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# The Relationship between Cerebral Hemisphere Volume and Receptive Language Functioning in Dyslexia and Attention-**Deficit/Hyperactivity Disorder**

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## Abstract

Because poor comprehension has been associated with small cerebral volume and there is a high comorbidity between developmental dyslexia, ADHD, and specific language impairment, the goal of this study was to determine if cerebral volume is reduced in dyslexia and ADHD in general, as some suggest, or if reduction in volume corresponds with poor receptive language functioning regardless of diagnosis. Participants included 46 children with and without dyslexia and ADHD, ages 8-12 years. Results indicated that cerebral volume was comparable between those with and without dyslexia and ADHD overall. However, when groups were further divided into those with and without receptive language difficulties, children with poor receptive language had smaller volumes bilaterally as hypothesized. Nonetheless, the relationship between cerebral volume and receptive language was not linear; rather, our results suggest small volume is associated with poor receptive language only in those with the smallest volumes in both dyslexia and ADHD.

#### **Keywords**

Dyslexia; Attention-Deficit/Hyperactivity Disorder; Magnetic Resonance Imaging

Developmental dyslexia and specific language impairment are common neurodevelopmental disorders that share about a 30% comorbidity<sup>1</sup>. Hence, of particular interest to this paper is whether the reduction in cerebral hemisphere volume occasionally seen in dyslexia is related to poor receptive semantic/syntactic functioning. This issue is pertinent as research suggests individuals with developmental language disorder present with smaller cerebral volume than controls. For example, Preis and colleagues<sup>2</sup> found a 7% forebrain reduction in developmental language disorder, and Herbert and colleagues<sup>3</sup> found developmental language disorder is associated with a smaller cerebral cortex. As many believe specific language impairment is due to some form of generalized deficit, rather than one limited to language per se when receptive language is affected  $^{3-9}$ , it is not surprising that bilateral cerebral hemisphere volume is reduced in this population  $^{10}$ . Consistent with this, intelligence often is at least mildly reduced in specific language impairment 10, and intellectual functioning is positively correlated with bilateral cerebral volume in general<sup>2</sup>, 11-15.

Specific language impairment tends to be diagnosed when children have unexplained oral language deficits that extend beyond their nonverbal intellect  $^{7, 16}$ . Although children with specific language impairment typically have deficits in the comprehension and/or expression of semantics, syntax and grammatical morphemes  $^{7, 16, 17}$ , many also have deficits in phonological processing, including phonological awareness and phonological short-term memory  $^{17-20}$ . In addition, children with specific language impairment often are poor readers, meeting most psychometric definitions of dyslexia, particularly when language problems continue into the school years  $^{16}$ .

Children with dyslexia commonly present with poor phonological processing  $^{21,22}$ , which may include deficits in phonological awareness  $^{23-26}$ , rapid retrieval of phonological material from long-term memory  $^{27-29}$ , and phonological short-term/working memory  $^{30-33}$ . The breadth and chronic nature of these problems has led some to suggest that dyslexia should be considered a developmental language disorder, where the central feature is poor phonological processing which affects word identification and spelling  $^{34,35}$ . In addition to poor phonological processing, deficits also have been found in speech perception, articulation, semantics, syntactic processing, and verbal memory in this population  $^{16,34,36,37}$ .

Given the overlap between dyslexia and specific language impairment, and given that both disorders present with a great deal of heterogeneity, what may be most important is the type of deficits seen. More specifically, deficits in phonological processing are associated with poor word identification, decoding, and spelling, whereas deficits in listening comprehension and other non-phonological linguistic skills are associated with poor reading comprehension <sup>12</sup>, <sup>34</sup>, <sup>36</sup>, <sup>38</sup>, <sup>39</sup>. This is true regardless of whether a child has been diagnosed with specific language impairment or dyslexia <sup>16</sup>. Because of these associations, Bishop and Snowling <sup>16</sup> proposed a two dimensional model of dyslexia and specific language impairment, with one dimension being phonological processing and the other being non-phonological linguistic skills including semantic, syntactic, and discourse-level processing. They suggested these two dimensions may be a better depiction of predictors of reading performance than the current dyslexia/specific language impairment classifications.

Recent work by Leonard and colleagues is consistent with this two dimensional model. When studying an adult dyslexia sample, Leonard and colleagues<sup>40</sup> found smaller cerebral hemisphere volume was associated with reduced listening comprehension, reading comprehension, and verbal intellect, whereas poor phonological processing and decoding but intact oral and written comprehension [called 'phonological dyslexia'] were associated with rightward cerebral asymmetry, leftward cerebellar asymmetry or symmetry, leftward asymmetry of the planum temporale, and duplication of Heschl's gyrus on the left. In subsequent studies they found a dissociation between phonological dyslexia and specific language impairment, with specific language impairment being associated with smaller, symmetrical structures in the perisylvian region and smaller cerebral hemisphere volume in general, and phonological dyslexia being associated with additional Heschl's gryi, larger language regions, and exaggerated planum asymmetries <sup>40-42</sup>. Although this research suggests dyslexia is associated with smaller hemisphere volume primarily when oral and written comprehension deficits are present, other research suggests hemisphere volume may be reduced in dyslexia in general <sup>43-45</sup>. The extent to which reduced cerebral volume in dyslexia is associated with poor non-phonological linguistic skills requires further examination.

