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INTRA-INDIVIDUAL VARIABILITY AMONG CHILDREN WITH ADHD ON A WORKING MEMORY TASK: AN EX-GAUSSIAN APPROACH

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Abstract

Intra-individual variability on a computer-based working memory task was examined among 25 children/adolescents with ADHD and 24 typically developing peers. Participants completed the Visual Serial Addition Task (VSAT) and reaction time data were fit to an ex-Gaussian distribution. ADHD participants demonstrated significantly more variable performance than controls, and effects of working memory load were observed. Event rate, however, had no influence on group differences in performance. Follow-up correlations revealed associations between VSAT performance and ADHD symptomatology. This study supports intra-individual variability as a hallmark feature of ADHD beyond the domain of response inhibition and reinforces the need to consider variability in ADHD more broadly.

Keywords

ADHD; Working memory; Reaction time; Variability

Attention deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed disorders in childhood, occurring in 3%–5% of school-age children (American Psychiatric Association, 1994) and accounting for almost half of pediatric clinical referrals (Barkley, 2006). While there is ongoing debate regarding causal models of ADHD (e.g., Barkley, 1997b; Coghill, Nigg, Rothenberger, Sonuga-Barke, & Tannock, 2005; Luman, Oosterlaan, & Sergeant, 2005; Nigg, 2005; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), researchers are increasingly citing intra-individual (i.e., *within*-subject) variability (IIV) in

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performance as a hallmark feature of the disorder (e.g., Band & Scheres, 2005; Castellanos et al., 2005; Castellanos & Tannock, 2002; Douglas, 1999, 2005; Lijffijt, Kenemans, Verbaten, & van Engeland, 2005). Defined as short-term changes in behavior that signal moment-to-moment fluctuations in task performance, IIV occurs over a period of seconds and is distinguished from systematic changes related to practice, learning, or variations in the clinical condition (Stuss, Murphy, Binns, & Alexander, 2003; Williams, Hultsch, Strauss, Hunter, & Tannock, 2005).

There is reason to believe that IIV may be a worthwhile candidate in the search for endophenotypes for ADHD (Castellanos et al., 2005; Castellanos & Tannock, 2002; Doyle et al., 2005; Kuntsi, Andreou, Ma, Borger, & van der Meere, 2005). As a quantifiable intermediate construct (between genes and behavior) that helps determine the risk of manifesting a disorder, an endophenotype must show evidence of heritability. Several studies have found IIV to be heritable (Andreou et al., 2007; Kuntsi & Stevenson, 2001; Nigg, Blaskey, Stawicki, & Sachek, 2004). In fact, in a study using a behavior genetic approach to examine a variety of psychological battery measures, IIV provided the highest heritability estimate and was the only task variable found to be statistically significant (Kuntsi & Stevenson). Gottesman and Gould (2003) further suggest that an endophenotype be found in unaffected family members of diagnosed individuals at a higher rate than in the general population. To this end, mothers of ADHD children have been shown to demonstrate significantly greater IIV compared to mothers of normal control children, even after covarying mothers' IQ and ADHD status (Nigg et al., 2004). Similarly, unaffected co-twins of ADHD individuals showed increased IIV compared to controls, even when subclinical ADHD symptoms were controlled (Bidwell, Willcutt, DeFries, & Pennington, 2007).

Castellanos and Tannock (2002) advocate that particular attention be paid to endophenotypes based in neuroscience. It is therefore noteworthy that functional brain-imaging studies lend support for the relevance of IIV in attentional processes and behavioral control (Bellgrove, Hester, & Garavan, 2004; Rubia, Smith, Brammer, & Taylor, 2007; Simmonds et al., 2007; Stuss et al., 2003). Rubia et al. (2007) found that decreased IIV in ADHD participants during an oddball task was associated with increased activation in the basal ganglia and thalamus, whereas lower IIV in controls was associated with increased temporal lobe activation. Based on imaging data acquired during a resting-state condition, Castellanos et al. (2008) speculate that the neural basis of IIV in ADHD may be due to dysfunctional synchronization between regions implicated in the "default network," including decreases in connectivity between the anterior cingulate, ventromedial prefrontal cortex, and posterior cingulate/precuneus regions. Nevertheless, the relationship between IIV and neurocognitive deficits in ADHD remains ambiguous

