



Lateralization of attention in adults with ADHD: Evidence of pseudoneglect

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Research Article

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Abstract

Background. We investigated whether adults with attention-deficit/hyperactivity disorder (ADHD) show pseudoneglect—preferential allocation of attention to the left visual field (LVF) and a resulting slowing of mean reaction times (MRTs) in the right visual field (RVF), characteristic of neurotypical (NT) individuals—and whether lateralization of attention is modulated by presentation speed and incentives.

Method. Fast Task, a four-choice reaction-time task where stimuli were presented in LVF or RVF, was used to investigate differences in MRT and reaction time variability (RTV) in adults with ADHD ($n = 43$) and NT adults ($n = 46$) between a slow/no-incentive and fast/incentive condition. In the lateralization analyses, pseudoneglect was assessed based on MRT, which was calculated separately for the LVF and RVF for each condition and each study participant.

Results. Adults with ADHD had overall slower MRT and increased RTV relative to NT. MRT and RTV improved under the fast/incentive condition. Both groups showed RVF-slowness with no between-group or between-conditions differences in RVF-slowness.

Conclusion. Adults with ADHD exhibited pseudoneglect, a NT pattern of lateralization of attention, which was not attenuated by presentation speed and incentives.

Introduction

Hemispheric asymmetry of the brain is universal in the animal kingdom, is well-supported by anatomical and molecular research [1], and offers cognitive survival advantages [1]. In humans, functional lateralization shows positive correlations with cognitive abilities as shown in functional magnetic resonance imaging (fMRI) studies [2]. Research involving patients after corpus callosotomy documented that left human hemisphere is dominant for language function, logical thinking, or local processing, whereas the right hemisphere is oriented toward visuospatial attention and global processing [3]. These differences are underlined by specific changes in gray matter volume or white matter density [4].

Because humans are binocular, and their brains have an optic chiasm, signals from the left visual hemifield (LVF) and the right visual hemifield (RVF) are contra-lateralized in the brain, such that information from LVF of both eyes is sent to the right hemisphere and vice versa. However, when it comes to allocation of attention, the right hemisphere tends to attend to both visual fields, whereas the left hemisphere allocates attention predominantly to RVF [5].

The right hemispheric dominance for visuospatial attention [6,7] is often referred to as “pseudoneglect,” a phenomenon where neurotypical (NT) individuals show small but robust attentional bias to the left [8,9]. However, studies in children and adults with attention-deficit/hyperactivity disorder (ADHD) suggest atypical hemispheric asymmetries at both structural and functional levels [10–12].

Over three decades ago, it was noted that children with ADHD resemble adults with right hemispheric dysfunction [13]. Since then, a link between ADHD and a rightward attentional bias was documented in boys with ADHD in a line bisection task [14], as well as in young adults with ADHD who made more LVF (but not RVF) omission errors in a cancellation tasks compared to NT individuals [15]. A similar pattern of higher mean LVF versus RVF omission errors was found in adults with ADHD compared to NT individuals in a letter cancellation task [16].

The cognitive-energetic model of ADHD focuses on the role of arousal, postulating that cognitive deficits seen in people with ADHD result from a reduced energetic state [17]. According to this model, the optimization of under-arousal (low energetic state) in people with ADHD results in reduction of attentional lapses and faster, less variable, and more accurate responses.

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Findings described above gave rise to a hemispheric hypoarousal hypothesis of attentional dysfunction, which was further supported by findings showing that methylphenidate normalizes performance in the line bisection task in children with ADHD [18]. Neuroscientific evidence lends some support to this hypothesis, as healthy children with a dopamine transporter (DAT1) risk variant for ADHD [19] were found to have poorer attention in the LVF in a visual orienting task [20]. This is potentially important as in children with ADHD, inattention to stimuli in the LVF can be improved (including normalization of performance in the line bisection task) by methylphenidate treatment which blocks the DAT1 [18,21]. The DAT1 variant [19] was also reported to be associated with disturbed patterns of activation in fMRI studies in both adults and children with ADHD, including the left dorsal anterior cingulate cortex (ACC) [22]. ACC plays a crucial role in many higher level functions, including attention allocation, reward processing [23], or boredom [24]. Additionally, a previous study focusing on patients with spatial neglect identified structural abnormalities within right putamen, caudate nucleus, pulvinar, and superior temporal gyrus as the neurological basis for spatial neglect [25]. Analogously, recent meta-analyses in children and adults with ADHD found reduced volumes in the right putamen [26] and consistent under-activation in the right caudate nucleus during cognitive tasks [12].

