

Johnson *et al.*
Neuropsychologia (in press)

Response variability in Attention Deficit Hyperactivity Disorder: evidence for neuropsychological heterogeneity

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Johnson *et al.*
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Abstract

Response time (RT) variability is a common finding in ADHD research. RT variability may reflect frontal cortex function and may be related to deficits in sustained attention. The existence of a sustained attention deficit in ADHD has been debated, largely because of inconsistent evidence of time-on-task effects. A fixed-sequence Sustained Attention to Response task (SART) was given to 29 control, 39 unimpaired and 24 impaired ADHD children (impairment defined by the number of commission errors). The response time data was analysed using the Fast Fourier Transform, to define the fast-frequency and slow-frequency contributions to overall response variability. The impaired ADHD group progressively slowed in RT over the course of the 5.5 minute task, as reflected in this group's greater slow-frequency variability. The fast-frequency trial-to-trial variability was also significantly greater, but did not differentially worsen over the course of the task. The higher error rates of the impaired-ADHD group did not become differentially greater over the length of the task. The progressive slowing in mean RT over the course of the task may relate to a deficit in arousal in the impaired-ADHD group. The consistently poor performance in fast-frequency variability and error rates may be due to difficulties in sustained attention that fluctuate on a trial-to-trial basis.

Introduction

Increased variability in response time (RT) performance on cognitive tasks is one of the most consistent findings in research into attention deficit hyperactivity disorder (ADHD) (Hurks et al., 2005; Leth-Steensen, King Elbaz, & Douglas, 2000). Increased RT variability is consistent with explanatory accounts of ADHD that emphasise sub-optimal energetic states (Sergeant, 2005) and deficient extinction processes (Sagvolden, Aase, Johansen, & Russell, 2005). Variability in RT has also been proposed as a possible endophenotype with the potential to index genetic vulnerability to the disorder (Castellanos & Tannock, 2002; Kuntsi & Stevenson, 2001). Two recent molecular genetic studies have reported associations between performance variability measured on tasks of sustained attention and the 10-repeat allele of a variable number of tandem repeats (VNTR) within the dopamine transporter gene (DAT1) in ADHD (Bellgrove, Hawi, Kirley, Gill, & Robertson, 2005; Loo et al., 2003). These studies are noteworthy as the dopamine transporter is the main site of action of methylphenidate (MPH) and treatment with MPH reduces performance variability in ADHD (Castellanos et al., 2005). Recent neuropsychological lesion studies and functional brain imaging have demonstrated that increased intra-individual variability is not a simple consequence of general brain dysfunction, but may be related to the functioning of the frontal cortex and in particular the dorsolateral areas (Bellgrove, Hester, & Garavan, 2004; Stuss, Murphy, Binns, & Alexander, 2003). These lines of evidence support the contention that increased intra-individual variability is a manifestation of fluctuating top-down attentional control (Barkley, 1997; Stuss et al., 2003). Castellanos and colleagues recently suggested that catecholaminergic deficiency may impair top-down control, thus giving rise to relatively

Johnson *et al.*
Neuropsychologia (in press)

frequent lapses of attention, as indexed by greater variability, which may underpin deficits such as sustained attention in ADHD (Castellanos et al., 2005).

The existence of a sustained attention deficit in ADHD remains controversial, in part because of the inconsistent demonstration of deficits in performance over the course of the task (time-on-task) (Heinrich et al., 2001; van der Meere, Shalev, Borger, & Gross-Tsur, 1995; van der Meere, Wekking, & Sergeant, 1991). Nevertheless, meta-analytic studies of neuropsychological function in ADHD demonstrate that deficits in sustained attention are of moderate to large effect size (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Neuropsychological heterogeneity within samples of children with ADHD (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005) has likely contributed to inconsistent reports of sustained attention deficits. The Sustained Attention to Response Task (SART) (Robertson, Manly, Andrade, Baddeley, & Yiend, 1997) differs from traditional continuous performance tasks (CPTs), in that the response contingencies are reversed. Thus in the SART, the participant must withhold a response to an infrequent target, rather than respond. The CPT may provide a degree of exogenous support, as the rarity of the target captures attention. By contrast, withholding a response in the context of routine action, as is required by the SART, requires participants to adopt a controlled stance if they are to overcome the automatised act of button pressing. This demand is particularly apparent in a fixed-sequence version of the task, in which the digits 1-9 are presented in a predictable and repeating sequence and the subject is simply required to withhold their action to the 3. Performance on this predictable but repetitive task is prone to rapid automatisisation. Imaging studies of this task find robust activation within right-lateralised frontoparietal attentional networks (Manly et al., 2003) that are thought to be

Johnson *et al.*
Neuropsychologia (in press)

dysfunctional in ADHD (Silk et al., 2005; Sowell et al., 2003). Not surprisingly, a number of studies have indicated that children with ADHD have manifest difficulties on different versions of the SART (O'Connell, Bellgrove, Dockree, & Robertson, 2004; Shallice et al., 2002). Performance on the SART has been linked to allelic variation within a number of catecholaminergic candidate genes for ADHD (DAT1)(Bellgrove, Hawi, Kirley et al., 2005), (DRD4) (Bellgrove, Hawi, Lowe et al., 2005).

Castellanos *et al* recently proposed a novel method for analysing RT data in order to capture any periodic patterns that may exist within the moment-by-moment fluctuations in response time performance in ADHD (Castellanos et al 2005). The analysis technique employed – the fast Fourier transform (FFT) – provides an alternate view of a series of RT data. It measures the power of periodic changes in RT at different temporal frequencies, or in other words, the degree to which periodic patterns of a certain time-scale exist within the RT data series (see Figure One for further explanation). Applied to RT data, any periodically recurring patterns of responding within the data series are manifest as peaks of power at particular frequencies. Importantly, all information contained in the original RT time series remains after the FFT transformation. For instance, integrating power over the entire frequency range (by calculating the area under the spectrum) equates to the overall variance in the data, i.e., the square of the standard deviation of RT. Thus breaking up the frequency range into sections enables the measurement of components of variability defined by specific time-scales.

In the study of Castellanos *et al*, the ADHD children showed significantly more variability in reaction time within the frequency range 0.02-0.07 Hertz (Hz), compared with the controls, as measured by FFT power within this range. Frequencies slower than

Johnson *et al.*
Neuropsychologia (in press)

0.03 Hz were removed from the data using a methodology to smooth the data (detrending using cubic splines). Thus more gradual components of variability, including incidences of slowing of RT over the task block, were not examined.

In the present study using the SART, we sought to extend the principle of variability analysis through spectral techniques and thus further explore the underlying nature of RT variability in ADHD. RT data on the fixed sequence SART is highly suitable for FFT analysis for several reasons. The repetitive structure and fixed ISI allows *a priori* characterization of discrete points and ranges on the frequency scale in terms of the behaviour underlying them; this deterministic structure allows valid group averaging and between-group comparisons. Also, the long duration of a SART block (225 trials, 5.5 min) affords the examination of very low frequencies, encompassing slow cycles or even gradual, incremental slowing or speeding over the course of the task. This ability to separate types of variability according to temporal characteristics is what distinguishes the FFT analysis from traditional measures of mean and standard deviation of RT. Moreover, these newer techniques may yield potentially interesting measures for use in molecular genetic studies of ADHD.

SART RT variability may be broken down into three components. (1) Gradual variability, which has a slow temporal characteristic; (2) Trial-to-trial variability, which has a fast temporal characteristic; and (3) Sequence-specific variance, which is a measure of the consistency and distinctiveness of a particular RT pattern. Slow and fast variability and sequence-specific variance are readily measurable from the FFT spectrum. In contrast, variability measured simply as standard deviation over a task run represents the combined influence of these components but provides no indication of relative contributions.