The debate over the best way to conceptualize dyslexia and specific language impairment has relevance to the debate in the literature over the best way to define dyslexia. Several researchers suggest the discrepancy definition should be abandoned, with focus being placed solely on poor decoding ability<sup>23</sup>, <sup>46</sup>, <sup>47</sup>. This change in definition was suggested as poor readers with and without an IQ discrepancy are comparable in phonological awareness<sup>23</sup>, <sup>47</sup>, the 'core'

deficit in developmental dyslexia  $^{26}$ ,  $^{30}$ ,  $^{48}$ ,  $^{49}$ . Nonetheless, those who meet the traditional discrepancy definition may be more likely to have deficits limited to phonological processing and decoding skill whereas poor readers who do not have a discrepancy may be more heterogeneous as a group, including those who have phonological and non-phonological linguistic deficits  $^{16}$ ,  $^{34}$ . Hence, the latter group may be more likely to include individuals with smaller cerebral hemisphere volumes given the literature reviewed above. Furthermore, the two groups may differ slightly in genetic contributions. Whereas aspects of phonological processing have been linked to chromosome  $^{50}$ , non-phonological linguistic deficits have been linked to chromosome 19, particularly poor expressive language functioning  $^{51}$ . Clearly the best definition of dyslexia to use when conducting neurobiological research requires further examination.

Along with dyslexia and specific language impairment sharing a high comorbidity, dyslexia and Attention-Deficit/Hyperactivity Disorder (ADHD) share about a 15-40% comorbidity <sup>52</sup>, <sup>53</sup>, and ADHD and specific language impairment share about a 31-60% comorbidity <sup>1</sup>, <sup>54</sup>. In addition, several researchers have reported reduced cerebral hemisphere volume in ADHD, with a 3-8% reduction in cerebral volume being found <sup>55-59</sup>. However, a study by Filipek and colleagues <sup>60</sup> failed to find a reduction in cerebral hemisphere volume in ADHD. Non-phonological linguistic deficits are common in ADHD, including poor pragmatic language functioning <sup>61-63</sup>, reduced oral comprehension <sup>1</sup>, <sup>61</sup>, <sup>64</sup>, and poor syntax formation <sup>65</sup>. Nevertheless, limited research has been conducted to determine whether smaller cerebral volume in ADHD is related to worse non-phonological linguistic functioning.

The primary purpose of this project was to examine cerebral hemisphere volume in dyslexia and ADHD and the extent to which reduced volume in these disorders is related to poor receptive language functioning. Based upon prior literature suggesting smaller cerebral volume is associated with worse comprehension  $^{40}$ ,  $^{41}$ , it was hypothesized that cerebral hemisphere volume would be reduced in dyslexia and ADHD when weaknesses in receptive language were present as opposed to being reduced in dyslexia and ADHD in general. The second purpose of this study was to examine cerebral volume in relation to the two domains of linguistic functioning: phonological and non-phonological. Given the literature reviewed, it was hypothesized that cerebral volume would be positively correlated with non-phonological linguistic skills but there would be a limited relationship between cerebral volume and phonological skills.

## **Methods**

#### **Participants**

Approval was obtained from the Human Subjects Committee of the University of Georgia Institutional Review Board before the study commenced. Participants were recruited by a laboratory focused on dyslexia and ADHD. They included 10 children with dyslexia, 13 children with comorbid dyslexia and ADHD, 13 children with ADHD and 10 typically developing controls, ages 8 – 12 years. For the dyslexia group, participants were 90% Caucasian and 70% male. For the dyslexia/ADHD group participants were 100% Caucasian and 77% male. For the ADHD group, participants were 92% Caucasian and 77% male, and for the control group participants were 100% Caucasian and 50% male. Exclusionary criteria applied to all participants and included neurological disorder, psychiatric disorder (except ADHD), medical conditions (except allergies and asthma), and measured intelligence below 80. No child was on medication for ADHD on the day of testing per parent report.

**Dyslexia**—Dyslexia was defined following State of Georgia criteria for a Specific Learning Disability in reading. State criteria were consistent with the *Individuals with Disabilities Education Act* (IDEA) at the time of data collection and required at least a 20 point standard

score discrepancy between measured intelligence and academic achievement in reading, with reading being lower, which could not be accounted for by sensory or motor difficulties, inadequate educational opportunities or mental retardation<sup>66</sup>. State criteria have since changed when IDEA requirements for a learning disability were modified in 2004. For the purposes of this study, the discrepancy required was between measured intellect as assessed by the Wechsler Intelligence Scale for Children-Third Edition<sup>67</sup> (WISC-III) and word identification as assessed by the Reading subtest of the Wide Range Achievement Test-Third Edition<sup>68</sup> (WRAT-3) since poor word identification is the primary feature of developmental dyslexia.