Increased IIV in ADHD has been demonstrated on a number of paradigms including stop-signal (Alderson, Rapport, & Kofler, 2007; Klein, Wendling, Huettner, Ruder, & Peper, 2006; Lijffijt et al., 2005), sustained attention to response (Bellgrove, Hawi, Kirley, Gill, & Robertson, 2005; Johnson, Robertson, et al., 2007; Shallice et al., 2002), choice reaction time (Geurts et al., 2007; Leth-Steensen, Elbaz, & Douglas, 2000), and Go/No-Go or continuous performance (CPT; Epstein et al., 2006; Heiser et al., 2004; Hervey et al., 2006; Klein et al., 2006; Kuntsi et al., 2005; Teicher, Ito, Glod, & Barber, 1996). However, only three known studies have examined IIV on *working memory tasks* in ADHD (Karatekin, 2004; Klein et al., 2006; Piek et al., 2004). Karatekin identified more variable reaction times (RTs) among ADHD participants on a working memory (WM) task and demonstrated that increased IIV is not attributable simply to greater fatigue in ADHD, finding no difference in performance between a baseline condition administered both first and last in the sequence of tasks. Klein and colleagues (2006) examined IIV using a number of paradigms; however, the

largest effect size for IIV was observed on the WM n -back test. Although results for a 2-back condition could not be reported because participants had difficulty understanding that task, the authors found a significantly greater increase in IIV from the 0-back to 1-back tests among ADHD participants compared to controls, indicating that WM load can substantially impact IIV among children with ADHD. Understanding the possible interaction between attentional lapses and WM load in ADHD could help isolate critical components involved in executive functioning deficits associated with ADHD and suggest possible neuronal substrates for future exploration. Taken together, these results suggest that IIV may be an important marker in WM processing in ADHD; however, none of these studies utilized an active manipulation component considered to be a key element in WM (Baddeley, 2003), nor did they apply a putatively more sensitive RT analytical approach described as follows.

The aforementioned ADHD WM studies and indeed most IIV studies in ADHD report the standard deviation of the reaction time (SDRT) across trials, a summary statistic for data assumed to fall on a normal Gaussian distribution. However, RT distributions among ADHD participants are usually — if not always — positively skewed (Douglas, 1999, 2005; Epstein et al., 2006; Leth-Steensen et al., 2000). The positive skew in ADHD participants is attributable to some extremely slow responses along with a majority of RT responses in the normal range. Thus, ADHD performance is better characterized by fitting RT data to an ex-Gaussian distributional model that represents RT as the sum of a normally distributed random variable and an exponentially distributed random variable to account for the positive skew (Leth-Steensen et al.; Luce, 1986; Ratcliff, 1979). Three parameters describe the ex-Gaussian distribution: μ (μ) and σ (σ), respectively, describe the mean and standard deviation of the normal component, and τ (τ) describes the mean and standard deviation of the exponential component. Conceptually, μ reflects the modal performance, whereas σ describes variability in the normal component of the curve, and τ reflects the skew attributable to extremely slow responses at the tail of the distribution.

Only four known studies have applied ex-Gaussian modeling to examine IIV in ADHD (Epstein et al., 2006; Geurts et al., 2007; Hervey et al., 2006; Leth-Steensen et al., 2000). Three of these showed τ to be a sensitive measure of group differences (Epstein et al., 2006; Hervey et al.; Leth-Steensen et al.), one of which demonstrated that the largest effect of stimulant medication on CPT performance was to reduce the positive skew captured by τ (Epstein et al.). Children with ADHD also appear to show increased variability in the normal part of the curve as indicated by σ (Epstein et al.; Hervey et al.). Although the Geurts et al. study failed to show significant differences between ADHD participants and typically developing controls on τ or σ , the authors suggest that their two-choice RT task lasting 3 minutes may have been too short to allow differences on IIV to emerge, and the authors also propose that tasks placing greater demands on WM might be associated with greater IIV. Finally, results based on mean RT suggest that ADHD children respond more slowly than controls, whereas analyses using the corresponding ex-Gaussian parameter (μ) have shown that participants with ADHD do *not* respond more slowly (Geurts et al.; Leth-Steensen et al.). When a normal distribution is assumed, the more frequent excessively slow responses made by ADHD participants pull the estimate of mean RT higher (i.e., mean RT appears slower). When an ex-Gaussian model is used, however, the mean RT in the normally distributed portion of the curve (μ) can be examined separately from the positive skew (τ). Thus, using an ex-Gaussian approach, ADHD participants have been found to demonstrate *faster* overall CPT responding (Hervey et al.) with stimulant medication improving performance by *slowing* overall RT (Epstein et al.). These studies underscore ex-Gaussian modeling as a valuable method for elucidating the differential processing of children with ADHD.

Although no known studies of WM in ADHD have used ex-Gaussian modeling, Schmiedek, Oberauer, Wilhelm, Süß, and Wittmann (2007) used this technique to examine WM performance among healthy university students. They found tau to be the strongest predictor of WM capacity in that population. Based on theories of controlled attention and goal maintenance, their results converge with Leth-Steensen et al.'s (2000) assertion that occasional lapses of attention and/or lapses in WM produce slow RTs on a number of trials, thus contributing to the distributional tail captured by tau.