Crucially however, and somewhat consistently with the cognitive-energetic model [17], level of arousal might have a modulating effect on the symptoms of spatial neglect both in patients with brain lesions and people with ADHD. It has been established that increasing alertness can help to overcome the perceptual spatial neglect in right-hemisphere patients [27]. It has been found that under lower perceptual load in a flanker task, children with ADHD exhibit hyper-distractibility in the RVF compared to the LVF (i.e., higher interference effect for RVF vs. LVF target displays)—an opposite pattern of interference effects compared to NT children (who show greater interference for LVF vs. RVF target displays) [28].

Recent studies investigating adults with ADHD identified neuroanatomical correlates of the dominant role of the right hemisphere in visuospatial attention. For example, the superior longitudinal fasciculus shows hemispheric asymmetry in volume [29], and the white matter microstructure of the superior longitudinal fasciculus is compromised in adults with ADHD [30]. Additionally, the reduced microstructural integrity of the superior longitudinal fasciculus is associated with reaction time abnormalities typical of adults with ADHD [31].

Apart from classic tasks mentioned above, such as the line bisection task or the letter/shape cancellation tasks, hemispheric differences can be studied using other simple cognitive tasks, where stimuli are randomized and presented separately in the LVF or RVF. Based on speed and accuracy of responses in the LVF and RVF, it is possible to make inferences about the underlying hemispheric processes [11]. Therefore, in this study we employed a lateralized version of the Fast Task [32], a four-choice reaction-time task where stimuli were presented in the LVF and RVF, to investigate differences in mean reaction time (MRT) and reaction time variability (RTV) in adults with ADHD and NT adults between slow/no-incentive and fast/incentive conditions.

Increased intra-individual variability in reaction times (RTV) might be a marker of ADHD as it is one of a few cognitive performance measures consistently producing reliable results in people with ADHD during speeded reaction time tasks [33–35]. It has been proposed that the increased RTV in people with ADHD

might represent fluctuations in attention related to disrupted sensitivity to reward and an underlying arousal deficit [36]. RTV and MRT in individuals with ADHD can be investigated with the Fast Task, where a slow/no-incentive condition is followed by a fast/incentive condition in which the event rate is increased and performance incentivized [32,37]. Improvements or normalization in the ADHD group in RTV and MRT under the fast/incentive condition is well-documented in two large meta-analyses showing small to medium effect sizes [33,34].

Therefore, we expect that in this study adults with ADHD will show overall increased MRT and RTV relative to NT group, as well as a relative improvement in both measures under the fast/incentive condition of the Fast Task. In the lateralization analyses, we expect a typical pattern of pseudoneglect in the NT group, that is, a preferential allocation of attention to the LVF and a resulting prolongation of reaction times in the RVF (i.e., RVF-slowness). As suggested by the research discussed above, we expect an opposite pattern of results for the ADHD group, that is, inattention to the left (rightward bias) resulting in longer reaction times in the LVF (LVF-slowness). Furthermore, we hypothesize that this pattern of results would be more pronounced in the slow/no-incentive condition of the Fast Task relative to the fast/incentive condition, with a possibility of adults with ADHD normalizing the rightward bias in the fast/incentive condition, due to the purported effect an elevated level of arousal has on normalizing spatial neglect [27,28,38].

Methods

Sample

The sample for this study consisted of 43 adults with ADHD and 46 NT adults, who volunteered to participate and did not differ in IQ (ADHD = 109.3 ± 15.7, NT = 108.4 ± 11.7, $t(87) = 0.312$, $p = 0.756$). We used G*Power 3.1 for sample size estimation. Previous meta-analytic analyses of RTV [34] reported bias-corrected Hedges' $g = 0.57$. With power = 0.80 and alpha = 0.05, the projected sample was $N = 80$, indicating suitability of the achieved sample size. Adults with ADHD were recruited from South London and Maudsley Adult ADHD Outpatient Service. Ethics approval was granted by the Joint South London and Maudsley (SLaM R&D Number: R&D2016/039) and Institute of Psychiatry Research Ethics Committee (REC Reference: 15/LO/2067). All study participants gave full informed consent. Table 1 shows patient background characteristics.

Table 1. Background characteristics of the study sample.

	Participants with ADHD ($N = 43$)		Neurotypical participants ($N = 46$)	
	Mean	SD	Mean	SD
Gender	16 females, 27 males		26 females, 20 males	
Age (years)	37.16	10.06	29.37	9.06
IQ	109.28	15.67	108.37	11.65
ADHD symptom severity ^a	32.70	10.61	7.26	7.04
ADHD functional impairment ^b	3.07	3.57	17.98	5.73

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; SD, standard deviation.