The discrepancy definition was chosen over the poor reader definition for a few reasons. First, by using a discrepancy definition we have a more stringently-diagnosed group with which to test our first hypothesis. Second, many studies on the neurobiological basis of dyslexia utilize a discrepancy definition, facilitating comparison amongst studies. Third, those who meet the discrepancy definition may be more likely to have a genetic/neurobiological basis to their disorder <sup>69</sup>; poor readers without a discrepancy may be more likely to have a stronger environmental basis to their disorder <sup>70</sup>. Fourth, participants were recruited by means of a free, written psycho-educational report, and the State of Georgia criteria required use of a discrepancy definition at the time of data collection.

**ADHD**—ADHD was diagnosed through a multi-modal procedure using multiple informants. The process entailed a semi-structured clinical interview to verify DSM-IV criteria were met (Schedule for Affective Disorders and Schizophrenia for School-Age Children, updated with DSM-IV criteria<sup>71</sup>) as well as multiple questionnaires completed by the parents and teachers to ensure the level of attention problems, hyperactivity and/or impulsivity were of sufficient severity to warrant diagnosis. Parent and teacher questionnaires completed included the Child Behavior Checklist<sup>72</sup> (CBCL), the Child Behavior Checklist-Teacher Report Form<sup>73</sup> (TRF) and the Swanson, Nolan, and Pelham checklist<sup>74</sup> (SNAP). The process of diagnosis used has been shown to be reliable in previous research<sup>75</sup>.

Based upon the semi-structured interview and the questionnaires, 3 children had ADHD-Predominately Inattentive type (ADHD-PI) and 10 had ADHD-Combined type (ADHD-C) in the dyslexia/ADHD group, and 3 had ADHD-PI and 10 had ADHD-C in the ADHD group. ADHD severity was mild for those with ADHD and dyslexia/ADHD, and the two groups did not differ in ADHD severity as assessed by the questionnaires.

#### **Neuropsychological Assessment**

All participants underwent a battery of neuropsychological measures after informed consent was obtained from the parent and informed assent was obtained from the child. Receptive and expressive language functioning were evaluated with the Clinical Evaluation of Language Fundamentals-Revised (CELF-R). This test measures semantic and syntactic language functioning, although the latter is better represented by the Expressive Language composite score, whereas semantic functioning is represented in both the Receptive and Expressive Language composite scores. CELF-R Sentence Assembly was used as a measure of syntactic functioning, and CELF-R Recalling Sentences was used a measure of rote verbal short-term memory. WISC-III Vocabulary was used as a measure of semantic functioning, and WISC-III Digit Span was used as a measure of phonological short-term memory. Phonological awareness was assessed with the Elision subtest from the Comprehensive Test of Phonological Processing — Experimental Version (CTOPP). Rapid naming was assessed with the number/letter composite from the Rapid Automatized Naming test (RAN). Measures of academic achievement included the Wide Range Achievement Test-Third Edition (WRAT-3) and the Woodcock Reading Mastery Test — Revised (WRMT-R) Word Attack and Passage Comprehension subtests.

## **MRI** Acquisition

Magnetic Resonance Imaging (MRI) scans were conducted on a .6 Tesla scanner (Health Images, Atlanta, Georgia). The protocol utilized 15 3-D, gapless, 3.1mm slices [TR=51; TE=10 (prior to 9/23/95) or TE=13 (after 9/23/95)]. All scans were assessed by a board certified neurologist and found to be within normal limits.

#### **Cerebral Hemisphere Measurement**

Images were traced in the coronal plane using a digitizing tablet and the publicly available software program, Scion Image for Windows (Scion Corporation, 2000). This software program is the Windows-based version of NIH IMAGE. Published studies were used as guidelines to determine measurement parameters <sup>40, 81</sup>. Each hemisphere was traced on every 4<sup>th</sup> slice in the coronal plane, starting at the most anterior slice in which a hemisphere was detectable and continuing until it was no longer present caudally. Each hemisphere was measured separately. Measurements included all gray/white matter encompassed by the dura but excluded the ventricles; optic nerve, tract, and chiasm; corpus callosum; fornix; and septum pallusidum. Cavalieri's rule was used to correct for overprojection when calculating volume <sup>82</sup>.

An asymmetry ratio was calculated as prior researchers have revealed atypical asymmetry in those with dyslexia  $^{83}$  and those with specific language impairment  $^{41}$ . The following formula was used for the interhemispheric coefficient of asymmetry  $^{84}$ : Left-Right/[(Left+Right)\*0.5)]. A positive value indicates leftward asymmetry, and a negative value indicates rightward asymmetry.