Johnson *et al.*
Neuropsychologia (in press)

It has been suggested that fluctuating top-down control, as indexed by increased RT variability, may be a partial explanation for impaired sustained attention (Bellgrove, Hawi, Kirley et al., 2005; Castellanos et al., 2005; Stuss et al., 2003). Working from the hypothesis that neuropsychological heterogeneity within ADHD samples may conceal clinically important deficits, we adopted a heterogeneity reduction technique recently advocated by Nigg and colleagues (Nigg et al., 2005). Impairment on the SART was defined as a commission error score that was 1.5SD above the mean commission error rate for control participants. This cut-off is consistent with criteria used to define clinically significant impairment, in for example, inattention or hyperactivity/impulsivity. If a score was greater than 1.5 standard deviations (SD) from the control commission error rate - the primary index of sustained attention - the child was placed into an “impaired ADHD” subgroup. A score within 1.5 SDs of the control mean defined an “unimpaired ADHD” subgroup. It was of interest whether neuropsychologically impaired and unimpaired ADHD groups would differ from controls in terms of sustained attention and the spectral content of the time-series data, using measures of peak amplitude and area under broad portions of the power spectra.

Methods

Participants

Twenty-nine control children (1 female, 2 left-handed) and sixty-three children with ADHD (10 females, 8 left-handed) participated in the study. There was no significant difference between the ages of the control children (age range 9 – 15 yrs; mean 11.2, SD 1.7 yrs) and the children with ADHD (age range 8 – 15 yrs; mean 11.3 yrs, SD 2.0 yrs).

Johnson *et al.*
Neuropsychologia (in press)

Data from 22 ADHD children had previously been published (Bellgrove, Hawi, Kirley *et al.*, 2005)

Exclusion criteria for participation in the study included known neurological conditions, pervasive developmental disorders, serious head injuries and below average intelligence (below 70 on the WISC-III). Control children were also excluded if they had first degree relatives with ADD or ADHD.

The ADHD participants were recruited as part of an ongoing genetic study (Kirley *et al.*, 2002). Children with ADHD were either referred by consultant psychiatrists or recruited through support groups. Diagnosis was confirmed by psychiatrists using the parent form of the Child and Adolescent Psychiatric Assessment (CAPA) (Angold *et al.*, 1995). All ADHD children met DSM-IV diagnosis for ADHD (American Psychiatric Association, 1995). Eighty-two percent of the ADHD participants had a diagnosis of ADHD combined type (ADHD-CT), 10% were of the ADHD inattentive type (ADHD-IN) and 8% were of the ADHD hyperactive type (ADHD-H). Fifty-four parents of the ADHD children completed the Conners' Parent Rating Scale – Revised: Long Version (CPRS-R:L)(Conners, 1997) (see Table 1). Forty-three percent of the children with ADHD met diagnostic criteria for oppositional defiant disorder and 18% met diagnostic criteria for conduct disorder. Any stimulant medication was withdrawn for at least 24 hours prior to testing. Intelligence levels of all children were measured using the WISC-III (Weschler, 1992). The control children were recruited from a number of Dublin schools. These schools varied widely in terms of the socio-economic status of the surrounding suburbs. Parental occupation was noted for 46 ADHD children and 28 control children and socio-economic status was estimated using the occupation sub-scale of the Hollingshead Index

Johnson *et al.*
Neuropsychologia (in press)

of Social Position (Hollingshead, 1965). Consent was obtained from parents of all children and the experimental work was conducted under the approval of local ethical committees in accordance with the Declaration of Helsinki.

Insert Table 1 about here

Apparatus and Procedure

Participants were presented with a repeating fixed sequence of digits (1 – 9) on a laptop computer. A single digit appeared on the screen for 313 ms; a mask was then presented for 125 ms, after which a response cue (a bold cross) appeared for 63 ms, followed by a second mask for 375ms and a fixation cross for 563 ms. The total inter-stimulus interval was 1439 ms (digit onset to digit onset). Participants were instructed to respond, using a button press, to every digit (go-trial) except ‘3’ (no-go trial). They were asked to respond when the response cue appeared on screen 125 ms after the digit was extinguished, or 438 ms from the start of the trial. The response cue was used to limit the impulsive response style of the ADHD children and to reduce any speed/accuracy trade-offs (Bellgrove, Hawi, Kirley et al., 2005). Participants performed 225 trials, representing 25 runs of the 1 to 9 sequence, lasting approximately 5.5 minutes.

Data Analysis

The 225 RTs per participant were analysed for errors of **commission** (responses made on the no-go digit 3), **omission** (non-responses on the go-trials). **Mean** and **standard deviation** of the RTs on the go-trials were calculated.

For each participant the sequence of 225 RTs was analysed using a fast Fourier transform (FFT). Grand average spectra were also calculated per group for descriptive purposes

Johnson *et al.*
Neuropsychologia (in press)

(see Figure 1). Due to the natural 1-9 frequency of the predictable, fixed-sequence SART, meaningful interpretation of group averaged spectra could be made, as spectral peaks coincided across participants.

Data preparation for FFTs: To calculate the FFTs, a continuous stream of data was needed. RTs for the digit 3 were linearly interpolated from the RTs at digits 2 and 4. Similarly, RTs of less than 100 ms (errors of omission and extremely short responses) were replaced with values interpolated from the RTs of the preceding and following digits. For the fast-frequency area under the spectra (FFAUS) and principle SART peak analyses (see below), individual RT data were detrended, subtracting out any linear components, which were analysed separately. We reasoned that very low frequency shifts in the data might be related to meaningful gradual changes in response time over the course of the task (for instance, slowing in RT over the task). For this reason, linear detrending was employed rather than higher-order detrending that might involve cubic splines, as in (Castellanos et al., 2005)).

Data analysis of FFTs: The RT data were analysed according to Welch's averaged, modified periodogram method. The RT data were analysed both over the entire task (full-run) (225 data points per individual) and in a first-half of the SART task vs second-half analysis (half-by-half). The full time series was first divided into 7 segments of 75 data points, with an overlap of 50. Each segment was Hamming-windowed and zero-padded to length 450. The FFT was then calculated for each segment. For the full-run analyses, the FFT for each segment was averaged across the 7 segments to provide a spectrum per individual. For the half-by-half analysis, the first three FFT segments were averaged in the first half and the last four segments were analysed in the second half.

Johnson *et al.*
Neuropsychologia (in press)

Any segments of 75 data points where there were over 10 errors of omission (not necessarily occurring together) were excluded in the FFT. Subsequently, for the full-run analyses, 19 impaired-ADHD children, 37 unimpaired-ADHD children and 29 controls were included in the FFAUS and principle SART peak analyses. For the half-by-half analyses, the exclusion criteria left 16 impaired-ADHD, 36 unimpaired-ADHD and 28 controls in the analysis.

In relating measurements from the FFT spectra to components of variability, a distinction was made between variance arising from task structure (e.g. strategic speeding and slowing at particular points within the 1-9 sequence) and that arising from true variability not related to the sequence. The former is measured by taking the power at a discrete frequency in the spectrum, while the latter is measured by calculating the area under the spectrum (AUS) over a broad band of interest.

The AUS represents a measure of the ‘power’ or overall variance in the signal. Two forms of the AUS were calculated. The **FFAUS** encompassed all sources of variability faster than once per SART cycle (0.0772 Hz) (area under curve to the right of dotted line in Figure.1). Any trial-to-trial variability was captured in this calculation. The **Slow Frequency Area Under Spectra (SFAUS)** encompassed all sources of variability slower than once per SART cycle (area under curve to the left of dotted line in Figure.1). Any variability that occurred over any time period greater than one SART cycle was captured in this calculation. This measure captured any gradual change in variability. To ensure that all low frequencies were encompassed in the SFAUS, the time series was not divided into segments. Any subject who made more than 30 omission errors in total over the course of the task was eliminated from this analysis. Subsequently, 12 impaired-ADHD,

Johnson *et al.*
Neuropsychologia (in press)

32 unimpaired-ADHD and 29 control children were included in the SFAUS analysis.

