the preceding statistical/methodological rationale.

RESULTS

Demographic Data. 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 without these variables as covariates. Means, SDs, and between-group contrasts are presented in Table 2.

Behavioral Inhibition (BI). SSRT and stop-signal delay 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).

Working Memory Mediators of SSRT

Working Memory Mediator Effect on SSRT. Two ANCOVAs were conducted to examine the role of overall visuospatial and phonological working memory on SSRT performance. SSRT was not significantly different between the two groups when the overall visuospatial/central executive working memory system was entered as a covariate, $F(1, 21) = .250$, p = ..62. Phonological working memory, however, was not a significant covariate of SSRT ($p > .05$). Additionally, examination of unique phonological buffer/loop, visuospatial buffer/loop, and central executive WM components indicated that they were not significant covariates of SSRT (all $p > .05$).

DISCUSSION

The purpose of this study was to examine potential mediators, particularly working memory, of SSRT performance. Although children with ADHD were found to have significantly longer SSRTs relative to children in the typically developing group, the non-significant SSD suggests that between-group differences are attributable to MRT differences, rather than deficits of behavioral inhibition. These findings are consistent with previous examinations of SSD (Alderson et al., 2007; Alderson et al., 2008) that suggested SSRT performance deficits do not reflect behavioral inhibition, but rather a more general attention/cognitive processing deficit.

Findings from this study demonstrated that SSRT between-group differences were not significant after accounting for visuospatial working memory. Additionally, the findings suggest that SSRT between-group differences result from an interaction between central executive and VS buffer/loop processing, rather than the individual components alone. Collectively, these findings are in direct contrast of extent BI models of ADHD that suggest performance on the stop-signal task is upstream from higher order executive functions such as self-regulation, internalization of speech, and working memory.