## Results

## **Group Descriptive Data**

To ensure diagnostic groups differed where appropriate, those with dyslexia (dyslexia and dyslexia/ADHD) and without dyslexia (ADHD and controls) were compared using ANOVA on relevant descriptive data. The entire sample was analyzed again, comparing those with ADHD (dyslexia/ADHD and ADHD) and without ADHD (dyslexia and controls). This procedure was chosen instead of directly comparing the four groups as cerebral hemisphere volume was examined using a  $2 \times 2$  MANOVA, comparing those with and without dyslexia and ADHD. Those with and without dyslexia were comparable in age, handedness, Full-Scale IQ (FSIQ), and Performance IQ (PIQ). They differed in Verbal IQ (VIQ), F(1,44)=4.46, p < . 05, as is common in this population. When using chi-square they were comparable in gender and ethnicity. In terms of Index scores, groups were comparable in WISC-III Perceptual Organization and Processing Speed, but they differed in Verbal Comprehension [F(1,44)=3.92, p = .05 and Freedom from Distractibility [F(1,44)=7.16, p = .01]. As a result, VIO was used as a covariate in the 2 × 2 MANCOVA on hemisphere volume. In terms of academic achievement, those with and without dyslexia differed in all areas assessed: WRAT-3 Reading  $[\underline{F}(1,44)=46.24, p < .001]$ , Spelling  $[\underline{F}(1,44)=26.67, p < .001]$  and Arithmetic  $[\underline{F}(1,44)=15.82, p < .001]$ p < .001], and WRMT-R Word Attack [F(1,44)=35.38, p < .001] and Passage Comprehension [F(1,44)=28.83, p < .001]. In contrast, those with and without dyslexia were comparable on parent and teacher CBCL Attention Problems. See Table 1 for descriptive data.

In terms of those with and without ADHD, groups were comparable in age, race, gender, handedness, FSIQ, VIQ, and PIQ when using the statistical procedures described above. They also were comparable on the academic achievement measures. See Table 1. Groups differed significantly on the ADHD scales: CBCL Attention Problems,  $\underline{F}(1,42)=49.55$ ,  $\underline{p}<.001$  and TRF Attention Problems,  $\underline{F}(1,39)=9.75$ ,  $\underline{p}<.01$ .

## Cerebral Hemisphere Volume in Dyslexia and ADHD

Given the primary purpose of this study, children with and without dyslexia and ADHD were compared on right and left hemisphere cerebral volume and the asymmetry ratio using a  $2 \times 2$  MANCOVA with VIQ as the covariate. This approach was chosen as it allows for analysis of the interaction between dyslexia and ADHD, which was of interest given the high comorbidity between the two disorders. The omnibus main effects and interaction were not significant [Fs (3,39) < 1.0]. In addition, none of the univariate ANOVAs were significant.

Because the heterogeneity of dyslexia and ADHD could have lessened group differences, the relationship between cerebral volume, reading ability, and ADHD symptom severity was examined in the total sample. None of the correlations between size of the right and left hemispheres and WRAT-3 Reading, WRMT-R Passage Comprehension, and WRMT-R Word Attack were significant when using Pearson correlations, with all  $\underline{r}$ s < .10. The parent Swanson, Nolan, and Pelham checklist was used to examine symptoms of ADHD as it includes separate scales for inattention, hyperactivity, and impulsivity. In contrast to reading, bilateral hemisphere volume was moderately correlated with ADHD symptom severity, with smaller size being related to worse inattention [right  $\underline{r}$  = -.40,  $\underline{p}$  < .05; left  $\underline{r}$  = -.38,  $\underline{p}$  < .05], hyperactivity [right  $\underline{r}$  = -.41,  $\underline{p}$  < .05; left  $\underline{r}$  = -.41,  $\underline{r}$  < .05; left  $\underline{r}$ 

#### Receptive Language and Cerebral Hemisphere Volume

As a first step in determining the relationship between cerebral volume and receptive language in dyslexia and ADHD, all participants were divided into two groups: those with and without receptive language weaknesses. Children with below average CELF-R Receptive Language composite scores (i.e., below 85) were assigned to the poor receptive language group; those with average or better Receptive Language composites (i.e., 85 or greater) were assigned to the group without receptive language deficits. This resulted in 16 children with poor receptive language and 30 children with intact receptive language. Chi-square was utilized to determine if the two groups differed in the presence of dyslexia or ADHD. Results were not significant ( $\underline{X}^2$ =4.29,  $\underline{p}$ >.10), and percentages of receptive language weaknesses by group were consistent with what one would expect given the comorbidities between dyslexia, ADHD and specific language impairment  $\underline{1}$ ,  $\underline{51}$ - $\underline{53}$ . See Table 2.