The data were not detrended in the SFAUS analysis, as the linear components of the RT variation over the entire task were of analytical interest. In a separate test, the linear component in isolation was analysed by fitting regression lines to the RTs of each participant using a first order polynomial fit (linear). The **slope of the regression line** was then calculated.

The peak power at a particular point in the spectra measures consistency and distinctness of a particular RT pattern. Healthy adult control subjects show a significant slowing in RT on digit 1 relative to digits 9 and 2 in preparation for the upcoming no-go response on the SART (Dockree et al., 2004). If this average pattern is consistently reproduced on every 1 – 9 sequence, we would expect to find a peak in the spectra at the **principle SART peak (PSP)** of 0.0772 Hz (reciprocal of 9 digits x 1.439 second inter-stimulus interval). The power of the PSP was calculated and divided by the FFAUS, normalising for trial-to-trial variability. This measure reflected any sequence-specific variance.

These 8 dependent variables were calculated per participant and averaged per group. All measures were analysed using analysis of variance (ANOVA), *t*-tests, regression and Bonferroni-adjusted pair-wise comparisons where appropriate.

Results

The criterion for subdividing the ADHD participants into impaired and unimpaired groups was a score of 1.5 SD above the control commission error mean (8.7 errors).

Twenty-four ADHD children made over 8.7 commission errors (impaired-ADHD group) and 39 children made less (unimpaired-ADHD group). Using one-way ANOVAs, there

Johnson *et al.*
Neuropsychologia (in press)

was no significant difference between the impaired- (mean 89.8, SD 13.9), unimpaired-ADHD (mean 97.8, SD 15.1) and control (mean 96.7, SD 8.8) groups in terms of IQ. There was no significant difference in age between the impaired- (mean 10.8, SD 2.0 yrs), unimpaired-ADHD (mean 11.7, SD 2.0 yrs) and control (mean 11.3, SD 1.7 yrs) groups. There were no significant differences between the impaired and unimpaired ADHD children on the Conner's Parent's Rating Scale Global Index, Inattentive sub-scale or the Hyperactive sub-scale (see Table One). Most children in the impaired- and unimpaired-ADHD groups were diagnosed with the Combined-type ADHD. Using chi-square tests, the number of children in the impaired- and unimpaired-ADHD groups did not vary in terms of oppositional defiant disorder diagnosis or conduct disorder diagnosis. The control, impaired- and unimpaired-ADHD groups also did not differ in terms of socio-economic class, as determined by the parental occupation sub-scale of the Hollingshead Index of Social Position (Hollingshead, 1965).

Validity of the FFT-based model of variability

The ability of the variability components derived from the FFT analysis (SFAUS, FFAUS and PSP) to predict SD of RT was analysed using linear multiple regression. A significant association was found between the three components and the SD of RT, [$R^2 = 0.905$ (adjusted $R^2 = 0.901$); $F(3,69) = 220.13$, $p < 0.001$]. This suggests that the three components account for over 90% of the predicted value of the SD of RT.

Linear Regression of RT

The slope of the regression line, fitted to the RTs of each participant, was calculated and analysed with one-sample *t*-tests to test if the slope of the regression lines varied significantly from zero. Only the slope of the impaired-ADHD group (mean 4.4, SD 7.8)

Johnson *et al.*
Neuropsychologia (in press)

was significantly different from zero [$t(1,23) = 2.8, p < 0.01$], and this positive slope indicated a significant slowing in RT over the SART. The slope of the regression lines of the control group (mean 0.0, SD 5.2) and the unimpaired-ADHD group (mean 0.6, SD 5.7) were not significantly different from zero. To investigate if there was a difference in the slope of the regression lines between the three groups, a one-way ANOVA was calculated and a significant Group difference was found, [$F(2,89) = 3.88, p < 0.024, \eta_p^2 = 0.08$]. Pair-wise comparisons suggested that the mean RT regression slope of the impaired-ADHD group was significantly steeper than that of the control group ($p < 0.034$) and there was a trend towards a difference between the two ADHD groups ($p > 0.063$). The unimpaired-ADHD and control groups did not differ significantly.

Insert Figure 1 about here

Slow Frequency Area Under Spectra

The group average FFT spectra are shown in Figure 1. Group averages of the SFAUS, specific for the frequency bands slower than one SART cycle, were calculated. A one-way ANOVA suggested a significant Group main effect, [$F(2,70) = 4.90, p < 0.01, \eta_p^2 = 0.12$]. Pair-wise comparisons suggested that the SFAUS of the impaired-ADHD group was significantly greater than that of the unimpaired-ADHD group ($p < 0.08$), or control group ($p=0.05$). There was no significant difference between the control and unimpaired-ADHD groups.

Mean RT

The impaired-ADHD group (mean 455, SD 93 ms), the unimpaired-ADHD group (mean 456, SD 87 ms) and the control group (mean 467, SD 114 ms) did not differ significantly

Johnson *et al.*
Neuropsychologia (in press)

in their mean RTs, when compared across the entire task. The group means were within the 63 ms response cue, demonstrating that participants complied with instructions. Since RT slowed over time for the impaired-ADHD group, the mean RT scores were calculated for the first and second halves of the task and analysed using a Group by Half two-way ANOVA (see Figure 2). The number of data points in each half were equated by eliminating the first 9 RTs arising from the task. There was a significant main effect for Half [$F(1,89) = 10.4$, $p < 0.002$, $\eta_p^2 = 0.10$], which was modified by a significant Group by Half interaction, [$F(2,89) = 6.5$, $p < 0.002$, $\eta_p^2 = 0.13$]. There was no significant Group difference. Pair-wise comparisons showed that the interaction arose from the increase in mean RT for the impaired-ADHD group between the two halves of the SART task (1st half: mean 424, SD 90 ms; 2nd half: mean 483, SD 112 ms), ($p < 0.001$). This increase did not occur with the unimpaired-ADHD (mean 448, SD 94 ms; 460, SD 94 ms) and control groups (mean 467, SD 110 ms; 463, SD 125 ms). There were no other significant interactions.

Insert Figure 2 about here

Standard Deviation of RT

To investigate if variability in RT varied over the two halves of the task, the SD of RT scores were calculated for the first and second halves of the task. This was analysed with a Group by Half two-way ANOVA. Significant main effects of Group [$F(2,89) = 13.1$, $p < 0.001$, $\eta_p^2 = 0.23$] and Half were found [$F(1,89) = 26.5$, $p < 0.001$, $\eta_p^2 = 0.23$]. These were modified by a significant Group by Half interaction [$F(2,89) = 3.2$, $p < 0.044$, $\eta_p^2 = 0.07$] (see Figure 2). Pair-wise comparisons indicated that all three groups were significantly more variable in the second half and the impaired-ADHD group was always

more variable than the other two groups, which did not differ. The differential increase in variability in the second half of the impaired-ADHD group gave rise to the interaction.

Fast Frequency Area Under Spectra

The FFAUS was calculated for each half of the trial and compared using a Group by Half two-way ANOVA. A significant Half main effect was found [$F(1,74) = 8.05$, $p < 0.006$, $\eta_p^2 = 0.10$]. The RTs in the second half were significantly more variable than those in the first half. A significant Group main effect was found [$F(2,74) = 5.69$, $p < 0.005$, $\eta_p^2 = 0.13$]. The impaired-ADHD group was significantly more variable than either the unimpaired-ADHD group ($p < 0.025$) or the control group ($p < 0.004$). The unimpaired-ADHD and control groups did not differ. No interaction was found. For all three groups, the level of fast variability increased in the second half of the task, but the impaired-ADHD group was not differentially more variable than the other groups in the second half.

Sequence-specific variance (Principle SART Peak)

The peak amplitude FFT for each half was calculated and compared using a Group by Half two-way ANOVA (half-by-half spectra are shown in Figure 3). A significant interaction was found between Half and Group [$F(2,74) = 4.23$, $p < 0.018$, $\eta_p^2 = 0.10$]. Pair-wise comparisons suggested that the interaction was driven by the greater peak amplitude of the impaired-ADHD group in the first (mean 4.2, SD 2.0), relative to second (mean 2.0, SD 1.3) ($p < 0.005$) half. Neither the unimpaired-ADHD or control groups differed in their peak amplitudes between the two halves. There was no significant difference between the three groups in either the first or second halves ($p > 0.05$).

