

Hemispheric Functioning in Children With Subtypes of Attention-Deficit/Hyperactivity Disorder

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Objective: The authors investigated line bisection performance in children with Attention-Deficit/Hyperactivity Disorder (AD/HD) subtypes. Previous research with neurotypical children found a rightward bias with right-hand use and a leftward bias with left-hand use; however, research with AD/HD participants has failed to similarly measure the effects of hand use, which was the focus of this study. **Method:** Line bisection was used to measure differences in right hemisphere functioning in children (7 to 12 years) with AD/HD-I and AD/HD-C. **Results:** Initial AD/HD group findings (without subtype differentiation) replicated previous research. However, further subtype analyses showed that the ADHD-I and ADHD-C groups perform significantly differently. Specifically, the ADHD-I group showed a leftward bias, irrespective of hand use, and the ADHD-C group showed a rightward bias, irrespective of hand use. **Conclusion:** These findings suggest that the subtypes represent two distinct disorders and that, unlike ADHD-C, ADHD-I may not be the result of right hemisphere dysfunction. (*J. of Att. Dis.* 2006;10(1)20-27)

Keywords: *line bisection; ADHD-I; ADHD-C; hand use; frontostriatal*

Introduction

Attention-Deficit/Hyperactivity Disorder (AD/HD) is a neurodevelopmental disorder characterized by three main features—inattention, hyperactivity, and impulsivity (American Psychiatric Association, 2000)—and is often accompanied by behavioral, emotional, or learning problems (R.T. Brown et al., 2001). AD/HD affects between 4% and 12% of the general population of 6- to 12-year-olds (R.T. Brown et al., 2001), and between 30% and 60% of children who develop AD/HD will continue to display symptoms in adulthood (Mannuzza, Klein, & Moulton, 2003).

The *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text revised; *DSM-IV-TR*) includes descriptions of three subtypes of AD/HD; ADHD-Combined Type (ADHD-C), ADHD-Predominantly Inattentive Type (ADHD-I), and ADHD-Hyperactive-Impulsive Type (American Psychiatric Association, 2000).

However, recent imaging and behavioral studies indicate that the disorder may more accurately include two subtypes: ADHD-C (incorporating both the ADHD-C and ADHD-Hyperactive-Impulsive subgroups) and ADHD-I. For example, using magnetic resonance imaging (MRI), Farmer (2002) reported that children with ADHD-I had smaller right parietal and bilateral dorsolateral region volumes and a larger brainstem area and children with ADHD-C had a smaller left parietal and right dorsolateral region when compared with healthy control children. Functionally, ADHD-C participants performed more poorly on the Wisconsin Card Sorting Test (WCST) than ADHD-I participants. The WCST is believed to be a measure of the ability to shift response set, monitor performance, and respond to feedback (Grodzinsky & Diamond,

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1992) and task performance is associated with neural networks within the prefrontal cortex (Monchi, Petrides, Petre, Worsley, & Dagher, 2001). Differential task performance on a task thought to engage the prefrontal cortex is further support that there may be structural and functional differences between the two subgroups.

In a study of comorbidity, Weiss, Worling, and Wasdell (2003) found that children diagnosed with ADHD-I displayed more internalizing disorders and learning disabilities than children with ADHD-C. In addition, these children were 2 to 5 times more likely to have speech and language problems, suggesting that different regions of the brain may be implicated in the development of ADHD-I and ADHD-C (Weiss et al., 2003). Consistent with these recent research findings, this study will therefore address AD/HD as a disorder of two subtypes.

The etiology of AD/HD is still largely unknown, despite many attempts to find the cause, including early suggestions of a minimal brain dysfunction (Lubar, 1991) and the notion that one's diet may contribute to the development of the disorder (Colquhoun, 1994; Feingold, 1975). However, evidence is growing to support the idea that it is mainly the right hemisphere in individuals with AD/HD (with no differentiation between subtype) that is dysfunctional (Heilman, Voeller, & Nadeau, 1991; Sheppard, Bradshaw, Mattingley, & Lee, 1999), which is partially based on the observations that the symptoms of AD/HD are similar to those seen in patients with acquired right hemisphere lesions (Mesulam, Waxman, Geschwind, & Sabin, 1976). Further evidence of the involvement of the right hemisphere in the development of AD/HD comes from functional neuroimaging (Bench et al., 1993) and neuropsychological (Riccio, Reynolds, Lowe, & Moore, 2002) studies reporting right hemispheric dominance for attention. Furthermore, in a functional magnetic resonance imaging (fMRI) study of AD/HD in children, Rubia et al. (2001) reported that difficulties in focusing and sustaining attention were specifically attributed to underactivity of the frontostriatal regions in the right hemisphere.