Next, participants with and without poor receptive language were compared on the WISC-III using MANOVA to determine if the poor receptive language group had generalized impairment as suggested by previous research<sup>3-10</sup>. As seen in Table 3, groups differed on all Indices, Verbal Comprehension [ $\underline{F}(1,42)=15.97$ ,  $\underline{p}<.001$ ], Perceptual Organization [ $\underline{F}(1,42)=49.05$ ,  $\underline{p}<.001$ ], Freedom from Distractibility [ $\underline{F}(1,42)=14.91$ ,  $\underline{p}<.001$ ], and Processing Speed [ $\underline{F}(1,42)=6.09$ ,  $\underline{p}<.05$ ], along with Full-Scale IQ [ $\underline{F}(1,44)=37.52$ ,  $\underline{p}<.001$ ]. Children with poor receptive language also had global linguistic deficits, performing worse on the CELF-R Expressive Language composite [ $\underline{F}(1,38)=13.39$ ,  $\underline{p}=.001$ ], CELF-R Recalling Sentences subtest [ $\underline{F}(1,38)=16.73$ ,  $\underline{p}<.001$ ], CTOPP Elision [ $\underline{F}(1,38)=7.47$ , $\underline{p}<.01$ ], WISC-III Digit Span [ $\underline{F}(1,38)=11.25$ ,  $\underline{p}<.01$ ] and rapid naming time [ $\underline{F}(1,38)=6.11$ ,  $\underline{p}<.05$ ] when using MANCOVA with the Perceptual Organization Index as the covariate.

Lastly, those with and without poor receptive language were compared on cerebral volume using MANCOVA with Full-Scale IQ as a covariate, controlling for unequal cell sizes. Full-Scale IQ was significant for left [ $\underline{F}(1,43)=5.09$ ,  $\underline{p}<.05$ ] and right [ $\underline{F}(1,43)=5.21$ ,  $\underline{p}<.05$ ] hemisphere volumes but not asymmetry [ $\underline{F}(1,43)<1.0$ ]. Omnibus tests were significant [ $\underline{F}(3,41)=4.44$ ,  $\underline{p}<.01$ ], as were the univariate ANOVAs for left [ $\underline{F}(1,43)=13.38$ ,  $\underline{p}=.001$ ] and right hemisphere volume [ $\underline{F}(1,43)=13.23$ ,  $\underline{p}=.001$ ]. Asymmetry was not significant [ $\underline{F}(1,43)<<1.0$ ]. See Table 4.

## Receptive Language and Cerebral Volume in Dyslexia and ADHD

To address the primary purpose of this study, those with and without poor receptive language were compared on cerebral volume within the dyslexia and ADHD groupings. Of the children with dyslexia, 9 had poor receptive language and 13 had intact receptive language. Using ANCOVA with Full-Scale IQ as a covariate, groups differed on left [ $\underline{F}(1,19)=6.07$ , p<.05] and right [ $\underline{F}(1,19)=5.10$ , p<.05] hemisphere volume, with poor receptive language being associated with smaller volume. When examining children with ADHD, 12 had poor receptive language and 14 had intact receptive language. ANCOVA with Full-Scale IQ as a covariate revealed those with poor receptive language had smaller right [ $\underline{F}(1,23)=16.72$ , p<.001] and left [ $\underline{F}(1,23)=19.83$ ,  $\underline{p}<.001$ ] hemisphere volumes than those with average or better receptive language.

#### Cerebral Hemisphere Volume and the Two Linguistic Dimensions

Given the secondary purpose of this study, the relationship between hemisphere volume and linguistic ability was examined in an exploratory fashion using Pearson correlations in the total sample (see Table 5). All correlations between hemisphere volume and linguistic functioning were small, and only one correlation between volume and linguistic functioning was significant at the .05 level: right hemisphere volume and number/letter naming time. When examining children with dyslexia specifically, asymmetry was negatively correlated with CELF-R Recalling Sentences ( $\underline{r}$ =-.42,  $\underline{p}$  < .05), indicating rightward asymmetry was moderately associated with better performance. When examining children with poor receptive language (regardless of dyslexia or ADHD diagnosis), leftward asymmetry was moderately correlated with better WISC-III Vocabulary performance ( $\underline{r}$ =.51,  $\underline{p}$  < .05), and left hemisphere volume was moderately correlated with CELF-R Sentence Assembly ( $\underline{r}$ =.50,  $\underline{p}$  = .05).

The lack of a significant relationship between the Receptive Language composite and hemisphere volume in the total sample was surprising given those with poor receptive language had smaller volumes as a group. Thus, a scatter plot of the relationship between receptive language and hemisphere volume was formed using the total sample (see Figure 1). Those with the smallest hemisphere volumes tended to have below average Receptive Language composites. However, once volume surpassed 1460cm<sup>3</sup> on the left and 1420cm<sup>3</sup> on the right, the relationship between receptive language and hemisphere volume became erratic. When participants were ordered according to left hemisphere volume, 8/10 of those with the smallest volumes (less than 1460cm<sup>3</sup>) had poor receptive language. Of these 8, 3 had ADHD, 4 had dyslexia/ADHD, and 1 had dyslexia. Nonetheless, the remaining 2 children had Receptive Language composites of 125 (control) and 128 (ADHD). When participants were ordered according to right hemisphere volume, 7/8 of those with the smallest volumes (less than 1420cm<sup>3</sup>) had poor receptive language, with the remaining child having the Receptive Language composite of 125 (control). The 7 with small right hemisphere volume included the same participants as the 8 with small left hemisphere volume with the exception of one child with dyslexia/ADHD.