Insert Figure 3 about here

To identify the pattern of responding to the SART task that corresponded to the PSP, the mean RT at each SART digit was calculated for the two halves of the task. As seen in Figure 4, the speeding on digit 2 was the most striking and common pattern amongst the three groups and the mean RT on this digit was analysed using a Group by Half two-way ANOVA. A significant Group by Half interaction was found [$F(2,89) = 3.83, p < 0.025, \eta_p^2 = 0.08$]. Pair-wise comparisons indicated that the mean RT at digit 2 for the impaired-ADHD group was significantly faster in the first half (mean 357 ms, SD 94) than the second half (mean 426 ms, SD 120), ($p < 0.001$). The unimpaired-ADHD and control groups did not vary across the two halves. The mean RT on digit 2 of the impaired-ADHD group was significantly faster than that of the unimpaired-ADHD ($p < 0.038$) and control groups ($p < 0.015$) in the first half. There was no difference between the groups in the second half.

Insert Figure 4 about here

The SD of RT on digit 2 was also analysed with a Group by Half two-way ANOVA. Significant Half and Group main effects were modified by a significant Group by Half interaction [$F(2,89) = 3.67, p < 0.029, \eta_p^2 = 0.08$]. Pair-wise comparisons indicated that the SD of RT at digit 2 for the impaired-ADHD group was significantly more variable in the second half (SD 209, SD 122) compared with the first (SD 132, SD 71) ($p < 0.001$). The unimpaired-ADHD and control groups did not vary across the two halves. There was no difference in SD of RT on digit 2 between the three groups in the first half. In the second half, the response variability on digit 2 of the impaired-ADHD group was

Johnson *et al.*
Neuropsychologia (in press)

significantly greater than the unimpaired-ADHD ($p < 0.005$) and control groups ($p < 0.013$).

Commission Errors

The number of commission errors made in each half was analysed using a Group by Half two-way ANOVA. There was a significant main effect of Group for the number of commission errors made, [$F(2,89) = 76.4, p < 0.001, \eta_p^2 = 0.63$], with the impaired-ADHD group (mean 6.1, SD 2.2) making significantly more commission errors compared with the unimpaired-ADHD (mean 2.3, SD 1.3) and control groups (mean 2.3, SD 1.6). The unimpaired-ADHD and control groups did not differ. There was also a significant main effect of Half, [$F(1,89) = 7.04, p < 0.009, \eta_p^2 = 0.07$], with all groups making more commission errors in the second half (mean 3.6, SD 2.4) compared with the first half (mean 3.0, SD 2.4). There was no significant interaction.

Omission Errors

The number of omission errors was analysed in each half of the task. A significant Group main effect for omission errors was found, [$F(2,89) = 17.0, p < 0.001, \eta_p^2 = 0.28$], with the impaired-ADHD group making significantly more omission errors (mean 8.8, SD 6.1) than the unimpaired- (mean 3.6, SD 5.6) and control groups (mean 2.1, SD 2.9). The unimpaired-ADHD and control groups did not differ. There was also a significant Half main effect, [$F(1,89) = 6.9, p < 0.01, \eta_p^2 = 0.07$], with all groups making more omission errors in the second half (mean 5.1, SD 6.0) compared with the first half (mean 3.8, SD 5.5). There was no significant interaction.

Clinical measures

The three Conners' indices did not correlate significantly with any of the dependent measures.

Discussion

The aim of this study was to investigate the nature of response variability on a sustained attention task in children with ADHD. By subdividing the ADHD group into impaired and unimpaired groups according to the level of commission errors made, a clear pattern of deficit in the impaired-ADHD group was discerned, enabling a deeper understanding of the nature of response time variability in ADHD. First, the impaired-ADHD group progressively slowed in mean RT performance over the 5.5 minute task (slope of linear regression, mean RT), whilst the unimpaired-ADHD and control groups kept a constant response time. The impaired-ADHD group showed greater variation in response time in the low frequency bands than the other two groups, as the power of the SFAUS was greater for this group. This variation is most likely due to the progressive slowing over the course of the task. We suggest that this progressive slowing reflects a deficit in arousal in the impaired-ADHD group. Second, all three groups became more variable as the task progressed (SD of RT in the two halves); however this difference was most distinct in the impaired-ADHD group. The response performance to digit 2 in the first and second halves (peak amplitude of PSP) is an excellent example of the impaired-ADHD group's slowing in RT and the increase in SD of RT over the course of the task (see Figure 4). Third, the impaired-ADHD group was always more variable in the fast-frequency trial-to-trial variability than the other two groups. All three groups became more variable as the task progressed, but the impaired-ADHD group did not become

Johnson *et al.*
Neuropsychologia (in press)

differentially more variable. This result was mirrored in the error rates. The impaired-ADHD group always made more errors of commission (by definition) and omission than the other groups, demonstrating a robust sustained attention deficit. All three groups made more errors in the second half of the task, compared with the first half, but the error rates of the impaired-ADHD group did not differentially increase in the second half (no interaction). We suggest that the impaired-ADHD group demonstrated a deficit in sustained attention throughout the course of the task, which was not differentially influenced by a time-on-task or arousal effect. Overall, these results suggest that the impaired-ADHD group displayed two key deficiencies – an arousal deficit over the 5.5 minute task and a sustained attention deficit, demonstrated in fast, moment-to-moment variability. These results suggest that the application of FFT analysis techniques is informative and discriminative about the underlying nature of response variability in ADHD.

In terms of the current models of ADHD, the hypothesised arousal deficit is consistent with the cognitive-energetic (Sergeant, 2005) and dynamic developmental (Sagvolden et al., 2005) models of ADHD. The sustained attention deficit is consistent with the ADHD model of executive dysfunction (Barkley, 1997; Pennington & Ozonoff, 1996) and again the dynamic developmental model (Sagvolden et al., 2005). An anatomical basis for the arousal and sustained attention systems is discussed below.

Previous CPT studies with normal subjects have found a progressive increase in RT over long time periods (~ 60 minutes) (Paus et al., 1997). Studies on children with ADHD have been less conclusive. Some studies on CPT and sustained attention in children with ADHD have reported progressive slowing in RT over intermediate time periods (~14

Johnson *et al.*
Neuropsychologia (in press)

minutes) (Epstein et al., 2003; Shallice et al., 2002) and some have found no change (Loo et al., 2003; van der Meere & Sergeant, 1988). In studies examining RTs over shorter testing periods (~5 minutes), differences in slow shifts in RT performance between ADHD and control children have either not been tested (Bellgrove, Hawi, Kirley et al., 2005; O'Connell et al., 2004) or have not been found (Heinrich et al., 2001). In the current study, reducing the heterogeneity of the ADHD group (through sub-division according to commission errors) allowed a clearer dissociation in performance of the ADHD groups over this shorter timeframe. The progressive slowing in RT by the impaired ADHD group may be due to a gradual decrease in arousal levels over the course of the 5.5 minute period. This would be consistent with a disruption to a lower-level arousal system, possibly involving the reticular formation, the noradrenergic locus coeruleus (Nigg, 2005) and/or the anterior cingulate (Critchley, Melmed, Featherstone, Mathias, & Dolan, 2002; Paus et al., 1997).

The traditional measures of mean and SD of RT blend the entire range of temporal characteristics of RT variability and so by their very nature do not allow a parcellation of temporally distinct forms of variability. The impaired-ADHD group was more variable in RT than the other groups and this variability increased differentially in the second half of the trial. This increased variability in RT (SD of RT) reflects a combination of the slowing in RT over the task and the increased fast-frequency trial-to-trial variability in RT of the impaired-ADHD group. The differential effect in the second half is likely a reflection of the low-frequency component.

