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ORIGINAL ARTICLE

Grey matter volume in developmental speech and language disorder

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Abstract

Developmental language disorder (DLD) and developmental speech disorder (DSD) are common, yet their etiologies are not well understood. Atypical volume of the inferior and posterior language regions and striatum have been reported in DLD; however, variability in both methodology and study findings limits interpretations. Imaging research within DSD, on the other hand, is scarce. The present study compared grey matter volume in children with DLD, DSD, and typically developing speech and language. Compared to typically developing controls, children with DLD had larger volume in the right cerebellum, possibly associated with the procedural learning deficits that have been proposed in DLD. Children with DSD showed larger volume in the left inferior occipital lobe compared to controls, which may indicate a compensatory role of the visual processing regions due to sub-optimal auditory-perceptual processes. Overall, these findings suggest that different neural systems may be involved in the specific deficits related to DLD and DSD.

Keywords Language · Speech · Child · VBM · MRI

Introduction

Language and speech provide the means for a child to engage and learn from their environment, as well as express their ideas and needs. For most children, language and speech development is spontaneous and effortless. However, around 2–15% of children, depending on age, have significant problems with the acquisition of language and/or speech for no apparent reason (Campbell et al. 2003; Eadie et al. 2015; McLeod and Harrison 2009; Shriberg et al. 1999).

Developmental language disorder (DLD) is diagnosed when a child has significant difficulties comprehending and/or producing language despite exposure to an adequate language learning environment and the absence of sensory or frank neurological impairments (Bishop et al. 2016; Reilly et al. 2015; Tomblin 2015). The term DLD encompasses many sub-phenotypes with potential impairments across syntax, morphology, phonology, and/or semantics (Leonard 2015). By contrast, children with developmental speech disorder (DSD) have difficulties accurately producing the vocal sounds of their native language appropriate for their age. The phenotypes of children with DSD are also variable and can include errors that reflect problems with articulatory (i.e.,

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phonetic) and/or phonological (i.e., phonemic) aspects of speech production (Dodd et al. 2018a). Longitudinal studies have also shown that the phenotypes for children with DSD change over time, with one common presentation including children who demonstrate phonological errors at one time-point and later experience articulation errors (Dodd et al. 2018a, b). DLD and DSD often persist into adolescence and adulthood and are associated with an increased risk of psychosocial, academic, and occupational difficulties (Law et al. 2009; Lewis et al. 2000, 2015; McKean et al. 2017; Schoon et al. 2010).

The etiology of DLD and DSD is considered to be a complex interaction between genetics, environment, and neurobiology (Graham and Fisher 2013). Although findings are inconsistent, structural brain anomalies have been associated with DLD and DSD (Liégeois et al. 2014; Mayes et al. 2015; Morgan et al. 2016). There is some evidence to suggest that the key language regions (e.g., inferior frontal and posterior temporal regions) in DLD groups have increased volume in the right and/or reduced volume in the left hemisphere in contrast to controls (De Fossé et al. 2004; Herbert et al. 2005; Soriano-Mas et al. 2009; Kurth et al. 2018), although other studies do not support this trend (Preis et al. 1998). Furthermore, anomalies in the inferior frontal and posterior temporal regions have also been reported in other communication disorders such as dyslexia and stuttering (Beal et al. 2013; Richlan et al. 2013). The striatum (putamen and caudate nucleus) are also proposed as core regions associated with DLD due to their role in procedural learning (Krishnan et al. 2016; Ullman 2016) and larger putamen volume (Lee et al. 2013) and atypical (i.e., both increased and decreased) caudate volume (Badcock et al. 2012; Soriano-Mas et al. 2009) have been reported in DLD when compared to controls. In contrast to DLD, imaging research in DSD is scarce. One relatively recent study reported children with persistent speech sound errors to have larger grey matter volume compared to controls in bilateral posterior temporal regions and left supramarginal gyrus (Preston et al. 2014).