## **Discussion**

The primary purpose of this project was to examine whether reduced cerebral volume in dyslexia and ADHD is related to poor receptive language functioning. Based upon prior literature suggesting smaller cerebral volume is associated with worse language comprehension 40, 41, it was hypothesized that cerebral hemisphere volume would be reduced in dyslexia and ADHD when weaknesses in receptive language were present as opposed to being reduced in dyslexia and ADHD in general. The second purpose of this study was to examine cerebral volume in relation to the two domains of linguistic functioning: phonological and non-phonological 16. Based upon prior literature in the area 12, 34, 36, 39, 40, it was

hypothesized that cerebral volume would be positively correlated with non-phonological linguistic skills, but there would be a limited relationship between cerebral volume and phonological skills.

## Cerebral Hemisphere Volume in Dyslexia and ADHD

As hypothesized, cerebral volume was quite comparable between those with and without dyslexia when using the total sample. However, cerebral volume was reduced in children with poor receptive language and dyslexia compared to those with dyslexia but intact receptive language. Similar results were found when analyzing ADHD. In addition, children with and without receptive language deficits in general differed in cerebral volume. Given these findings, at first glance it appears that cerebral hemisphere volume is only reduced in dyslexia and ADHD when poor receptive language is present, consistent with hypotheses and the work of Leonard and colleagues 40-42.

Nonetheless, small cerebral volume was associated with poor receptive language functioning only in those with the smallest volumes. For the rest of the sample the relationship between receptive language and cerebral volume was rather spurious. Even for children with the smallest volumes the relationship was not absolute, as one to two children with small volumes had excellent receptive language functioning, depending on the hemisphere. In addition, children with poor receptive language had multiple cognitive weaknesses, including mildly reduced verbal and nonverbal intellect, slower processing speed, and global linguistic deficits compared to those with intact receptive language. Hence, although our findings are consistent with prior literature suggesting there are generalized deficits in individuals with poor receptive language  $^{3-5}$ ,  $^{7-9}$ , it is difficult to ascertain if small volume is associated with poor receptive language per se, or if it is associated with one or more of the deficits which often accompany poor receptive language. Further research is indicated to make these differentials.

Although children with and without ADHD did not differ in cerebral volume, a moderate relationship was found between cerebral volume and symptoms of ADHD in the total sample; this was true for inattention, hyperactivity, and impulsivity. These relationships likely were not mediated by linguistic functioning given the small correlations between receptive language and inattention, hyperactivity, and impulsivity (rs < .20) and the small relationship between receptive language and cerebral volume in the total sample. Hence, our results are partially consistent with prior research finding ADHD symptomotology is associated with reduced cerebral volume <sup>57, 58</sup>. It is likely that our participants with and without ADHD did not differ in volume due to our sample being largely comprised of children with mild ADHD. Nonetheless, what is informative from our study is the moderate relationship between cerebral volume and ADHD symptoms, suggesting the relationship between the two may be more continuous in nature.

#### Relationships between Cerebral Volume and Linguistic Ability

When examining linguistic skills comprising the phonological dimension in the total sample, the relationships between cerebral volume and phonological awareness, phonological short-term memory, word recognition, and decoding skill were quite limited. Hence, these findings are partially consistent with the work of Leonard and colleagues <sup>40</sup>, <sup>41</sup> who suggested that the phonological dimension may be better associated with aspects of brain morphology other than cerebral volume. Nonetheless, we did not find a linear relationship between cerebral volume and non-phonological linguistic functions in the total sample either, including semantic and syntactic oral language functioning and reading comprehension. Although this could be related to low power, the correlations were small.

When analyzing subgroups, there was a moderate relationship between rightward asymmetry and better verbatim sentence repetition in dyslexia. While the rightward nature of this relationship is surprising given traditional views on language, it is consistent with recent literature suggesting rightward asymmetry of the supramarginal gyrus is associated with better phonological short-term memory in those with dyslexia and/or ADHD<sup>85</sup>. Furthermore, findings are consistent with prior literature which suggests there is a biological contribution to phonological short-term memory performance in particular in developmental dyslexia <sup>16</sup>. Further research with a large sample is indicated to assess the relationship between cerebral volume and phonological short-term memory and whether it differs between those with and without poor phonological processing.

For those with receptive language weaknesses, there was a moderate relationship between leftward asymmetry and better vocabulary knowledge. There also was a moderate relationship between left cerebral volume and syntax formation. Hence, further research on the relationship between cerebral volume and semantic and syntactic functioning in those with poor receptive language is warranted. While replication in those with specific language impairment is required, it also would be of interest to determine if this relationship is found in other populations with non-phonological linguistic deficits such as autism. In addition, it would be of interest to assess the role of environmental contributions to this relationship. For example, do children with larger volumes but poor receptive language functioning have worse or more numerous environmental risk factors? Do children with small volumes but intact receptive language have more environmental protective factors in place?