The FFAUS measure reflects fast-frequency trial-to-trial variability without contamination by the low-frequency components (the slowing over time). The poor

Johnson *et al.*
Neuropsychologia (in press)

performance of the impaired-ADHD group on the fast-frequency variability, commission and omission errors is suggestive of a loss of executive functional control, possibly involving the right hemisphere frontoparietal system (Robertson & Garavan, 2004), which may then be responsible for deficits in sustained attention (Bellgrove, Hawi, Kirley *et al.*, 2005). All three groups increased their fast-frequency trial-to-trial variability over the course of the task. The lack of a differential change in RT and error rate performance in the impaired-ADHD group over the length of the SART suggests that delay-aversion and/or motivational difficulties were not differentially affecting this group. Sustained attention may operate over short time periods, for example at 0.05 Hz (20 seconds) for a self-paced task such as the CPT (Castellanos *et al.*, 2005), or at 0.0772 Hz (13 seconds) for the response-cued SART. A deficit in sustained attention in the impaired-ADHD group may be related to a deficit in frontoparietal circuitry in ADHD (Silk *et al.*, 2005; Sowell *et al.*, 2003). Neuroimaging of children with ADHD performing this sustained attention test will help to clarify the exact areas of dysfunction. ADHD may therefore be associated with deficits in bottom-up (sub-cortical arousal) and top-down (fronto-parietal) systems that are necessary for cognitive control.

As hypothesised by Nigg and colleagues (Nigg *et al.*, 2005), there was a large degree of overlap in the performance of the control and ADHD children. Sixty-two percent of the total ADHD group fell into the unimpaired-ADHD group and this group did not differ from the control group on any measure. ADHD children may present with similar clinical symptoms but may have deficits in different pathways in the brain (Castellanos *et al.*, 2005). By sub-grouping according to a commission error rate, a deeper understanding of the nature of variability in ADHD was reached.

Johnson *et al.*
Neuropsychologia (in press)

In conclusion, the impaired-ADHD group showed a progressive increase in mean RT and increase in SD of RT over the course of the 5.5 minute SART, which we suggest is related to a deficit in arousal. This group also showed a consistently poor performance in fast-frequency variability in RT and in commission and omission error rates, which did not worsen differentially compared with the other two groups over the course of the task. These deficits may be due to particular difficulties in sustaining attention over much shorter time-periods and may be reflective of frontoparietal dysfunction.

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Johnson *et al.*
Neuropsychologia (in press)

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Johnson *et al.*
Neuropsychologia (in press)

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Johnson *et al.*
Neuropsychologia (in press)

Figure 1: Grand average of the fast Fourier transform (FFT) of the mean response time (RT) data on the fixed Sustained Attention to Response Task (SART) for each participant group. The Y axis represents the power of periodic changes in RT data. The X axis represents the different temporal frequencies, in Hertz (Hz). Three points are noted. (1.) A left-to-right downward slope along the X axis ($1/f$ characteristic) was observed in the spectra for all groups. This was especially pronounced in the impaired-Attention Deficit Hyperactivity Disorder (ADHD) group. This characteristic represents a slow change in RT, as there is greater power at the lower temporal frequencies. (2.) The FFT spectrum of the impaired-ADHD group was elevated on the Y axis along the entire frequency spectrum (X axis), in comparison with the unimpaired-ADHD and control averages. This represents increased variability of the impaired-ADHD group at all temporal frequencies. (3.) All groups showed a peak of activity around 0.0772 Hz (the Principle SART Peak (PSP)) (dotted line). This suggests that a particular pattern of response occurred at the same frequency (0.0772 Hz) often. Grand average spectra were calculated per group using the FFT function in MatLab 7.0 (The MathWorks, Natick, Massachusetts).

Figure 1

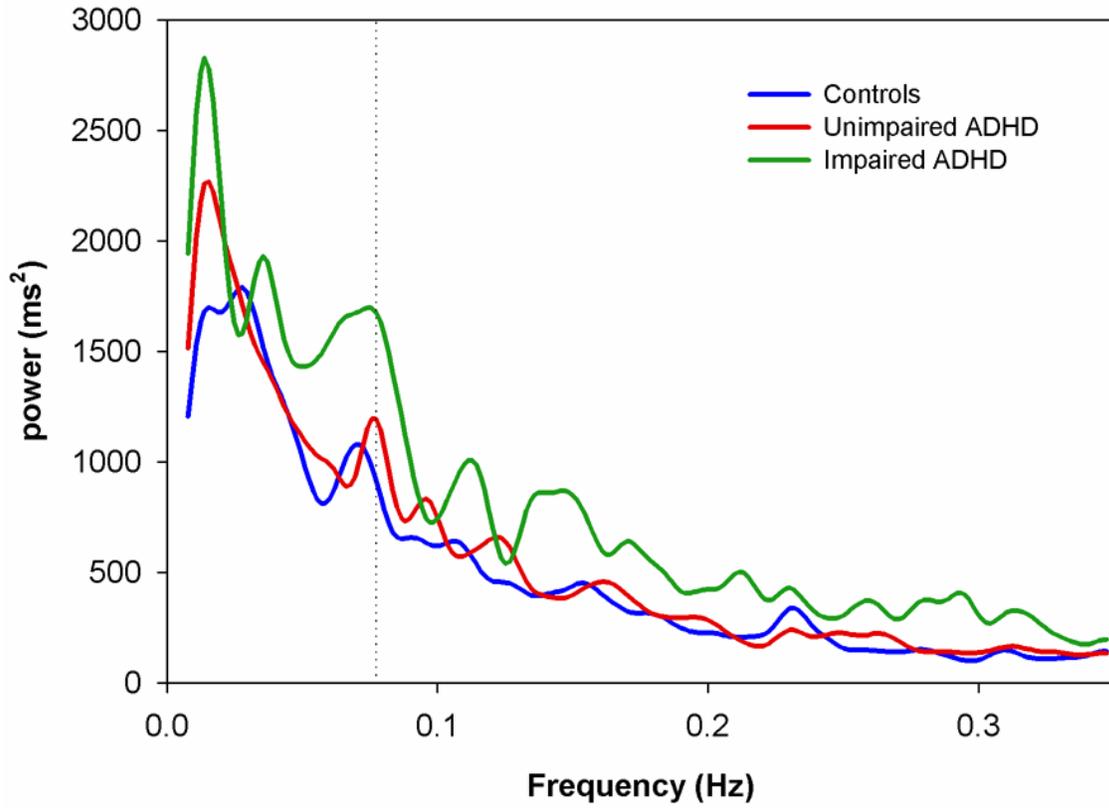


Figure 2: Mean (2A) and standard deviation (2B) of response time scores (with standard errors) for each participant group for the first and second halves of the fixed version of the SART.