Both traditional RT and ex-Gaussian approaches suggest that IIV among children with ADHD is sensitive to changes in stimulus presentation rate (Andreou et al., 2007; Kuntsi et al., 2005; Scheres, Oosterlaan, & Sergeant, 2001). In two studies using ex-Gaussian modeling and employing interstimulus intervals (ISIs) of 1, 2, and 4 seconds, the longer ISIs exerted a much more profound influence on CPT performance among ADHD children than controls by producing significantly slower and more variable responding (Epstein et al., 2006; Hervey et al., 2006). Furthermore, stimulant medication effects on reducing IIV were most pronounced at longer ISIs (Epstein et al.). These findings provide support for the notion that faster event rates help to optimize the activation or arousal state of children with ADHD.

The present study compares the performance of children/adolescents with ADHD and a group of typically developing control participants on a WM task employing an active manipulation component. The ISI and level of task difficulty were varied in order to examine the effects of event rate and WM load. In an effort to better capture IIV, RT data were fit to an ex-Gaussian distribution. It was hypothesized that ADHD participants would demonstrate higher levels of inconsistent responding than controls, as evidenced by increases in omission errors, sigma, and tau. These effects were expected to become more pronounced at slower event rates (i.e., longer ISIs) and at higher WM loads. Because the ADHD group was expected to show more *variable* responding rather than generalized performance deficits, group differences were not anticipated on mu or on response accuracy (after accounting for omission errors).

METHODS

Participants

Participants included 25 children/adolescents ages 7 to 14 years with ADHD–Combined Type (17 male, 8 female) and 24 typically developing controls ages 7 to 14 years (11 male, 13 female). ADHD participants were recruited through newspaper advertisements and flyers, support groups, the Children and Adults with Attention Deficit/Hyperactivity Disorder (CHADD) website, and a university-based ADHD clinic. Control participants were recruited through newspaper advertisements, flyers, and word-of-mouth.

Prior to enrollment in the study, demographic and initial eligibility information was collected using a telephone-screening interview. After enrollment, Hollingshead's (1975) method was used to determine socioeconomic status (SES) based on parental education and occupation. Potential candidates for the ADHD and control groups underwent the same screening and diagnostic procedures, including rating scales, interviews, and psychological testing. Each child's parent (usually the mother) completed the Conners' Parent Rating Scale–Revised: Long Version (CPRS-R:L; Conners, 1997) regarding behavior problems over the past month. Parent and child versions of the computerized Diagnostic Interview for Children and Adolescents (DICA-IV; Reich, Welner, & Herjanic, 1997) provided initial diagnostic information. An experienced licensed psychologist or a Master's level or higher clinically trained research assistant conducted a follow-up interview with the parent to confirm diagnoses. The Wechsler Intelligence Scale for Children – Third Edition (WISC-III;

Wechsler, 1991) evaluated participants' intellectual abilities and the Woodcock-Johnson Tests of Achievement – Third Edition (WJ-III; Woodcock & Mather, 2001) was used to help assess learning disabilities. Evidence of a math/reading disorder was considered present if there was a 1.5 *SD* or greater difference between IQ and WJ-III scores.

A licensed psychologist reviewed all diagnostic information to determine participants' eligibility. Information from the CPRS-R:L, the parent's DICA-IV responses, and the clinical interview were used to determine whether each participant met *Diagnostic and Statistical Manual of Mental Disorders*, text revision (*DSM-IV-TR*; American Psychiatric Association, 2000) criteria for ADHD - Combined Type. Other psychiatric diagnoses were based on information from the parent and child versions of the DICA-IV and the clinical interview.

Children/adolescents with ADHD were excluded if they met any of the following criteria: (a) Full Scale IQ (FSIQ) score below 85; (b) evidence of a *DSM-IV-TR* math/ reading disorder; (c) history of head trauma, neurological disorder, or major medical problem; (d) meeting *DSM-IV-TR* criteria for Major Depression, Bipolar Disorder, Obsessive Compulsive Disorder, or a psychotic disorder; or (e) a first-degree relative with a diagnosis of Schizophrenia or Bipolar Disorder. Control participants passed these same exclusion criteria and were also ineligible if they had a first-degree relative diagnosed with ADHD. All participants in the control group earned a *T*-score less than 65 (1.5 *SD* above the mean) on the Restlessness-Impulsivity, Cognitive Problems/Inattention, Hyperactivity, and ADHD Index subscales of the CPRS-R:L.

Participants' demographic and clinical characteristics are shown in Table 1. No group differences were found on gender, ethnicity, age, or parents' SES (Hollingshead, 1975). The FSIQ of participants in the ADHD group differed significantly from those in the control group, $t(1,47) = 2.38, p = .02$. This disparity is consistent with results of a meta-analysis examining FSIQs among ADHD participants and controls (Frazier, Demaree, & Youngstrom, 2004).