^aMeasured by the Barkley Adult ADHD Rating Scale [39].

^bMeasured by the Barkley ADHD Functional Impairment Scale [40].

Clinical measures

Adults with ADHD were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders—fifth edition criteria [41] using the Diagnostic Interview for Adult ADHD [42,43]—a structured clinical interview assessing the symptoms of ADHD in childhood and adulthood in adults. Wechsler Abbreviated Scale of Intelligence was used to measure IQ (Wechsler 2011). Adults with ADHD who were taking ADHD medication underwent 24–48-h washout phase. NT participants in the control group did not meet diagnostic criteria for ADHD. This was established via a short clinical interview and by applying the Barkley Adult ADHD Rating Scale, a self-rating questionnaire for adult ADHD symptoms [39], and the Barkley Functional Impairment Scale, a 10-item self-rating questionnaire for functional impairment related to ADHD [40]. We excluded participants with major co-occurring medical or mental health disorders including autism spectrum disorder, current episode of depression, major depressive disorder, bipolar disorder, addiction disorder, schizophrenia, antisocial personality disorder, anxiety with panic attacks, and any signs of psychosis or hypomania/mania.

Cognitive testing

We used a variant of the Fast Task [32,37] where the stimuli were lateralized to the LVF or RVF, that is, positioned in a concentric pattern around a central fixation cross. Participants were presented with four empty circles arranged in the upper-left, upper-right, bottom-left, and bottom-right corner of the screen. After a delay period, a circle designated as the target signal for that trial was filled in (colored in yellow). Participants were asked to make a compatible choice by pressing one of four corresponding buttons on a small numeric keyboard. Following a response, the circles disappeared from the screen and a fixed inter-trial interval of 2,500 ms followed. First, a practice session was administered, during which participants had to respond correctly to five consecutive trials. Then, two conditions followed, a slow/no-incentive condition and a fast/incentive condition. The slow/no-incentive condition consisted of 72 trials with a foreperiod of 8 s. The fast condition consisted of 80 trials with 1-s foreperiod and incentives. In both conditions, all trials contained targets, which were equally and randomly distributed across both visual fields. If a participant responded quicker than their MRT during the slow/no-incentive condition (based on the middle 94% of responses, excluding extremely fast and slow responses) for three consecutive trials, they won a smiley face. The number of won smiley faces appeared during the inter-trial interval instead of the fixation point and represented a reward. The Fast Task took about 20 min to complete. See Figure 1 for an illustration of the experimental paradigm.

Equipment and data recording

Data were recorded and the task administered using BGaze Player by Braingaze. All study participants used a chin-rest to facilitate recording.

Data processing

RTV was calculated as standard deviation of MRT for each study participant. In the lateralization analyses, MRT was calculated separately for the LVF and RVF for each condition and each study participant.

Statistical analyses

We used a 2 x 2 x 2 mixed analysis of variance (ANOVA) to investigate the effect of MRT and RTV between visual field (RVF vs. LVF) and task condition (slow/no-incentive condition vs. fast/incentive condition) as within-subject factors in both groups (ADHD group vs. NT group) with Bonferroni-corrected post-hoc tests. If the assumption of homogeneity of variances was violated in any analysis (assessed by Levene's test for equality of variances, $p < 0.05$), we reported Welch ANOVA and post-hoc tests with the Games-Howell correction.

Results

Mean reaction time

We found a main effect of task condition on MRT, $F(1, 83) = 182.811$, $p < 0.001$, partial $\eta^2 = 0.688$. Post-hoc tests showed speeding of MRT from slow/no-incentive to fast/incentive condition with a mean difference of 156 ms. We also found a main effect of group, $F(1, 83) = 5.372$, $p = 0.023$, partial $\eta^2 = 0.061$, with MRT 89 ms slower in the ADHD group between both conditions. There was statistically significant group-by-condition interaction, $F(1, 83) = 7.288$, $p = 0.008$, partial $\eta^2 = 0.081$, so that the difference between the ADHD group and the NT group was larger in the slow/no-incentive condition (mean difference = 120 ms), than in the fast/incentive condition (mean difference = 58 ms). Please see Figure 2 for the MRT data across task conditions and groups.