Figure 2A

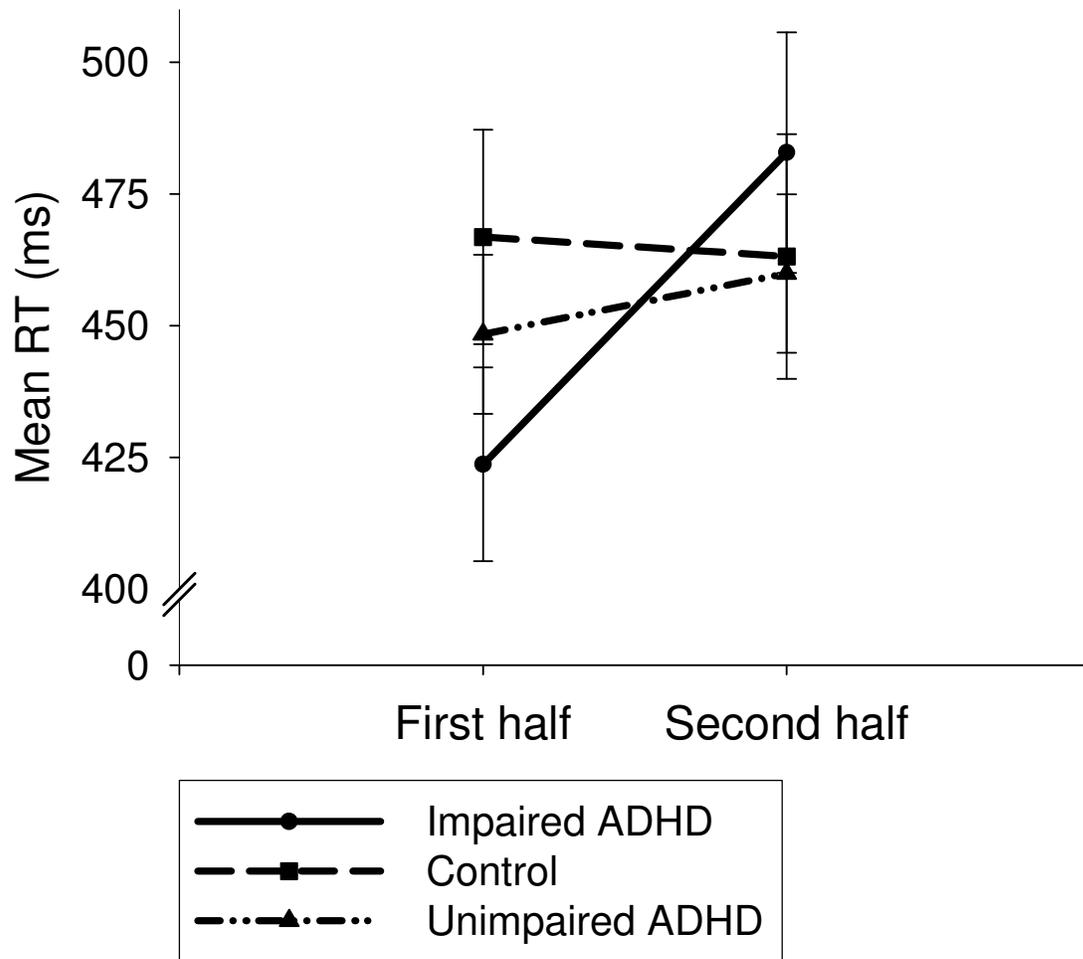
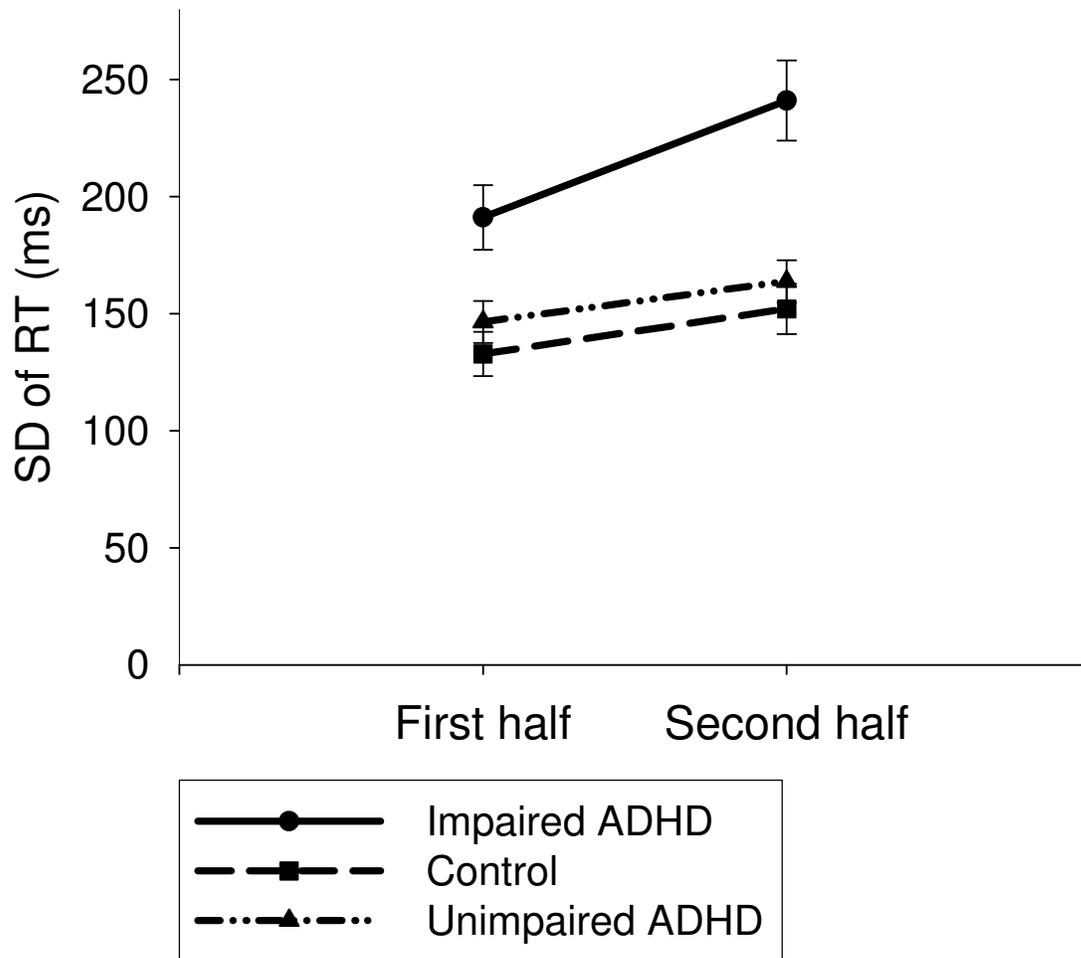


Figure 2B



Johnson *et al.*
Neuropsychologia (in press)

Figure 3: Grand average of the fast Fourier transform of the mean response time for each half of the fixed SART task, for the impaired-ADHD group (3A), the unimpaired-ADHD group (3B) and the control group (3C). Note that the principle SART peak (PSP) varies around 0.0772 Hz (dotted line) for the impaired-ADHD and control groups. The unimpaired-ADHD group's PSP falls directly on 0.0772 Hz for each half.