Taken together, our findings on the relationship between cerebral volume and linguistic functioning are consistent with the review by Bishop and Snowling  $^{16}$  which suggests that neurobiological bases to linguistic functioning are more likely to be found when well-defined groups are used. When heterogeneous groupings are used, the sample is more likely to include participants with various environmental and neurobiological contributors to their functioning. Perhaps heterogeneity served to reduce the relationships found between cerebral volume and linguistic functioning in the total sample.

## **Limitations and Future Directions**

First, as dyslexia was defined according to a discrepancy definition future research is warranted using the poor reader definition to determine if relationships weaken further, as a biological basis for dyslexia may be more readily found when a discrepancy definition is used 16, or if poor readers have smaller cerebral volumes as a group given the increased prevalence of nonphonological linguistic deficits in this group <sup>16</sup>. Second, both the dyslexia and ADHD groups were of mild severity; thus, it would be of interest to assess whether results differ from a sample with more severe deficits. Nevertheless, often greater severity of disorders is accompanied by a greater number and severity of comorbidities, something this study tried to avoid through its inclusion and exclusion criteria. Third, receptive language functioning was assessed with a cutoff score in our study, similar to the work of Leonard and colleagues 40. Hence, it would be beneficial to replicate this study using formal diagnostic procedures to determine presence or absence of specific language impairment rather than using a cut-off score. Fourth, as this study was conducted on a weak scanner, it would be beneficial to replicate this study using a stronger scanner allowing for use of more sophisticated technology (e.g., gray/white matter segmentation). Finally, as with most studies using MRI, our sample size was small. Hence, replication is required with a larger sample to test for differences in correlation values between groups (e.g., dyslexia, receptive language weaknesses, controls).

#### **Conclusions**

Of particular interest to the authors were the unusual relationships found between cerebral volume and language comprehension in our study given the work by Leonard and colleagues <sup>40-42</sup>. While not finding a continuous relationship between cerebral volume and receptive language in the total sample could be related to our sample composition and low power, it also could be that only those with the smallest volumes have this neurobiological contributor to their language comprehension and/or accompanying deficits, as opposed to there being a continuous relationship between volume and comprehension in general. Further research is indicated to investigate the relationship between cerebral volume and language comprehension in more detail, including examination of how various environmental factors may affect this relationship (e.g., maternal education, perinatal factors, quality of education, type of instruction).

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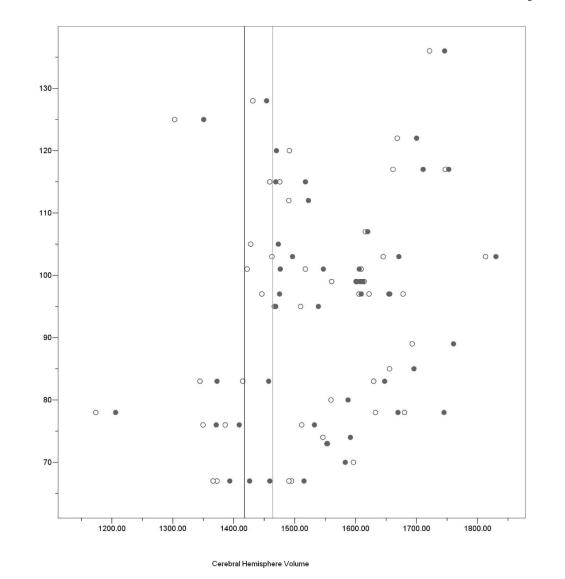
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right hemisphere
left hemisphere



**Figure 1.** Scatterplot of the relationship between receptive language and cerebral hemisphere volume. All hemisphere volumes left of the black line are less than 1420cm<sup>3</sup>. All hemisphere volumes left of the gray line are less than 1460cm<sup>3</sup>.