Reaction time variability

A similar pattern of results was found for the RTV. There was a main effect of task condition, $F(1, 83) = 28.517$, $p < 0.001$, partial $\eta^2 = 0.256$. Post hoc tests showed a reduction in RTV from slow/no-incentive to fast/incentive condition. We also found a main effect of group, $F(1, 83) = 9.508$, $p = 0.003$, partial $\eta^2 = 0.103$, with average RTV higher in the ADHD group. There was also a statistically significant group-by-condition interaction, $F(1, 83) = 6.158$, $p = 0.015$, partial $\eta^2 = 0.069$, so that the difference between the ADHD group and the NT group was larger in the slow/no-incentive condition, than in the fast/incentive condition. Please see Figure 3 for the RTV data across task conditions and groups.

Lateralization analyses

There was no statistically significant three-way interaction between visual field (LVF or RVF), task condition (slow/no-incentive vs. fast/incentive condition), and group (ADHD vs. NT) for MRT, $F(1, 83) = 0.327$, $p = 0.569$, partial $\eta^2 = 0.004$, as well as for RTV, $F(1, 81) = 1.841$, $p = 0.179$, partial $\eta^2 = 0.022$. There was also no statistically significant two-way interaction between visual field and group, for both MRT, $F(1, 83) = 0.009$, $p = 0.924$, partial $\eta^2 = 0.000$, and RTV, $F(1, 81) = 0.559$, $p = 0.457$, partial $\eta^2 = 0.007$. Finally, there was no statistically significant interaction between condition and visual field in the MRT analysis, $F(1, 83) = 2.832$, $p = 0.096$, partial $\eta^2 = 0.033$, as well as in the RTV analysis, $F(1, 81) = 1.182$, $p = 0.280$, partial $\eta^2 = 0.014$. Consistently with the above MRT and RTV analyses, we found a statistically significant two-way interaction between condition and group in the MRT, $F(1, 83) = 7.551$, $p = 0.007$, partial $\eta^2 = 0.083$, as well as RTV analysis, $F(1, 81) = 8.403$, $p = 0.005$, partial $\eta^2 = 0.094$. There was a main effect of condition in the MRT analysis, $F(1, 83) = 184.706$, $p < 0.001$,

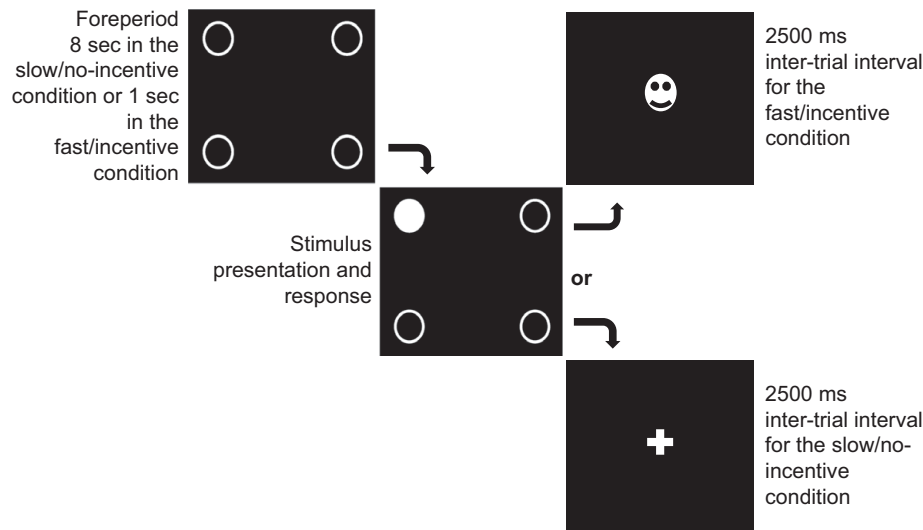


Figure 1. Illustration of the experimental paradigm (the Fast Task) with a slow/no-incentive condition and a fast/incentive condition.