One popular tool that is often used to quantify right hemisphere dysfunction is the line bisection task, which requires participants to bisect a horizontal line into two equal parts. Studies with clinical samples, including patients with right hemisphere damage, have been widely used to assess the role that the right hemisphere plays with respect to visuospatial tasks (Burnett-Stuart, Halligan, & Marshall, 1991; Clarke, 2001; Voeller & Heilman, 1988). Wilkinson and Halligan (2002) studied the performance of patients with left and right hemispheric damage on a line bisection task and found that patients with right hemisphere damage had greater difficulty with allocation of spatial attention than left

hemisphere damaged patients, and tended to bisect lines with a rightward bias.

In comparison with clinical samples, neurotypical adults tend to bisect lines to the left of center, irrespective of hand use (Hausmann, Ergun, Yazgan, & Güntürkün, 2002; McCourt & Garlinghouse, 2000; McCourt & Jewell, 1999). This phenomenon has been labeled "pseudoneglect" (Bowers & Heilman, 1980) and has been attributed to the differential roles that the left and right hemispheres play with respect to the allocation of spatial attention, with the right hemisphere having a stronger involvement with regard to visuospatial tasks than the left hemisphere (Heilman & Van Den Abell, 1980). This hemispheric dominance arises because whereas the left hemisphere predominantly directs attention to the right visual hemispace, the right hemisphere is assumed to direct attention to both sides of visual space (although the contralateral left side tends to be favored; Failla, Sheppard, & Bradshaw, 2003; Heilman & Valenstein, 1979; Mesulam, 1981). The findings of a number of studies support the involvement of the right hemisphere in spatial attention (Mapstone et al., 2003; Weintraub & Mesulam, 1987) and, as a consequence, for the task of bisecting horizontal lines (Hausmann et al., 2002).

Hausmann, Waldie, and Corballis (2003) studied neurologically normal children (aged 10 to 12 years) to determine if the same bias that was reported in healthy adults (Hausmann et al., 2002) was present in child and adolescent participants. The researchers found that although children showed the same leftward bias as adolescents and adults when bisecting lines with their left hand, when using their right hand, the children showed a rightward bias. Hausmann, Waldie, and Corballis (2003) suggested that this symmetrical neglect was due to an immature corpus callosum in children, which resulted in the two cerebral hemispheres operating relatively independently for some aspects of visuospatial attention.

Hand use has been emphasized as an important variable (Hausmann et al., 2002). Each hand is primarily controlled by the contralateral cerebral hemisphere. According to the Activation model (Kinsbourne, 1970), utilization of the left and right hands will activate the right and left hemispheres, respectively. Due to the underlying dominance of the right hemisphere in spatial attention (Failla et al., 2003; Heilman & Valenstein, 1979; Mesulam, 1981), an activation of the right hemisphere following left hand use might result in a larger leftward bias compared with a left hemisphere activation following right hand use. A stronger left bias using the left hand has been shown in several studies (Brodie & Pettigrew, 1996; Hausmann et al., 2002; McCourt, Freeman, Tahmahkera-Stevens, & Chaussee, 2001). However, due to the fact that

the leftward bias was still present when the right hand was used, an interhemispheric transfer of spatial information was believed to occur from the visuospatially dominant right hemisphere to the motor region of the left hemisphere, which controls the right hand (Failla et al., 2003; Hausmann, Waldie, & Corballis, 2003). This transfer most probably occurs via the corpus callosum. The relevance of the corpus callosum in line bisection has been shown directly in studies investigating patients with resection or damage of the corpus callosum (Corballis, 1995; Hausmann, Corballis, & Farbi, 2003; Kashiwagi, Kashiwagi, Nishikawa, Tanabe, & Okuda, 1990).