Interpretation of the current imaging literature in DLD is limited by small sample sizes (Badcock et al. 2012; De Fossé et al. 2004; Girbau-Massana et al. 2014), as well as variability across study methodology and findings. Much of the research has focused on specific brain regions of interest (e.g., Wernicke's or Broca's area) and/or incorporated manual methods to examine brain morphology (De Fossé et al. 2004; Gauger et al. 1997; Herbert et al. 2005; Preis et al. 1998), making findings difficult to compare across studies. Interpretation is further complicated by within- and between-study variability in the DLD sample's age (e.g., 5–17 years), language phenotype, and comorbid diagnoses (e.g., reading disorder or speech programming deficit; Badcock et al. 2012; Girbau-Massana et al. 2014; Soriano-Mas et al. 2009). Developmental information is rarely reported which is important given the proposed link between past developmental language trajectories and causal mechanisms (Snowling et al. 2016; Zambrana et al. 2014). Further research addressing the limitations of previous imaging work is warranted.

Given that DSD and DLD are highly comorbid and have some overlap in their symptomatology and etiological risk factors (Peterson et al. 2007), it is of interest to know whether there are similarities in their underlying neurobiology. This can be explored both by comparing children with DLD or DSD to appropriate typically developing control subjects, and by investigating if there are detectable differences when the affected groups are directly compared to one another. A better understanding of the neurobiological association or dissociation between these disorders may inform our understanding of any unique neurobiological characteristics, with the potential to provide insight into distinct causal pathways.

The aim of the current study was to investigate grey matter volume in 9–11 year old children with and without language or speech difficulties. Our primary aim was to compare children with DLD or DSD to a typically developing control group. In addition, children with DLD and DSD were directly compared to each other. Within-group heterogeneity was minimized using a participant sample of similar age, and a history of consistent developmental language or developmental speech difficulties from preschool to early adolescence. Differences in grey matter volume were investigated using whole-brain voxel-based morphometry (VBM), including small-volume correction for multiple comparisons in particular brain regions relating to specific hypotheses. Based on significant findings reviewed above, it was hypothesised that children with DLD, compared to controls, would show a) reduced volume of the left and/or larger volume of the right inferior frontal gyrus (IFG) and posterior superior temporal gyrus (pSTG), b) atypical (i.e., smaller or larger) caudate volume, and/or c) larger putamen volume when compared to controls. Children with DSD were predicted to show larger grey matter volume in the pSTG bilaterally and the left supramarginal gyrus when compared to the typically developing controls. Given the dearth of research directly comparing children with DLD and DSD, this part of our study is exploratory in nature and our approach was to test for significant differences in regional grey matter volume between these groups using whole-brain analyses.

Materials and methods

Participant identification

The children in this study were identified through the Early Language in Victoria Study (ELVS), a community

longitudinal cohort study of language in 1910 children. Recruited between 8 and 10 months of age, language and speech development was monitored over nine subsequent waves via parent and teacher questionnaires and face-to-face assessments (Reilly et al. 2018). A subset of this cohort who met the inclusion criteria for the present study was invited to take part.