NIH-PA Author Manuscript Participant Descriptive Data NIH-PA Author Manuscript

Table 1

NIH-PA Author Manuscript

Variable	Dyslexia		Dyslexia/ADHD	HD	ADHD		Controls	
	Mean	SD	<u>Mean</u>	SD	<u>Mean</u>	$\overline{\mathrm{SD}}$	Mean	SD
Age (years)	10.28	1.35	9.54	0.89	9.44	1.05	06.6	1.06
Edinburgh	95.00	5.27	80.00	28.36	86.54	25.93	86.43	33.75
WISC-III								
Full-Scale IQ	08.66	12.51	105.31	17.41	104.92	15.15	111.90	12.26
Verbal IQ <sup>a</sup>	97.80	11.70	103.84	19.88	106.38	13.16	117.40	15.94
Verbal Comprehension Index $^a$	100.10	11.86	104.31	20.67	108.23	14.02	116.60	15.43
Freedom from Distractibility Index $^b$	88.40	10.81	96.62	15.42	97.46	11.52	113.60	14.50
Performance IQ	102.50	13.47	106.23	14.31	102.84	16.83	103.60	9.31
Perceptual Organization Index	106.60	13.78	108.15	16.23	104.00	18.44	102.50	7.26
Processing Speed Index	93.60	14.69	96.83	9.17	96.31	12.30	108.11	14.80
WRAT-3								
$Reading^{\mathcal{C}}$	79.00	12.16	81.77	9.04	101.54	11.69	111.00	15.62
${ m Spelling}^{C}$	81.56	11.33	85.31	7.26	95.15	8.40	107.10	13.30
Arithmetic <sup>c</sup>	86.56	11.40	92.23	11.68	100.92	12.01	105.70	7.66
WRMT-R								
Word Attack <sup>c</sup>	77.90	13.33	82.00	69.7	99.38	11.86	106.70	17.47
Passage Comprehension <sup>C</sup>	75.30	14.52	82.54	9.73	93.62	11.07	108.60	12.82
CBCL								
Parent form Attention Problems $^d$	55.90	6.35	00.89	6.63	69.85	6.80	53.14	5.84
Teacher form Attention Problems $^e$	60.30	60.6	69.91	13.41	00.69	11.83	56.14	7.88

Note. Edinburgh is measured in percent of tasks performed with the right hand. CBCL is in T-scores, and the rest of the measures are in standard scores.

 $<sup>^{\</sup>it a}{\rm Those}$  with and without dyslexia differed at p  $\leq$  .05.

 $<sup>\</sup>ensuremath{^{b}}\xspace$  Those with and without dyslexia differed at  $\ensuremath{\underline{p}}=.01.$ 

<sup>&</sup>lt;sup>c</sup>Those with and without dyslexia differed at  $\mathbf{p} < .001$ .

 $<sup>^{</sup>d}\mathrm{Those}$  with and without ADHD differed at p<.001.

 $<sup>^{\</sup>mbox{\it e}}$  Those with and without ADHD differed at p<.01.

 Table 2

 Frequencies of Diagnosis by Receptive Language Group

Variable	<u>Dyslexia</u>	<u>Dyslexia/ADHD</u>	<u>ADHD</u>	Controls
CELF-R Receptive < 85	3	6	6	1
CELF-R Receptive $\geq 85$	7	7	7	9

Note. CELF-R Receptive is the CELF-R Receptive Language composite score. Receptive language groups did not differ significantly in diagnostic frequency.

 Table 3

 Cognitive Functions by Receptive Language Group

¥7	Poor Receptive Language		Intact Receptive Language	
Variable				
	<u>Mean</u>	<u>SD</u>	<u>Mean</u>	<u>SD</u>
WISC-III				
Full-Scale IQ ***	91.81	9.24	112.70	11.83
Verbal IQ ***	94.44	11.33	112.47	15.60
VCI***	95.19	11.14	112.64	15.27
FDI***	87.75	8.23	103.89	15.46
Performance IQ***	90.69	8.84	110.93	10.04
POI***	91.50	7.21	112.43	10.61
PSI*	92.06	9.50	101.79	13.99
CELF-R Expressive ***	75.69	6.63	98.36	13.28
CELF-R Recall***	6.38	2.03	10.72	2.78
CTOPP Elision**	14.31	4.57	18.88	4.91
WISC-III Digit Span **	7.25	1.29	10.56	3.06
RAN Number/Letter Time *	44.25	11.75	36.72	10.01

Note. CELF-R Recall and WISC-III Digit Span subtests are in scaled scores; CTOPP Elision subtest and RAN Number/Letter Time are in raw scores; the rest are in standard scores. CELF-R Expressive is the CELF-R Expressive Language composite score. VCI is the Verbal Comprehension Index; FDI is the Freedom from Distractibility Index; POI is the Perceptual Organization Index; and PSI is the Processing Speed Index.

p < .05.

<sup>\*\* &</sup>lt;u>p</u> < .01.

<sup>\*\*\*</sup> p < .001.

 Table 4

 Cerebral Hemisphere Size by Receptive Language Group

Variable	Poor Receptive Language		Intact Receptive Language	
	<u>Mean</u>	<u>SE</u>	<u>Mean</u>	<u>SE</u>
Left hemisphere volume *	1444.57	35.14	1618.25	23.43
Right hemisphere volume*	1419.26	34.94	1590.96	23.29
Asymmetry ratio	.018	.006	.017	.004

Note. Means are adjusted for group differences in WISC-III Full-Scale IQ.

p = .001.

 Table 5

 Pearson Correlations between Hemisphere Volume and Linguistic Functioning in the Total Sample

Variable	<u>Left Hemisphere</u>	Right Hemisphere
CELF-R Receptive Composite	.24	.24
CELF-R Expressive Composite	.17	.19
CELF-R Sentence Assembly	.16	.15
CELF-R Recalling Sentences	.11	.18
WISC-III Vocabulary	04	06
WISC-III Digit Span	.05	.07
CTOPP Elision	.06	.02
RAN Number/Letter time	25	30*

<sup>\*</sup>p < .05.