Similar to neglect patients with right hemispheric damage (Burnett-Stuart et al., 1991; Clarke, 2001; Voeller & Heilman, 1988), individuals with AD/HD show a strong rightward bias when bisecting horizontal lines, presumably as a result of a disturbance in the right frontal lobe network. In a study using a computerized line bisection task, Sheppard et al. (1999) presented children with unmedicated AD/HD (aged 8 to 12 years) with lines of varying length on a computer screen and instructed these participants to use a response box to move a cursor along each line toward the judged midpoint. The cursor was moved to the left by using the left index finger on the left response button and to the right by using the right index finger on the right response button. Sheppard et al. (1999) found that children with AD/HD (with no differentiation between subtypes) bisected lines with a rightward bias, whereas healthy control children showed a slight leftward bias, and suggested that the difference in bias between AD/HD and control participants resulted because children with AD/HD perceived the left side of the line to be slightly shorter or less noticeable than the right as a result of reduced ability to direct attention to the left side of space. However, the lateralized spatial deficit in AD/HD could be attributed to a higher level of left hemispheric activation resulting in the rightward shift of attention, which could in turn produce a slight left hemispace neglect, similar to that seen in patients with right hemispheric damage (Wilkinson & Halligan, 2002).

A number of studies have been conducted to investigate which specific right hemispheric structure is predominately involved in line bisection performance, with varying results. Fink, Marshall, Weiss, Toni, and Zilles (2002) used fMRI with healthy adult participants and reported that, as one may expect of a task involving visuospatial attention, the superior parietal cortex was activated during task performance. However, activation of the frontostriatal region has also been found for tasks that require visuospatial attention and specifically line bisection discrimination. Using single photon emission computer tomography (SPECT) and normal healthy

adults, Marshall et al. (1997) found an increase in regional cerebral blood flow in the right dorsolateral prefrontal cortex, as well as the superior temporal lobe, during perceptual line bisection task performance.

If AD/HD is the result of a dysfunctional right hemisphere, as suggested by Heilman et al. (1991) and Sheppard et al. (1999), and the line bisection task employs the right hemisphere dorsolateral prefrontal cortex (Marshall et al., 1997), we would expect participants with AD/HD to show a rightward bias, whereas non-AD/HD participants would show a symmetrical neglect based on the Activation model (Kinsbourne, 1970). Furthermore, based on the reported structural and functional differences between the subtypes of AD/HD (Farmer, 2002), it was further predicted that differences between the ADHD-I and ADHD-C groups would exist on line bisection task performance. Specifically, due to the reported involvement of the right dorsolateral prefrontal region during line bisection performance (Marshall et al., 1997) and the finding that this area is smaller in children with ADHD-C (when compared with healthy control children; Farmer, 2002), it was predicted that these children would show a rightward bias, irrespective of hand use due to the under-activation of the right dorsolateral prefrontal region and consequent reduced attention being directed to the left side of space (Sheppard et al., 1999). Children with ADHD-I were reported to have smaller bilateral dorsolateral prefrontal volume (Farmer, 2002); therefore, for this group, it was predicted that the normally dominant right dorsolateral region would take on a central role in task performance, resulting in a bias toward the left hemisphere (Sheppard et al., 1999).

In this study, manual line bisection performance was investigated in children with ADHD-I and ADHD-C who were matched with a neurotypical control group on the basis of gender, age, and cognitive ability. By measuring the effects of hand use, this study aimed to provide further information with regard to hemispheric functioning in children with ADHD-I and ADHD-C. Consistent with Sheppard et al. (1999), we expected to see an overall rightward bias when both ADHD-I and ADHD-C were treated as a collective disorder (AD/HD). We also expected to see line bisection differences according to subtype, as outlined above, thus providing further evidence that AD/HD is not a homogeneous disorder.

Method

Participants and Materials

Participants were recruited from nine schools in Auckland, New Zealand. All procedures were approved

Table 1
Mean Age (*SD*), Mean Wechsler Abbreviated Scale of Intelligence Score (*SD*), and Number of Participants With a Right-Hand Preference (RHP) for the ADHD-I, ADHD-C, and Control Groups

Group	Mean Age (<i>SD</i>)	Mean IQ (<i>SD</i>)	RHP	Brown ADHD-I Score	Brown ADHD-C Score
ADHD-I	8.59 (2.02)	100.80 (17.03)	12	62	—
ADHD-C	8.92 (2.22)	101.47 (16.29)	14	—	66
Control	8.86 (2.00)	100.27 (11.60)	14	—	—

Note: Brown ADHD-I and ADHD-C mean scores are presented for ADHD-I and ADHD-C participants, respectively. Each group was made up of 1 female and 14 males.

by the University of Auckland Human Participants Committee.