Measures

Working Memory task—Each participant completed the Visual Serial Addition Task (VSAT), a computer-based WM task based on the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977). The PASAT presents a series of single digits auditorily and participants respond by naming the sum of the two most recent numbers. The PASAT is frequently used as a measure of attentional processing in normal development and across clinical populations (see Tombaugh, 2006, for review), including adults and adolescents with ADHD (Jenkins et al., 1998; Katz, Wood, Goldstein, Achenbach, & Geckle, 1998; MacLeod & Prior, 1996; Schweitzer et al., 2004). Performance of ADHD children on the Children's PASAT (CHIPASAT; Dyche & Johnson, 1991) has been shown to be responsive to stimulant medication (Tannock, Ickowicz, & Schachar, 1995). We developed the VSAT to be an fMRI-compatible version of the PASAT for other studies, with participants performing serial addition of *visually* presented digits shown on a PC desktop computer running E-Prime version 1.1 software.

The VSAT demanded both maintenance and cognitive manipulation of stimuli over short periods of time (see Figure 1). Participants initially saw one digit at the top of the computer screen for 1.0 s, followed by a blank screen for a designated period of time (see description of ISIs below). A second digit then appeared at the top of the screen concurrently with a third digit in parentheses at the bottom, displayed simultaneously for 1.0 s. Participants decided whether the sum of the two consecutive numbers shown at the top of the screen equaled the number in parentheses at the bottom. Participants responded by pushing one of

two buttons held in each hand, using the right-hand button for “Yes/Correct” and the left-hand button for “No/Incorrect.” The task continued with a new digit at the top and a new potential sum in parentheses at the bottom for three blocks of 11 stimuli each, with a 1.0 s interval between each block, signified by a bold dash on the screen. A response was not possible until after the second stimulus in each block, resulting in a total of 30 response opportunities during the task (10 responses/block over three blocks).

Nine task conditions were created by manipulating the number set and the amount of time between the stimulus screens (i.e., the ISI). Similar to the CHIPASAT (Dyche & Johnson, 1991), different number sets were used to generate three WM loads: Low, Moderate, and High. Low Load stimuli ranged from 1–5 and could sum to no more than 6; at Moderate Load, stimuli ranged from 1–7 and summed to no more than 9; at High Load, the digits ranged from 1–9 with 18 as the maximum possible sum. Within each WM load, stimuli were presented at three different speeds (3.2, 2.8, and 2.4 s ISIs) consistent with the CHIPASAT (Dyche & Johnson), resulting in nine experimental sessions. Both WM load and ISI remained constant within each experimental session.

After performing a practice session containing Low Load stimuli presented at 3.2 s, participants completed the three Low Load experimental sessions. They next underwent a second practice session containing Moderate Load stimuli presented at 3.2 s, then completed the three Moderate Load experimental sessions followed by the three High Load experimental sessions. Within each WM load, sessions were presented from slowest to fastest ISI. Presentation order was not counterbalanced because pilot testing showed that children who began with higher load and/or faster trials experienced more frustration and were less likely to complete the testing.

As a result of a programming error, responses during the Moderate Load administration at 2.4 s were not properly captured. Because of the nature of repeated measures analysis, the present study considers data from six experimental sessions: Low, Moderate, and High Loads each administered at 3.2 s and 2.8 s ISIs.

VSAT performance measures included: (a) RT (in milliseconds); (b) omission errors; and (c) accuracy. Reaction time data were analyzed using an ex-Gaussian distribution (see Data Processing). Omission errors were calculated as the percentage of missed responses out of the 30 possible responses (i.e., number of missed responses divided by 30 then multiplied by 100). To avoid confounding accuracy with omission errors, accuracy was defined as the percentage of correct responses of all *attempted* responses within the session (i.e., excluding trials on which the participant did not respond). We thus examined participants' accuracy *when they responded*, apart from how often they failed to respond altogether.

Procedure

The protocol was approved by the University of Maryland School of Medicine's Institutional Review Board. Parents gave written consent for their child's participation. Participants age 13 and over gave written assent and children under 13 provided verbal assent.

Most participants completed testing in two visits (each lasting 2–3 hours) to reduce fatigue. Diagnostic/assessment procedures were completed during the first session and the VSAT was administered at the beginning of the second visit. The VSAT typically required approximately 45–60 minutes to complete (including instruction time and practice trials), with breaks provided as needed. With physician approval, ADHD participants receiving psychostimulant medication ($n = 16$) discontinued this treatment at least 24 hours before performing the VSAT. Parents received \$30 in grocery store certificates and a written report

of their child's IQ and achievement results. Participants received a \$50 bookstore gift certificate.

Data Processing

Prior to analyzing VSAT RT data, any single trial RT of less than 150 ms was considered an accidental key press and treated as a missing value (e.g., Williams et al., 2005). Across the 180 VSAT trials (six sessions each containing 30 response trials) for each participant, 0.93% of the data points were eliminated, with no significant group difference in the amount of data censored.