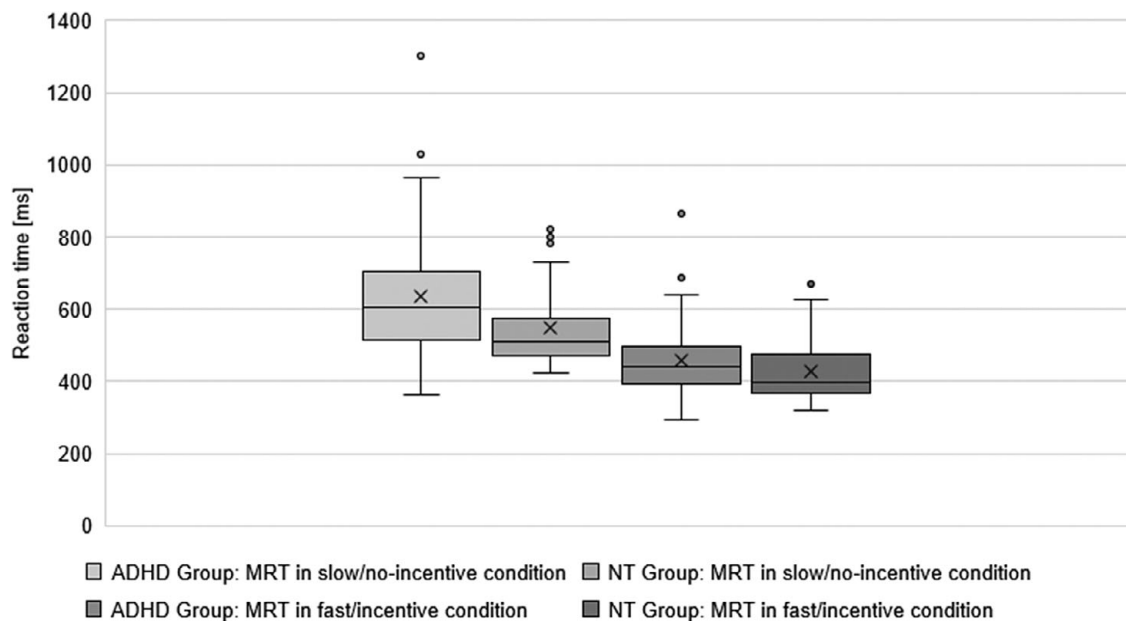


Figure 2. Boxplots showing mean reaction time (MRT) data from the slow/no-incentive and the fast/incentive condition of the Fast Task in the group of adults with ADHD and the neurotypical (NT) group. Boxes represent interquartile range with the median and mean (x). Whiskers indicate the maximum and minimum values (excluding the outliers which are represented by the dots). Abbreviations: ADHD, attention-deficit/hyperactivity disorder; MRT, mean reaction time; NT, neurotypical.

partial $\eta^2 = 0.690$, as well as in the RTV analysis, $F(1, 81) = 27.528$, $p < 0.001$, partial $\eta^2 = 0.254$.

We found a main effect of visual field in the MRT, $F(1, 83) = 3.978$, $p = 0.049$, partial $\eta^2 = 0.046$, but not in the RTV analysis, $F(1, 81) = 2.937$, $p = 0.090$, partial $\eta^2 = 0.035$. Only the overall effect of RVF-slowness was statistically significant, and there was no significant interaction with group or condition. See Figures 4–6 for summary of MRT data presented in this section.

Discussion

In lateralization analyses, we found the expected pattern of results for NT adults, consistent with pseudoneglect. Adults with ADHD showed the same pattern of lateralization of attention as NT adults.

There was no evidence to support the rightward bias resulting in longer MRT in the LVF in the ADHD group.

We found increased MRT and RTV in adults with ADHD relative to NT adults and a significant improvement in both groups across both measures under the fast/incentive condition of the Fast Task. The difference between adults with ADHD and NT adults was larger in the slow/no-incentive condition, than in the fast/incentive condition. These findings are in line with results of a recent meta-analysis investigating MRT and RTV in adults with ADHD [34]. Our results from MRT and RTV analyses showing improvement in the fast/incentive condition in the ADHD group might be linked to theories and results, including from Fast Task, indicating disturbed arousal as the source of task-unrelated activity leading to decreased cognitive performance [17,44]. The fact that performance is improved under more optimal arousal state in the fast/