Children with and without AD/HD were recommended as potential participants by specialists at each school. For children who were selected on the basis of suspected or diagnosed AD/HD, their symptoms were confirmed by administering a continuous performance task (Integrated Visual and Auditory—Continuous Performance Task; IVA-CPT; Sandford & Turner, 2000) and the Brown ADD Scales (T.E. Brown, 2001). The IVA-CPT is a computer-based program designed to identify symptoms of AD/HD and aid differential diagnosis of the subtypes of AD/HD (Sandford & Turner, 2000). The Brown ADD Scales are 50-item questionnaires given to parents and teachers and are designed to elicit information with regard to a child’s functioning in the home and school settings (T.E. Brown, 2001; mean normative scores = 50, standard deviation = 10). The participants who made up the control group had their non-AD/HD status confirmed using the IVA-CPT.

A total of 45 children (aged 7 to 12 years, mean age = 8.79 years, *SD* = 2.04 years) participated in this study: 15 were classified as ADHD-I (AD/HD without hyperactivity or impulsivity—predominantly inattentive type), 15 were classified as ADHD-C (AD/HD with hyperactivity and impulsivity), and 15 served as controls. The three groups were matched for gender, age, and level of cognitive ability.

The Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 2000) was used to measure cognitive ability, and handedness was assessed using the Edinburgh Handedness Inventory (EHI; Oldfield, 1971). The mean age, WASI, and hand preference scores for the total sample (*N* = 45) are presented in Table 1. For the ADHD-I and ADHD-C groups, mean Brown ADD Scale scores are also presented.

Stimuli and Procedures

Each experimental session lasted approximately 75 minutes and took place in a quiet room on the school grounds. Following the administration of the assessment

tools, the line-bisection task was administered. This task was identical to that used by Hausmann et al. (2002; Hausmann, Waldie, & Corballis, 2003) and was made up of 17 horizontal black lines ranging in length from 100 to 260 mm (in 20.0 mm intervals) presented on a sheet of white paper (A4 size). The mean length of all lines was 183.5 mm. Seven lines appeared in the middle of the sheet (mean length 20.0 mm), 5 lines had a midpoint in the left visual field (mean length 17.2 mm), and 5 lines had a midpoint in the right visual field (mean length 17.2 mm). Biases in line bisection were calculated by measuring the deviation from the midpoint in millimeters (mm) to 0.5 mm accuracy. Positive numbers indicate a rightward bias and negative numbers indicate a leftward bias.

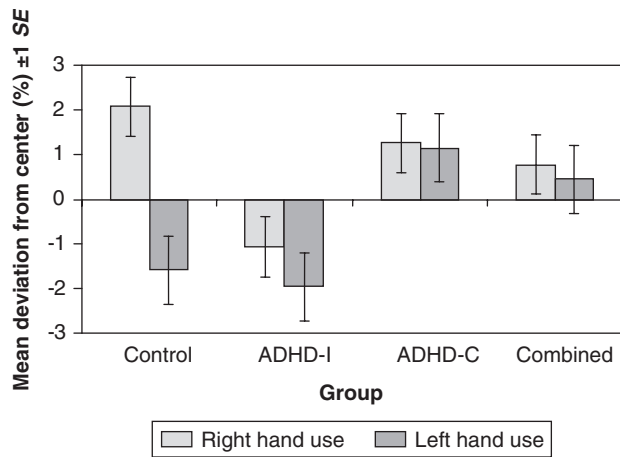
Results

A split plot analysis of variance (ANOVA) was performed on the bisection scores with group (ADHD-I, ADHD-C, Control) as a between-subjects variable and hand use (left, right) as a within-subjects variable. The analysis found a main effect for group, $F(1, 42) = 5.12, p = .029$. Irrespective of hand use, the ADHD-I group showed a leftward bias ($M = -1.51 \text{ mm}, SD = 3.46$), whereas the ADHD-C group showed a bias toward the right ($M = 1.20 \text{ mm}, SD = 2.87$). Pairwise comparisons (using Bonferroni correction) revealed this to be significant ($p < .001$).