Quantile maximum probability estimator (QMPE) software v.2.18 (Heathcote, Brown, & Cousineau, 2004) was used to derive ex-Gaussian distributional fits to the RT data from the VSAT. The QMPE program uses an iterative search routine that fits the ex-Gaussian model using continuous maximum-likelihood estimation. The mu, sigma, and tau parameters were computed for each participant's RT during each of the six experimental sessions. Data from one experimental session for one ADHD subject were excluded because the ex-Gaussian parameters failed to converge.

Statistical Analyses

Data were analyzed using SAS for Windows version 9.1. Threshold for significance for all analyses was set at $\alpha < .05$ (two-tailed). VSAT dependent measures (omission errors, accuracy, mu, sigma, and tau) were analyzed using separate repeated measures General Linear Mixed Models, with Group (two levels: ADHD or control) as the between-subjects factor, and WM Load (three levels: Low, Moderate, and High) and ISI (two levels: 3.2 and 2.8 s) as within-subject factors. Significant effects of WM load were followed by polynomial contrasts to test the type of trend (linear or quadratic) and subsequent pairwise comparisons. Follow-up correlations were conducted within the ADHD group to examine associations between VSAT performance and ADHD symptomatology.

In light of difficulties with multicollinearity between FSIQ and a diagnosis of ADHD (Barkley, 2006), we report VSAT analyses without FSIQ entered as a covariate. However, all analyses were repeated with FSIQ as a covariate and the pattern of results remained unchanged.

RESULTS

Preliminary Analysis of Math Ability

Math ability was assessed because significant between-group differences had the potential to confound interpretation of VSAT performance. Although a group difference was found on the WJ-III Calculation subtest, $F(1, 47) = 4.42$, $p = .04$, results of ANCOVA controlling for FSIQ revealed that this disparity was accounted for by global differences in FSIQ, $F(1, 46) = 0.37$, $p = .54$.

Performance on the VSAT

Mu—There was no significant main effect of Group nor interactions with Group for mu (Table 2). Results indicated a main effect of ISI in the expected direction, $F(1, 47) = 5.08$, $p = .03$, with participants demonstrating quicker RTs when the task was faster.

Sigma—As hypothesized, there was a significant main effect of Group for sigma, $F(1, 47) = 6.16$, $p = .02$, with ADHD participants demonstrating greater RT variability than controls. There were no significant two- or three-way interactions of WM Load or ISI with Group for sigma.

Tau—There was a significant main effect of Group for tau, $F(1, 47) = 10.15, p = .003$, with ADHD participants showing more RT variability than controls. There were no significant interaction effects of WM Load or ISI with Group for tau.

Omission errors—Results indicated a significant main effect of Group for omission errors,¹ $F(1, 47) = 7.54, p = .008$, but this effect was qualified by a significant Group by WM Load interaction, $F(2, 85) = 7.25, p = .001$. In looking at the pattern of omission errors over levels of increasing WM load by group, polynomial contrasts indicated a linear increase in omission errors for ADHD participants, $F(1, 24) = 39.09, p = .0001$, and a quadratic trend for controls, $F(1, 23) = 11.22, p = .003$. Controls made *fewer* errors at the Moderate Load level than at the other loads (Figure 2). While ADHD participants made more omission errors overall, this difference between groups was not significant at the Low Load, $F(1, 47) = 0.24, p = .63$, but was at the Moderate, $F(1, 44) = 10.30, p = .002$, and High WM Loads, $F(1, 41) = 8.99, p = .005$. The Group by ISI interaction was not significant nor was the three-way interaction (Group $\times$ Load $\times$ ISI).

Accuracy—There was no significant main effect of Group nor interactions with Group for accuracy (Table 2). As expected, we found a main effect of WM Load, $F(2, 85) = 10.64, p = .001$, with accuracy decreasing as the WM load increased.

Association between VSAT Performance and ADHD Ratings

Exploratory analyses within the ADHD group examined whether VSAT performance correlated with parent ratings of ADHD symptomatology (Table 3). VSAT measures were collapsed across ISI and WM load to reduce the experiment-wise error rate. Greater RT variability (as indicated by tau) correlated significantly with higher ratings of hyperactivity ($r = .49, p = .01$). Ratings of cognitive problems/inattention and restlessness/impulsivity showed a similar pattern (r s = .37 and .35, respectively) with tau, but these correlations failed to reach statistical significance (p s = .07 and .09, respectively). Interestingly, higher levels of hyperactivity ($r = .54, p = .005$) and restlessness/impulsivity ($r = .40, p = .049$) each correlated significantly with *slower* reaction times (μ).

DISCUSSION

In the present study, ADHD participants showed significantly more variable responding than controls on a WM task, according to several outcome measures. In addition, significant group differences on omission errors were found across increasing WM load, with ADHD participants showing a linear decrease in performance and control participants showing initial improvement followed by worsening. Contrary to expectation, event rate did not significantly impact group differences on any measure.