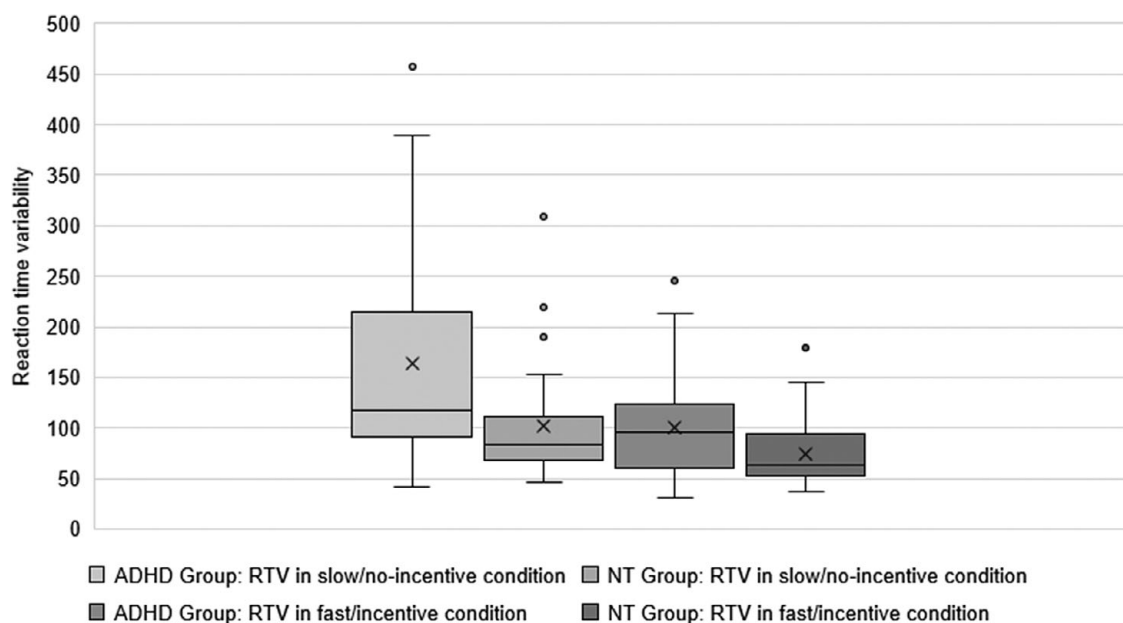


Figure 3. Boxplots showing reaction time variability (RTV) data from the slow/no-incentive and the fast/incentive condition of the Fast Task in the group of adults with ADHD and the neurotypical (NT) group. Boxes represent interquartile range with the median and mean (x). Whiskers indicate the maximum and minimum values (excluding the outliers which are represented by the dots). Abbreviations: ADHD, attention-deficit/hyperactivity disorder; NT, neurotypical; RTV, reaction time variability.

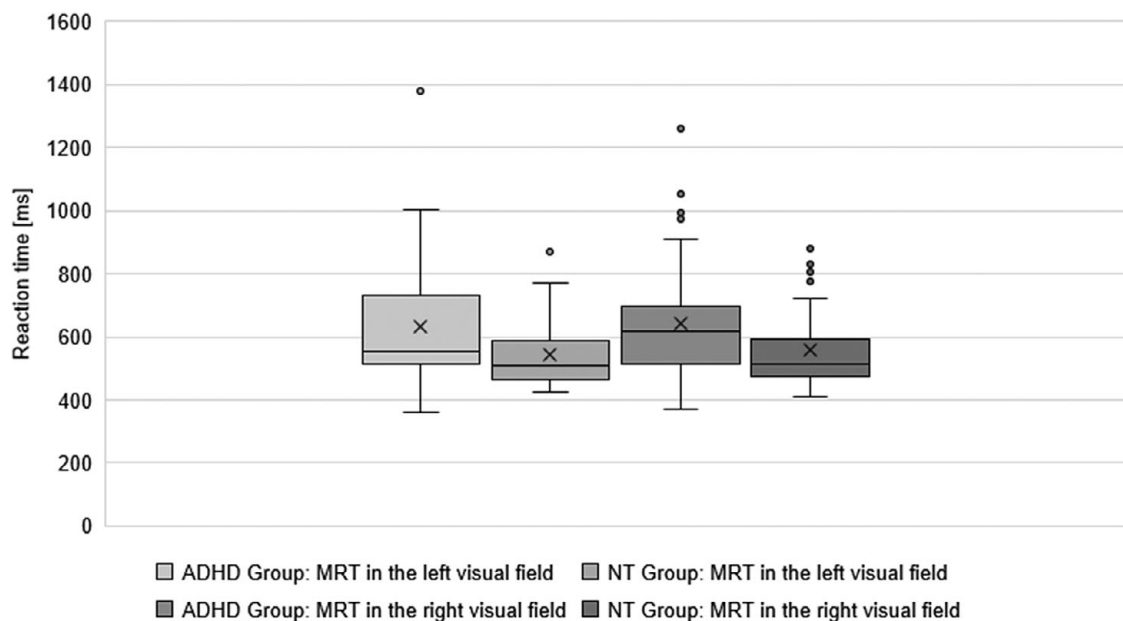


Figure 4. Boxplots showing mean reaction time (MRT) data from the left and right visual field in the slow/no-incentive condition of the Fast Task in the group of adults with ADHD and the neurotypical (NT) group. Boxes represent interquartile range with the median and mean (x). Whiskers indicate the maximum and minimum values (excluding the outliers which are represented by the dots). Abbreviations: ADHD, attention-deficit/hyperactivity disorder; MRT, mean reaction time; NT, neurotypical.

incentive condition suggests that internal processes became more task-oriented.