A significant interaction was revealed between group and hand use, $F(2, 42) = 4.337, p = .019$. Simple effects tests showed that for the control group, there was a significant difference in bias when using the left hand ($M = -1.58 \text{ mm}, SD = 2.42$) versus the right hand ($M = 2.07 \text{ mm}, SD = 2.22, p = .002$). However, there was no difference in performance between the left and right hands for the ADHD-I or ADHD-C groups ($p > .05$).

The data from ADHD-I and ADHD-C groups were also combined to create a clinical group ($n = 30$), and Figure 1 shows that this group displayed an overall rightward bias when bisecting lines with both the right and left hands. A paired-samples *t* test found no difference in biases as a function of hand use, $t(29) = 0.218, p = .829$

Figure 1
Mean Deviation From Center (mm) and
Standard Error Bars as a Function of Hand
Use for the Control, ADHD-I, ADHD-C,
and AD/HD Combined Groups



Note: Positive numbers indicate a rightward bias and negative numbers indicate a leftward bias.

(right hand: $M = 0.77$ mm, $SD = 3.38$; left hand: $M = 0.45$ mm, $SD = 4.25$).

Discussion

In this study, children with and without AD/HD (aged 7 to 12 years) performed a manual line bisection task designed to use spatial attention for which the right dorsolateral prefrontal region (Marshall et al., 1997) and the superior parietal cortex (Fink et al., 2002) are thought to be involved. Neurotypical children showed a symmetrical neglect—that is, a leftward bias with left hand use and a rightward bias when the right hand was used to bisect horizontal lines, consistent with other studies investigating children with the line bisection paradigm (Hausmann, Waldie, & Corballis, 2003; Roeltgen & Roeltgen, 1989; Sheppard et al., 1999). This pattern of biases has been attributed to an immature corpus callosum (Bradshaw, Spataro, Harris, Nettleton, & Bradshaw, 1988), whereby when the right cerebral hemisphere (activated by the left hand) is used, the contralateral left side of space is favored, resulting in a bias toward the left, and vice versa, consistent with Kinsbourne's (1970) activation model.

Moreover, the results of this study replicated previous findings of an overall rightward bias in line bisection in children diagnosed with AD/HD (Sheppard et al., 1999). Sheppard and colleagues suggested that the rightward bias noted in unmedicated children with AD/HD resulted

because these children had a reduced ability to direct attention to the left side of space, consistent with the right hemisphere dysfunction theory of AD/HD (Casey et al., 1997; Sandson, Bachna, & Morin, 2000; Stefanatos & Wasserstein, 2001), and attributed this to low levels of neural activity in the prefrontal structures of the right hemisphere and subsequent increased level of left hemispheric activation in children with AD/HD (Sheppard et al., 1999). However, in this study, this bias tendency only appeared when the results of both AD/HD subgroups are combined. When analyzing the line bisection results for each subgroup separately, we found a significant difference in the way the ADHD-I and ADHD-C groups bisected lines, with the ADHD-I group showing a leftward bias, irrespective of hand use, and the ADHD-C group showing a rightward bias, also when using either hand. The finding that the two subtypes differ in their functional cerebral organization supports the view that ADHD-I and ADHD-C represent two distinct disorders (Farmer, 2002; Milich, Balentine, & Lynam, 2001; Weiss et al., 2003). The right hemisphere dysfunction theory was only supported with findings from the ADHD-C group. The line bisection pattern in the ADHD-I group strongly suggests an underlying dysfunction that differs from that of the ADHD-C group.

It has been suggested that AD/HD is accompanied by an *underactivation* in frontostriatal structures of the right hemisphere (Bradshaw & Sheppard, 2000; Bush et al., 1999; Rubia et al., 2001). This underactivation might result in neglect of the left side of space, which might in turn shift spatial attention toward the right hemisphere (Sheppard et al., 1999) and thus lead to a robust rightward bias when bisecting horizontal lines. However, this model only fits to the results of the ADHD-C group. The well-known leftward bias (pseudoneglect) in healthy adult controls, which is similar to the bias of the ADHD-I group, is assumed to be the result of a right hemispheric activation based on the visuospatial character of the line bisection task (Fink et al., 2002; Marshall et al., 1997). Thus, we might conclude that the consistent leftward bias in the ADHD-I group might be the result of an overactivation of right frontostriatal structures, which increases the attention toward the opposite left side.