The ex-Gaussian distribution provided a good model to examine IIV. As expected, we did not find a significant group difference on μ between ADHD and control participants, a finding that is consistent with other studies using ex-Gaussian measures (e.g., Geurts et al., 2007; Leth-Steensen et al., 2000). Most studies suggesting that children/adolescents with ADHD respond more slowly than controls have used traditional Gaussian measures of RT (i.e., mean and SD), which fail to take into account the positive skew consistently found in ADHD (but see Johnson, Kelly, et al., 2007 for a notable exception). Positive skew causes the mean of the distribution to be pulled higher; thus, overall RT in a skewed distribution will appear to be slower. By contrast, the present findings support a small but growing body

¹The omission errors variable was positively skewed for both the ADHD and control groups (z -scores for skewness ranged from 1.15 to 4.54 across the six experimental sessions). A log transformation, $\log_{10}(x + 1.0)$, was used to normalize the distribution, and no z -score remained significantly different from zero after the transformation.

of literature demonstrating that after controlling for RT variability, ADHD participants respond as fast as (if not faster than) their typically developing peers (Geurts et al.; Hervey et al., 2006; Leth-Steensen et al.). On the other hand, the association of slower RTs (μ) with higher levels of both hyperactivity and restlessness/impulsivity *within* our ADHD group is consistent with the hypothesis that motoric behavior may serve a functional role by increasing autonomic arousal to help compensate for cortical under-arousal during WM tasks (Rapport, Kofler, Alderson, & Raiker, 2007). Rapport et al. have demonstrated higher levels of hyperactivity among ADHD and control participants during a WM task, with motoric behavior increasing linearly as a function of increasing WM demands. Although we did not measure participants' activity level *during* the VSAT, our results suggest an association between slower overall performance on this WM task and increased rates of hyperactivity more generally in a naturalistic environment. Taken together, it appears that further investigation of motoric behavior as a compensatory process on a neural level would be worthwhile.

As hypothesized, ADHD participants showed more IIV than controls in terms of both sigma (which captures variability in the normal component of the distributional curve) and tau (which represents extremely slow responses). Furthermore, the association between IIV and parent ratings of hyperactivity suggests relevance of ex-Gaussian variability measures to daily functioning. Our results provide further evidence that the IIV phenomenon in ADHD extends beyond traditional response inhibition paradigms. As part of the growing body of literature characterizing IIV as a ubiquitous phenomenon among children and adolescents with ADHD, demonstration of increased variability in WM functioning reinforces the value of IIV as a candidate endophenotype for the disorder (Castellanos et al., 2005; Castellanos & Tannock, 2002; Johnson, Kelly, et al., 2007; Klein et al., 2006). Ongoing investigation of the role of IIV in ADHD — and the associated influence of distinct paradigms and task-specific variables — may provide a route for gaining insights into the heterogeneous pathophysiology of ADHD (Doyle et al., 2005; Nigg et al., 2004; Sonuga-Barke, 2005; Sonuga-Barke & Castellanos, 2007).

Along with ex-Gaussian measures of IIV, omission errors provided another measure of inconsistent responding. As anticipated, ADHD participants demonstrated more omission errors than controls, indicating that they had difficulty responding steadily throughout the task. Interestingly, however, ADHD participants answered as accurately as controls *when they responded*. This result is consistent with Klein et al.'s (2006) finding that WM performance among children with ADHD becomes more variable but *not* more error prone as task demands increase. Thus, *fluctuations* in performance — rather than a global deficit — may better account for poorer WM performance among ADHD children/adolescents. This is important because it suggests that children with ADHD are capable of acquiring the basic skills required to perform WM tasks; their difficulty with such tasks appears not to be a learning issue, per se, but perhaps may be related to modulation of attentional resources (Johnson, Kelly, et al., 2007; Rubia et al., 2007; Sonuga-Barke & Castellanos, 2007). Then again, it is possible that participants with ADHD were less likely to respond if they felt they might be wrong and/or were more likely than controls to pause deliberately in order to “catch their breath” throughout the task. Although such behaviors were neither explicitly observed nor reported by participants in our study, additional research is warranted to determine whether our findings indicate true fluctuations in attention as opposed to these or similar alternative explanations.

If WM is impaired in ADHD, differences between ADHD and control participants arguably should be more pronounced at higher WM loads. In the present study, WM load appeared to influence omission errors, with the curvilinear pattern for control participants across increasing WM loads suggesting a possible practice effect between the Low and Moderate

loads that was not maintained at the High load. As previous WM studies demonstrate (Rapport et al., 2008), ADHD participants showed no benefit of practice; rather, increasing WM load taxed them in a conspicuously linear fashion. This explanation is consistent with practice effects widely reported on the PASAT for individuals *without* ADHD (Tombaugh, 2006) and evidence from a brain-imaging study that adults with ADHD failed to demonstrate improvement on the PASAT over three trials (Schweitzer et al., 2004). Although the interaction between diagnostic group and WM load was not statistically significant for the other VSAT measures, this same pattern was observed for several measures and is worthy of additional research. The lack of a significant effect on sigma and tau may signify that IIV in WM among ADHD participants is a highly stable characteristic not easily altered by manipulation of the VSAT number set (i.e., task difficulty).