Figure 3A

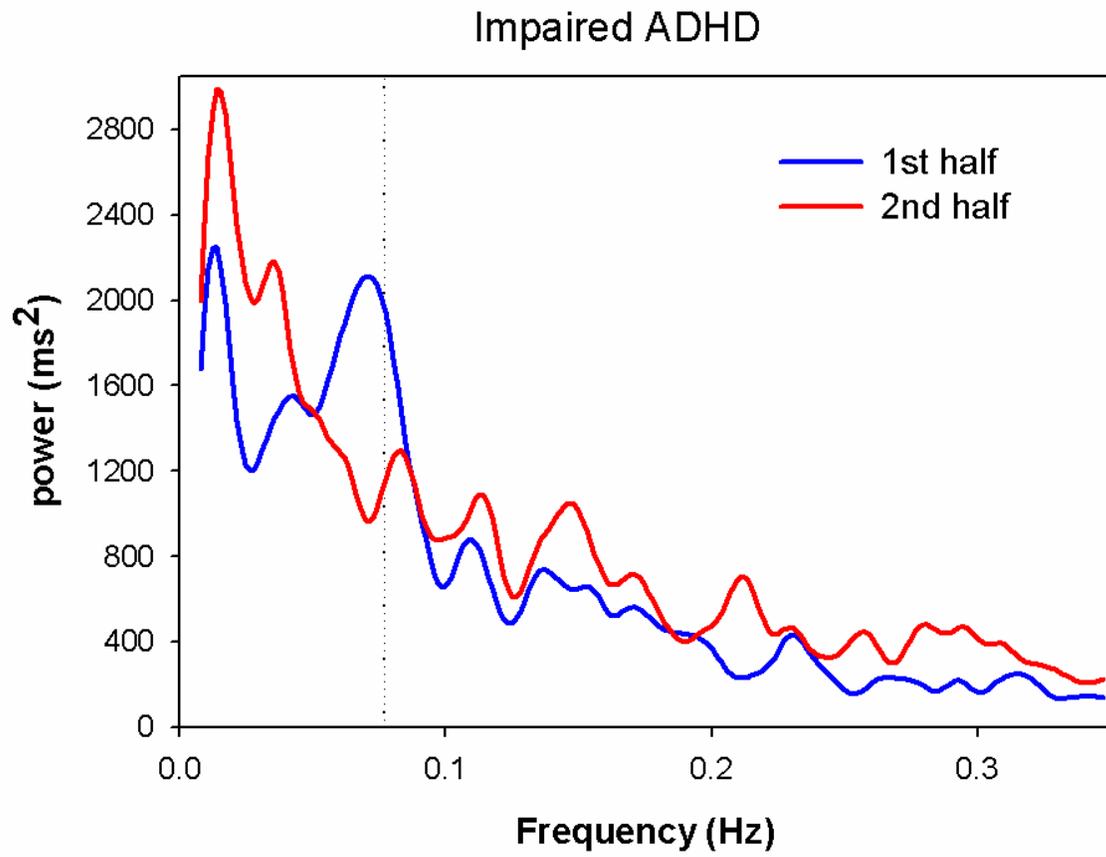


Figure 3B

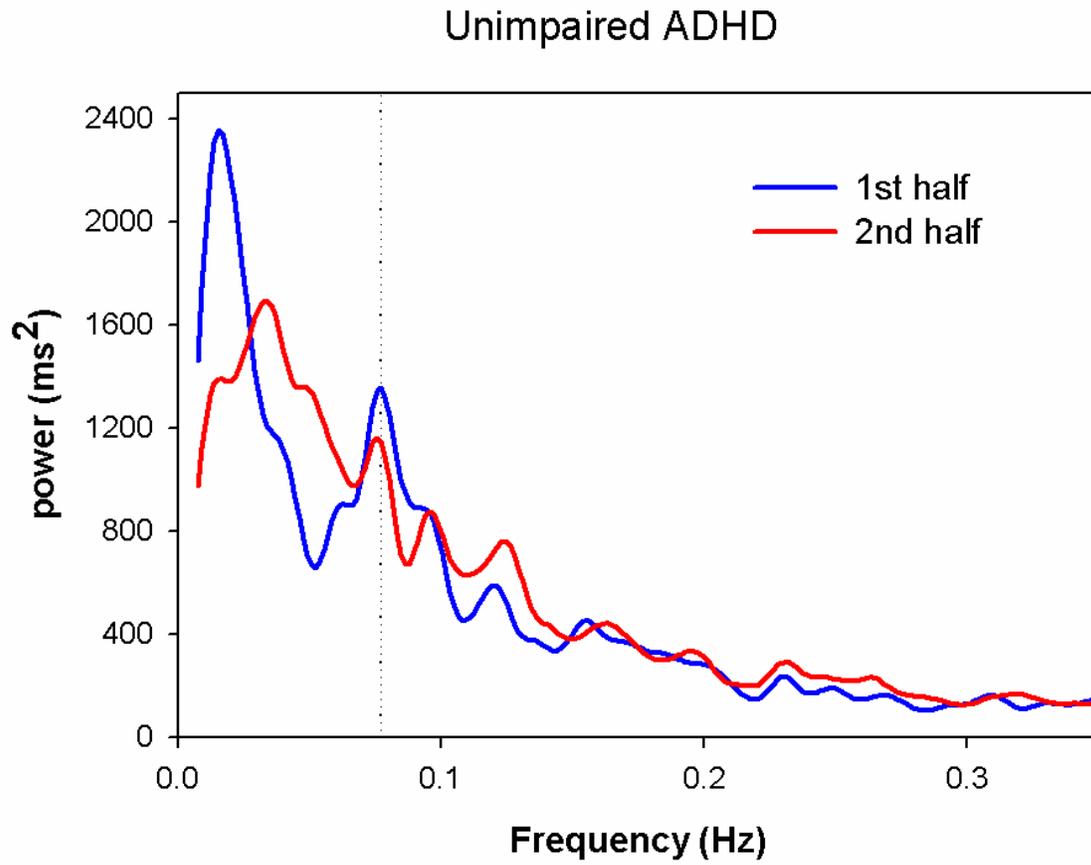


Figure 3C

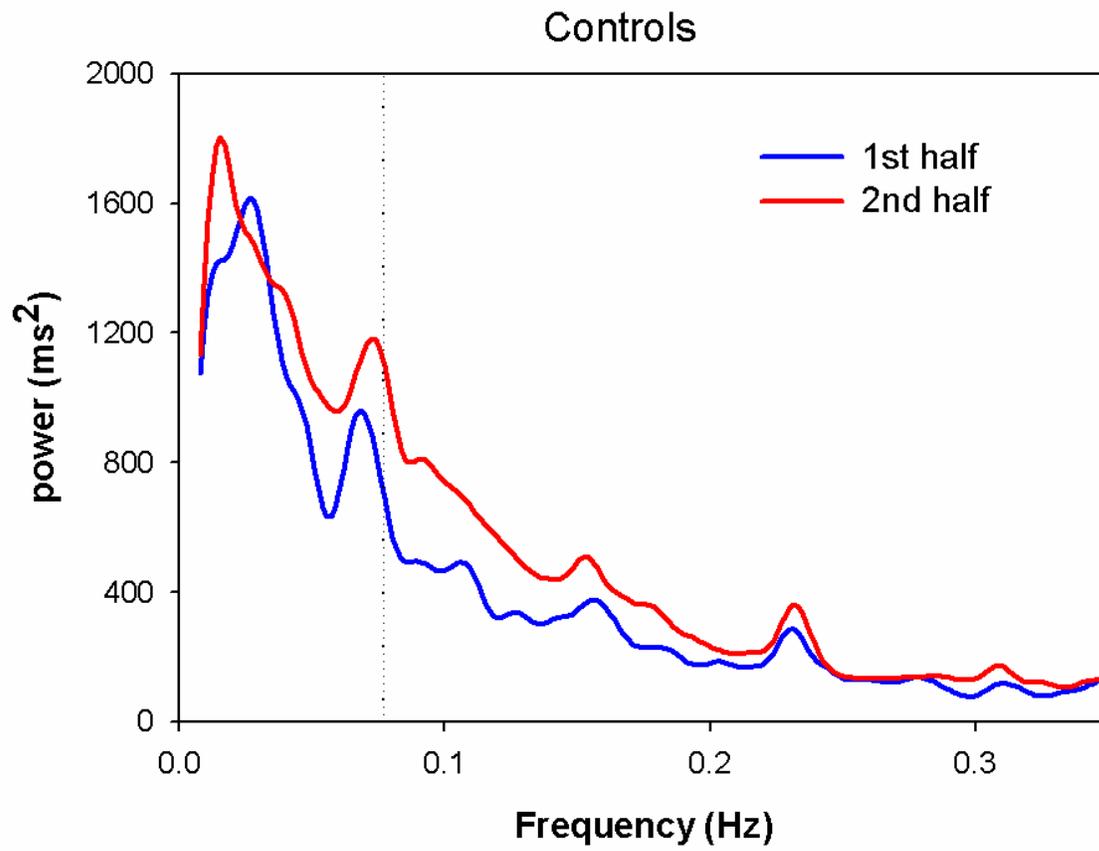


Figure 4: Mean (4A) and standard variation (4B) in response time scores (with standard errors) for each participant group for each digit for the first and second halves of the fixed version of the SART.