An alternative explanation is that the left bias found in the ADHD-I group is based on a dysfunction of the left hemisphere. Evidence of a left hemisphere dysfunction has been previously noted by MRI studies that have investigated the cerebral volume in children with AD/HD without differentiation between subtypes (Mostofsky, Cooper, Kates, Denckla, & Kaufmann, 2002; Overmeyer et al., 2001). These studies reported that in addition to a bilateral reduction in frontal gray matter, children with AD/HD showed a significant reduction in frontal white matter localized in the left hemisphere. Further evidence

of a potential left hemisphere impairment in AD/HD comes from studies showing decreased regional cerebral blood flow (rCBF) in frontal regions in the left hemisphere in patients with AD/HD (Lou, Henriksen, & Bruhn, 1984; Lou, Henriksen, Bruhn, Borner, & Nielsen, 1989) as well as a positron emission tomography study showing a decrease in the metabolic activation of the left anterior frontal lobe in boys with AD/HD during an auditory continuous performance task (Zametkin et al., 1993). Together, these findings suggested that a left hemisphere impairment was partially related to AD/HD; however, because AD/HD was previously treated as a homologous disorder by these researchers (Lou et al., 1984; Lou et al., 1989; Mostofsky et al., 2002; Overmeyer et al., 2001), it is difficult to determine whether the left hemispheric anomaly is related to ADHD-I, ADHD-C, or both.

Although we cannot decide between both hypotheses on the basis of this study, the results clearly suggest that the mechanisms underlying AD/HD subtypes differ fundamentally between ADHD-I and ADHD-C. Although both ADHD-I and ADHD-C are characterized by symptoms of inattention, the presence of a hyperactive/impulsive component in ADHD-C that is absent in ADHD-I may indicate that different brain regions are implicated. The inattention and defective response inhibition observed in children with AD/HD has been attributed to frontal lobe and striatal dysfunction (Heilman et al., 1991). In contrast, hyperactivity might be a consequence of a smaller cerebellum that has been noted in children with AD/HD compared with non-AD/HD children (Castellanos et al., 2001; Kim, Lee, Shin, Cho, & Lee, 2002). The cerebellum receives input from the primary and secondary motor cortex, brain stem motor nuclei, and the somatosensory and vestibular systems and is primarily responsible for the regulation of movement (Pinel, 1997). It is possible that these studies included predominantly ADHD-I or ADHD-C participants (although subtype analyses were not performed) and that the neurological differences noted may represent one subtype or the other.

A further factor to consider is the involvement of the interacting visual systems employed during the manual line bisection task and the behavioral response that was required from participants. Two neural pathways are involved in processing visual information: the ventral stream and the dorsal stream (Ungerleider & Mishkin, 1982). The ventral stream flows from the primary visual cortex to the inferotemporal cortex and is primarily involved in transforming visual information into object recognition and perceptual representations. The dorsal stream, which projects from the primary visual cortex to the posterior parietal cortex, uses information about an object located in extrapersonal space to direct behavioral

interactions, such as a reach, with that object (Goodale & Humphrey, 2001). The ventral and dorsal streams then project to the orbitofrontal (Merigan & Maunsell, 1993; Wilson, Scalaidhe, & Goldman-Rakic, 1993) and dorso-lateral prefrontal (Barbas & Pandya, 1989) cortices of the prefrontal lobe, respectively. Due to the goal-directed reaching component required of these participants, the posterior parietal cortex of the dorsal stream (specifically, the intraparietal sulcus) was involved in manual line bisection task performance (Kalaska, Cohen, Hyde, & Prud'homme, 1989). Therefore, contrary to previous research that implicated the right frontostriatal system in the development of AD/HD (Durstun et al., 2003; Rubia et al., 2001), the abnormal biases noted in these AD/HD participants may actually indicate an impairment of the posterior parietal cortex in these individuals. To test for this, a similar task that minimizes the reaching component and instead uses perceptual abilities, similar to the Landmark judgment-based test employed by Fink et al. (2002), could be used instead. Such a task may help to highlight further differences between the two subtypes of AD/HD and therefore warrants further investigation.

The importance of treating AD/HD as a heterogeneous disorder was highlighted through these findings of differential line-bisection performance by participants with ADHD-I and ADHD-C. Through the recognition of ADHD-I and ADHD-C as two distinct and independent subtypes of AD/HD, we may be better able to provide the most appropriate and beneficial methods of remediation, so that those with either subtype are able to function to the best of their ability.

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