We recognize that greater WM load and increasing time on task were procedurally confounded in the present study. Thus, differences in omission errors between the ADHD and control participants at various levels of the task might be attributable to increased WM load, sustained-attention demands, fatigue, or a combination of these factors. The overall findings nevertheless provide some evidence for the influence of WM load. First, accuracy decreased significantly for *both* groups at the highest WM load. If the differential pattern for omission errors across groups is attributable to greater fatigue and/or difficulties with sustained attention, we might expect a correspondingly larger decrement in accuracy among the ADHD participants than controls over the course of the task. Similarly, in light of evidence that RTs lengthen with increasing time on task for ADHD participants (Berlin, Bohlin, Nyberg, & Janols, 2003) and the lack of fatigue effects found by Karatekin (2004) on a WM task, the stability of overall RT (μ) in the current study suggests that fatigue alone does not account for observed group differences in omission errors across varying WM loads. Nevertheless, as pointed out by Castellanos, Sonuga-Barke, Milham, and Tannock (2006), definitive conclusions about the role of WM — above and beyond processes such as arousal and sustained attention — cannot be made unless appropriate control tasks are used. To that end, we have acquired data from another study in which a subset of these participants performed the VSAT while undergoing fMRI (Fassbender, personal communication, June 10, 2008). In that paradigm, the VSAT was repeatedly presented over time in an A, B, C design along with two control tasks involving parametrically lesser demands on higher order cognitive functioning: a simple matching task and a basic arithmetic task absent an active WM component. The results demonstrated that differences in IIV increase with cognitive demand from the least complex matching task to the arithmetic task to the VSAT and were not simply a function of time on task.

Our results did not support the hypothesis that group differences in IIV would be more evident at a slower event rate. It has been suggested that faster speeds improve performance in ADHD by reducing temporal delays contributing to problems with self-control (Barkley, 1997a) and/or by optimizing energetic levels critical to self-regulation (Andreou et al., 2007; Sergeant, 2005; Sergeant, Oosterlaan, & van der Meere, 1999). Such mechanisms may exist for simple RT tasks but not for higher order WM tasks, in which slower event rates allow more time for complex processing. This interpretation is consistent with studies of the PASAT that fail to show increased sensitivity to between-group differences at faster ISIs (Tombaugh, 2006). Alternatively, the difference between ISIs in the current study (0.4 s) may not have been large enough to produce a significant between-group effect.

These results have several implications. First, the VSAT yielded valuable outcome measures distinguishing the performance of ADHD children/adolescents from their typically developing peers. Second, our findings highlight the importance of WM impairments in ADHD with particular emphasis on IIV, and the relationship between parent ratings and IIV performance suggests that this phenomenon is linked to functional behavior. In addition to

replicating findings that IIV is a key element in ADHD, we were able to evaluate the responsivity of IIV to task variations such as WM load and event rate. As an objective measure relating to subjective ratings of ADHD symptomatology, the VSAT holds promise for future research on IIV. Task parameters can be easily modified to allow further investigation of WM load and event rate effects. Furthermore, intra-individual RT fluctuations found on the VSAT might lend themselves to oscillation pattern analysis as described by Castellanos et al. (2005). Thus, future research using WM tasks such as the VSAT may help elucidate how IIV pertains to different theories of ADHD, including Barkley's unified theory (Barkley, 1997b), the cognitive-energetic model (Sergeant, 2005), and models emphasizing reinforcement-response abnormalities (Sagvolden, Aase, Johansen, & Russell, 2005; Schweitzer & Sulzer-Azaroff, 1995; Sonuga-Barke, 2002, 2003). Ideally, research examining IIV in ADHD should be tested along the lines of the model outlined by Nigg and Casey (2005) that emphasizes neuroscientific integration of components of cognitive control and affect regulation within a developmental framework. Finally, our results may have implications for ADHD treatment in light of the WM training effects cited by Klingberg and colleagues (2005, 2002). To date, measures of IIV have not been reported in WM training studies. Additional research would do well to examine whether reductions in IIV contribute substantially to improvements in functioning after training.