Our lateralization findings stand in contrast with some previous studies investigating hemispheric and visual field effects in people with ADHD. There are several factors that might account for this discrepancy. Previous studies focused on children with ADHD, and only one involved young adults (college students) [15]. Another study used MRT to evaluate rightward bias in ADHD and identified an increased lateralized interference effect (i.e., a difference between congruent and incongruent trials in the RVF), but found that

reaction time data for target position showed differences only in response times between central versus peripheral targets, but not between LVF versus RVF targets [28]. Some earlier studies used cancellation or line bisection tasks, which focus on omission errors rather than reaction time [14,15]. These differences might account for the fact that we did not find the expected rightward bias (LVF-slowness). A closer scrutiny of the older studies reveals that some of the boys diagnosed with ADHD in fact made extreme line dissection errors in the opposite direction as expected (consistent with leftward bias) [14]. In a study involving adults with ADHD, the

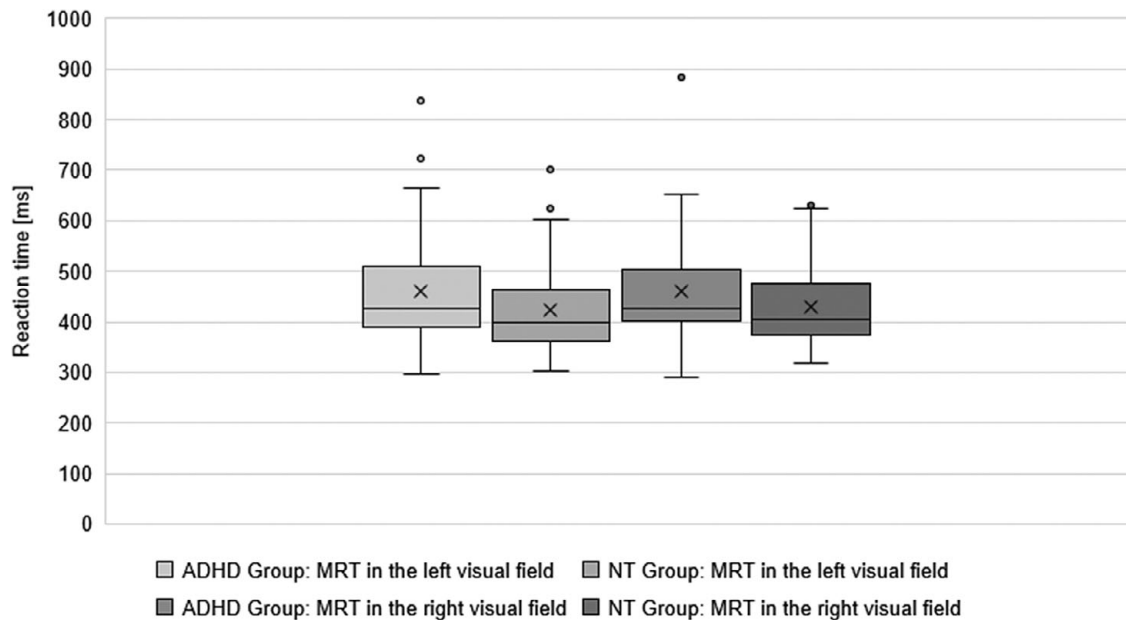


Figure 5. Boxplots showing mean reaction time (MRT) data from left and right visual field in the fast/incentive condition of the Fast Task in the group of adults with ADHD and the neurotypical (NT) group. Boxes represent interquartile range with the median and mean (x). Whiskers indicate the maximum and minimum values (excluding the outliers which are represented by the dots). Abbreviations: ADHD, attention-deficit/hyperactivity disorder; MRT, mean reaction time; NT, neurotypical.