Figure 4A

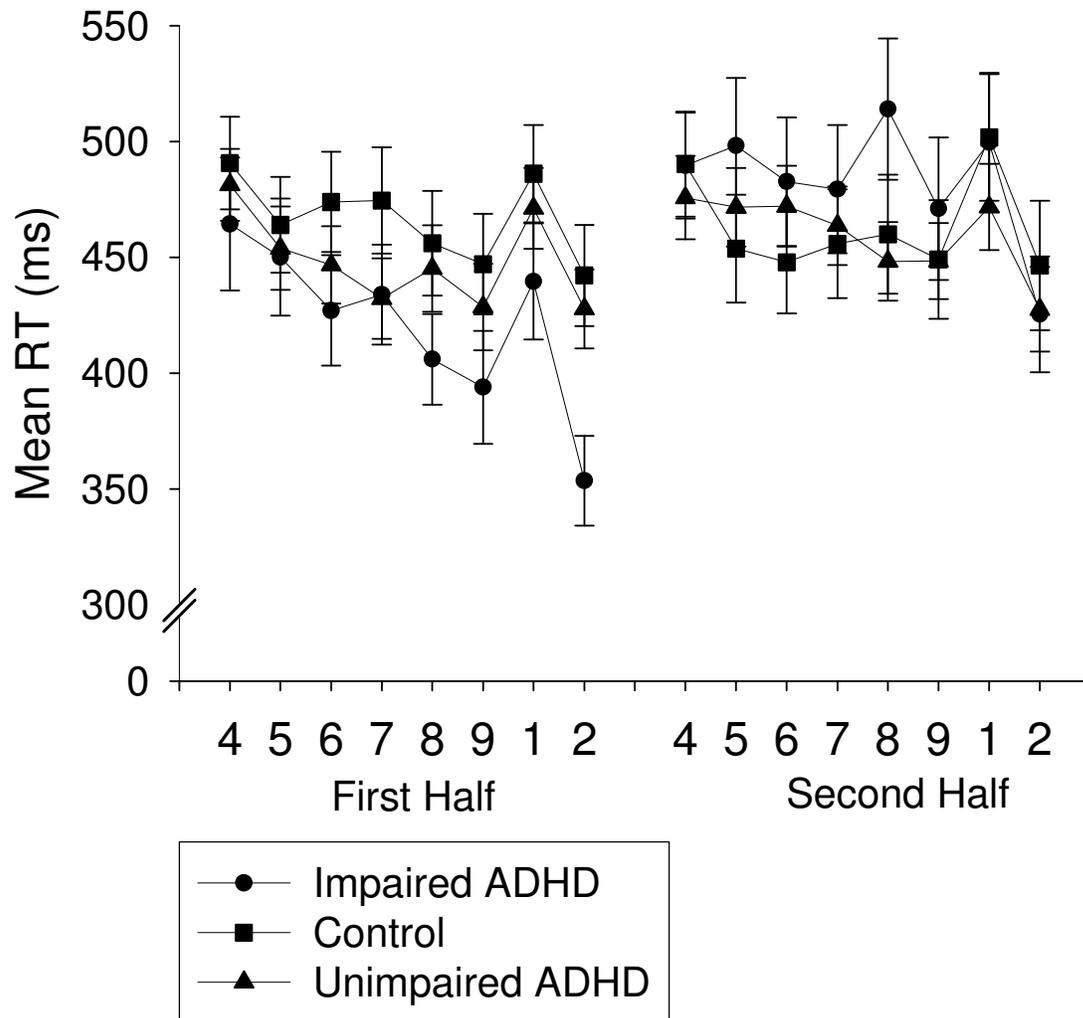


Figure 4B

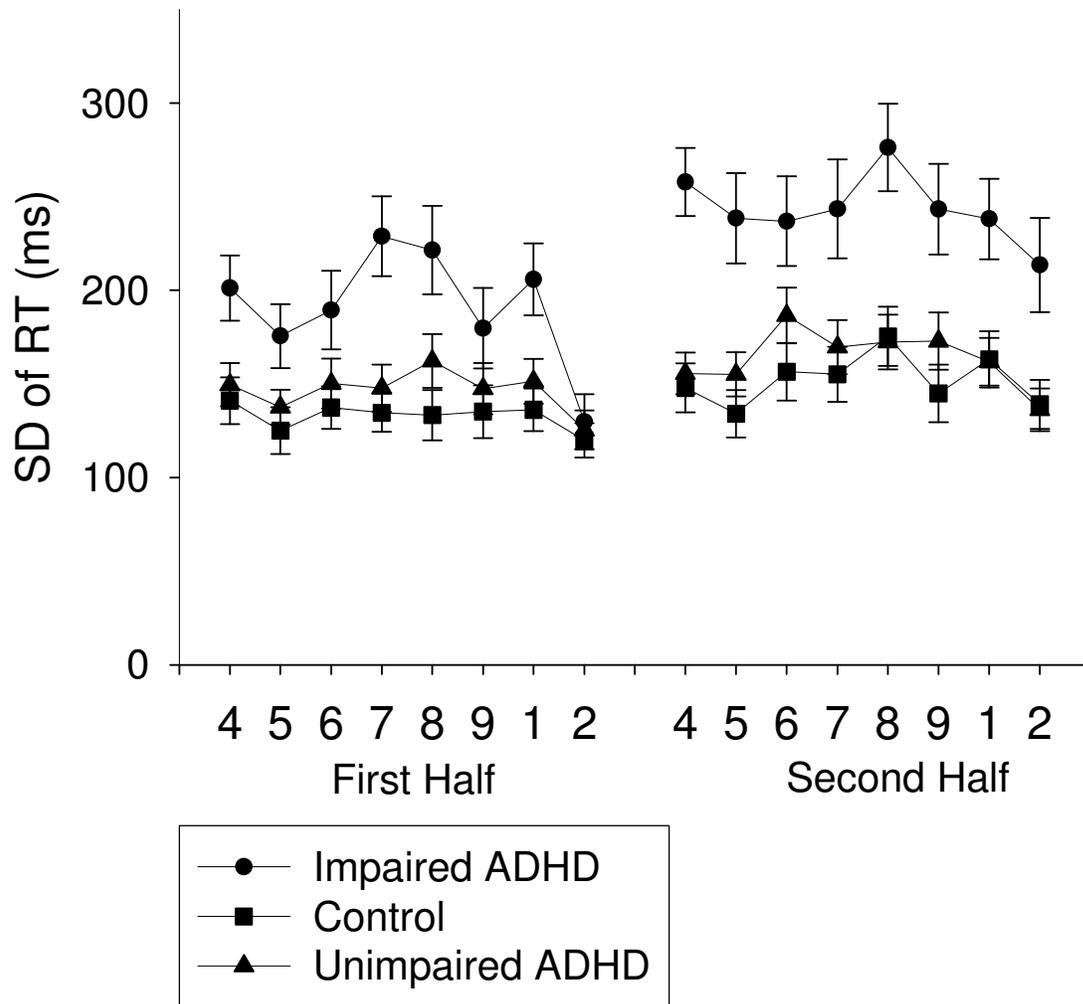


Table One

Table 1: Demographic and diagnostic information on the ADHD and control participants

Group	Unimpaired ADHD	Impaired ADHD	Control
Number	39	24	29
Age (mean, SD)	11.7 (2.0)	10.8 (2.0)	11.3 (1.7)
IQ (mean, SD)	97.8 (15.1)	89.9 (13.9)	96.7 (8.8)
SES (mean, SD)	3.3 (1.3)	3.4 (1.7)	3.8 (2.2)
Combined-type (count, % of group)	31 (79%)	21 (88%)	
Hyperactive/Impulsive (count, % of group)	2 (5%)	3 (13%)	
Primarily Inattentive (count, % of group)	6 (15%)	0 (0%)	
Number of Conners' Parental responses	36	21	
DSM IV: Inattentive Subscale (mean, SD)	72.9 (9.5)	72.8 (9.6)	
DSM IV: Hyperactive / Impulsive Subscale (mean, SD)	80.7 (11.3)	82.4 (11.3)	
Global Index: Total (mean, SD)	76.3 (10.5)	78.3 (8.7)	
Conduct Disorder diagnosis (count, % of group)	6 (15%)	5 (21%)	
Oppositional Defiant Disorder diagnosis (count, % of group)	17 (44%)	10 (42%)	