These findings should be interpreted in light of several limitations. First, we recommend replication in a larger sample to confirm the reliability of our findings. Although we obtained convergence on the ex-Gaussian parameters using the QMPE program, our sample size was small for that technique given the potential for bias (Brown & Heathcote, 2003; Heathcote et al., 2004; Heathcote, Brown, & Mewhort, 2002). Replication and extension are also important to determine the degree to which our results can be generalized. In the current study, participants in both groups tended to be of above average intelligence. Given correlations between intelligence and performance on the PASAT (Tombaugh, 2006), it remains an empirical question whether our results will extend to children of average or below-average intelligence. Nevertheless, scores on the PASAT are more highly associated with measures of attention than with intelligence (Tombaugh), thus supporting the relevance of the present findings. Also with regard to sample characteristics, additional research will be necessary to explore potentially important influences of gender and age and to determine whether increased IIV during WM tasks is specific to ADHD or characteristic of a wider range of conditions (Castellanos et al., 2005; Geurts et al., 2007; Verté, Geurts, Roeyers, Oosterlaan, & Sergeant, 2006). Although our results indicate that an important phenomenon of IIV is occurring among ADHD participants during a WM task, further research using appropriate control tasks will be necessary to tease out these effects.

In summary, these findings provide additional evidence that IIV is a fundamental aspect of ADHD. Methodologically, results of this study support the value of ex-Gaussian modeling to capture RT data. Above all, our findings suggest that cognitive impairments in children/adolescents with ADHD may be better understood by examining IIV in WM paradigms.

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Figure 1.
The Visual Serial Addition Task (VSAT). Schematic demonstrates example of the first three screens presented during the task.

Figure 2. Mean VSAT performance ($\pm SE$) of participants with ADHD (grey bars) and control participants (white bars) across increasing WM loads.

Table 1

Demographic and Clinical Characteristics of Participants in the ADHD and Control Groups.

	ADHD (<i>n</i> = 25)		Controls (<i>n</i> = 24)	
	Mean	<i>SD</i>	Mean	<i>SD</i>
Gender (<i>n</i>):				
Male	17		11	
Female	8		13	
Participant's ethnicity (<i>n</i>):				
Caucasian	20		16	
African American	4		4	
Asian	0		2	
Biracial	1		2	
Participant's age (years)	10.2	1.4	10.3	1.9
Full Scale IQ [*]	110.4	12.2	120.1	16.0
Parents' Socioeconomic Status	26.4	11.8	21.2	9.5
CPRS-R:L Scales:				
Cognitive Problems/Inattention ^{****}	70.4	10.4	46.1	4.4
Hyperactivity ^{****}	68.6	10.9	46.5	3.2
Restlessness-Impulsivity ^{****}	70.1	8.8	45.5	5.1
ADHD Index ^{****}	72.9	8.2	45.0	4.2

Note. CPRS-R:L = Conners' Parent Rating Scale-Revised: Long Version.

^{*}
p < .05;^{****}
p < .0001.

Table 2
VSAT Performance Across ADHD and Control Participants as a Function of WM Load.

	ADHD (<i>n</i> = 25)			Controls (<i>n</i> = 24)			Group × Load GLMM		
	Low Load		Moderate Load	Low Load		Moderate Load	High Load		High Load
	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	Mean (<i>SD</i>)	
Mu	931.5 (384.0)	915.0 (461.8)	875.8 (510.5)	892.7 (375.6)	812.3 (437.7)	917.1 (469.1)	0.10	0.75	1.00
Sigma	250.5 (194.6)	275.9 (225.7)	332.7 (208.2)	181.5 (145.0)	155.8 (137.5)	221.6 (207.9)	6.16*	2.29	0.36
Tau	342.9 (147.6)	359.8 (196.2)	462.3 (194.5)	285.2 (162.1)	254.9 (118.7)	292.4 (186.9)	10.15**	2.86	1.53
Omission errors (%)	9.3 (8.1)	14.8 (15.1)	19.5 (15.9)	11.5 (11.5)	5.5 (8.3)	9.7 (15.0)	7.54**	3.10*	7.25**
Accuracy (%)	78.7 (14.0)	76.1 (15.3)	67.2 (15.4)	80.0 (16.0)	79.7 (16.2)	71.8 (14.9)	1.21	10.64***	0.52

Note. Means are collapsed across ISI. GLMM = General Linear Mixed Model; Load = WM Load.

* $p < .05$;

** $p < .01$;

*** $p < .001$.

Table 3

Correlations Between VSAT Performance and Behavioral Ratings Within the ADHD Group ($n = 25$).

CPRS–R:L Scales	Accuracy (%)	Omission Errors (%)	Mu	Sigma	Tau
Cognitive Problems / Inattention	.30	–.02	.27	.17	.37
Hyperactivity	.41*	.27	.54**	.35	.49*
Restlessness-Impulsivity	.28	.23	.40*	.16	.35
ADHD Index	.27	.04	.22	.06	.13

Note. VSAT performance measures are collapsed across all levels of ISI and WM Load; CPRS–R:L = Conners' Parent Rating Scale–Revised: Long Version.

* $p < .05$;

** $p < .01$.