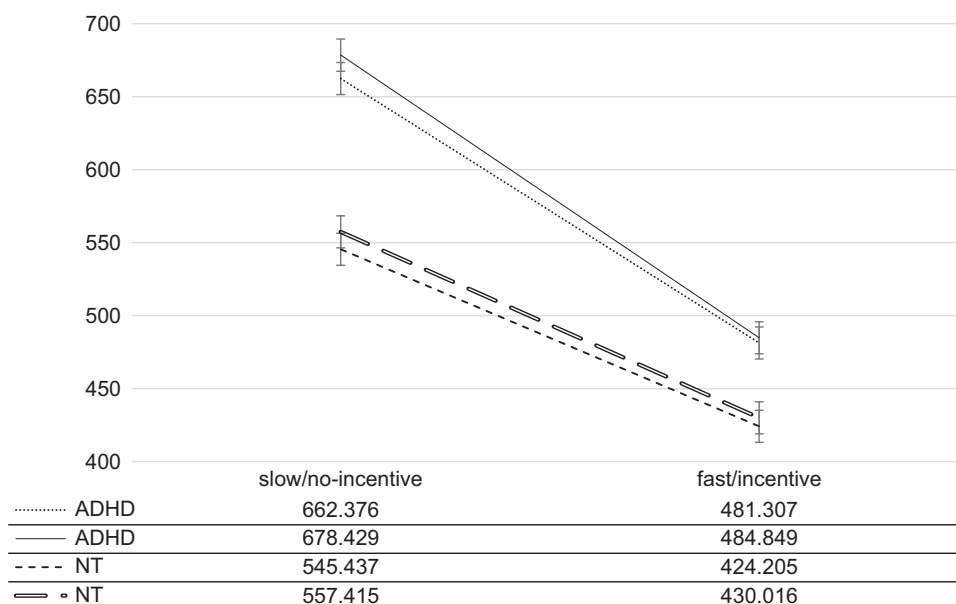


Figure 6. Mean reaction time in milliseconds in the group of adults with ADHD and the neurotypical group (NT) between the slow/no-incentive condition and the fast/incentive condition in the right visual field (RVF) and the left visual field (LVF). Error bars represent standard error. Abbreviations: ADHD, attention-deficit/hyperactivity disorder; LVF, left visual field; NT, neurotypical; RVF, right visual field.

case-control difference in LVF omission errors was only observed in a letter cancellation task and not in a shape cancellation task, suggesting a possible confounding by undiagnosed dyslexia [15].

As more studies involving samples of adults with ADHD are lacking, we can only speculate whether the behavioral manifestations of spatial neglect in people with ADHD simply normalize with age. Given a large overall slowing in MRT in adults with ADHD, a left-hemispheric disturbance may partially account for processing speed deficits and attentional lapses in the RVF. Future research on lateralization of attention in adults with ADHD could investigate

whether the underlying mechanisms leading to pseudoneglect in adults with ADHD is also no different to NT individuals. Below we offer a simple working hypothesis based on some recent findings regarding the default mode network (DMN).

The DMN includes nodes that are in both the left and the right hemisphere, but neuroimaging research suggests that this network is partially left-lateralized [45–47]. The DMN consists of interconnected cortical regions, including ventromedial prefrontal cortex and posterior cingulate cortex, which are activated (positively correlated) during rest and deactivated (anticorrelated) in response

to attentional task demands [48]. Individuals with ADHD have disturbed DMN connectivity leading to hyperactivation of the DMN during cognitive tasks [49], which results in a negative influence on task performance measures [50]. Such “DMN interference” [51] has been demonstrated in adults with ADHD [52] and interferes with normal vigilance as reflected in increased MRT [51,53]. Crucially, it has been found that increased activity in the DMN found in people with ADHD is lateralized to the left hemisphere during cognitive task performance [54] and that the activity in the left-lateralized areas of DMN in people with ADHD is highest in tasks using slow event rates [55]. Following this interpretation, overactivity of the DMN in the left hemisphere might lead to interference with on-task activity, resulting in poorer performance in the RVF. Moreover, the slow/no-incentive condition of the Fast Task is designed to induce low-arousal state and is reliably regarded by study participants as boring [32,37], and both low arousal and the feeling of boredom are strongly correlated with increased DMN activation [24,56,57]. To investigate whether DMN might play a role in lateralization of attention in adults with ADHD, a replication of our study in an fMRI scanner would be necessary.

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Conflict of Interest. Professor Asherson has received funds for consultancy on behalf of King’s College London to Shire, Eli-Lilly, and Novartis, regarding the diagnosis and treatment of people with attention-deficit/hyperactivity disorder (ADHD); has received educational/research awards from Shire, Eli-Lilly, Novartis, Vifor Pharma, GW Pharma, and QbTech; and was speaker at sponsored events for Shire, Eli-Lilly, and Novartis. All funds are used for studies of people with ADHD. The other authors report no conflicts of interest.

Data Availability Statement. The datasets generated in this study are available from the corresponding author on reasonable request.

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