Inclusion/exclusion criteria

Children were eligible for the current study if they had (a) no history of neurological condition (e.g., epilepsy and acquired brain injury), known hearing impairment, persistent stuttering (i.e., after the age of 5 years), or major developmental disorder (e.g., Autism Spectrum Disorder, Attention Deficit Hyperactive Disorder), (b) were a native English speaker, not a twin, and had a non-verbal IQ standard score of ≥ 80 on the Kaufman Brief Intelligence Test, Second Edition (KBIT-II; Kaufman and Kaufman 2004) at age 4 and the Wechsler Abbreviated Scales of Intelligence (WASI; Wechsler 1999) at age 7 years based on data collected as part of the ELVS. In addition, all participants were required to pass an MRI safety screen. Eligible children were required to meet additional group-specific criteria. Children in the DLD group were required to score 'below average' (i.e., at least one standard deviation below the mean) on the receptive or expressive language index score on the Clinical Evaluation of Language Fundamentals (CELF; Semel et al. 2006; Wiig et al. 2006) at ages 4 or 5, 7 years, and at the time of MRI scanning (9-11 years). Children in the DSD group were initially identified based on their performance on the Goldman Fristoe Test of Articulation, Second Edition (GFTA-2; Goldman and Fristoe 2000) at 4 years of age (i.e., performance below the 25th centile). In addition, children in the DSD group were required to have articulation and/or phonological errors at both 4 years of age and at time of scanning, which was assessed by two raters using the GFTA-2 and connected speech samples (Dodd et al. 2018a; b; Morgan et al. 2017; see section "Participant characteristics" for speech classification). All children in the DSD and typically developing group were required to have no history of language difficulty [i.e., a standard score within the average range on receptive and expressive language indices of the CELF (Semel et al. 2006; Wiig et al. 2006) at 4, 5, 7, and 9–11 years].

Participant characteristics

Participants included 19 children with DLD, 15 with DSD, and 45 typically developing controls aged between 9 and 11 years. Of these, nine children in total were excluded due to insufficient quality of T1-weighted images; two each from the DLD and DSD groups and five from the typically developing controls. Participant characteristics are shown in Table 1. Significant group differences were found in core, receptive, and expressive language, reading skills, and non-verbal intellectual abilities. As expected, post hoc *t* tests with Bonferroni adjusted alpha of $p < .017$ (i.e., adjusted for the three group comparisons) showed the children with DLD had significantly reduced language scores compared to the typically developing and DSD groups, whereas the typically developing and DSD groups displayed no significant differences. Children with DLD also had significantly reduced reading scores and non-verbal intellectual abilities compared to the typically developing and DSD groups; however, these abilities of the DLD group remained within the 'average' range. Reading scores and non-verbal intellectual abilities did not significantly differ between the typically developing and DSD groups. Speech ratings at 4 years of age revealed the children with DSD had speech sound errors consistent with phonological disorder ($n = 1$), phonological delay ($n = 2$), phonological disorder and phonological delay ($n = 2$), articulation disorder ($n = 4$), phonological disorder and articulation disorder ($n = 2$), phonological delay and articulation disorder ($n = 1$), and phonological disorder, phonological delay, and articulation disorder ($n = 1$). Speech

Table 1 Participant characteristics

	TD	DLD	DSD	Statistic	*P*
N	40	17	13	–	–
Age (months)	123(6)	123(3)	124(3)	$\chi^2(2) = .04$	.98
Sex (M:F)	19:21	10:7	3:10	$\chi^2(2) = 18.2$	<.000
Left, mixed, right handed	3, 2, 35	4, 1, 12	0, 1, 12	$\chi^2(X) = 4.8$	.22
CELF-4 (language)					
Rec	105(8)	83(9)	104(6)	$F(2) = 46.2$	<.000
Exp	108(10)	80(9)	106(10)	$F(2) = 52.6$	<.000
Core	106(9)	80(6)	105(9)	$F(2) = 64.6$	<.000
WASI-2 PRI (NVIQ)	102(10)	91(9)	104(11)	$F(2) = 10.1$	<.000
WRAT-4 reading[a]	109(11)	93(10)	105(10)	$\chi^2(2) = 17.1$	<.000

Values are Mean (Standard Deviation)

CELF-4 standard index scores and WASI-2 standard index scores are reported with a mean of 100 and a standard deviation of 15

Note. The Freeman–Halton extension of the Fisher's exact test was used for handedness due to the small frequency counts

TD typically developing, *DLD* developmental language disorder, *DSD* developmental speech disorder, *CELF-4* Clinical Evaluation of Language Fundamentals, Fourth Edition, *WASI-2 PRI* Wechsler Abbreviated Scale of Intelligence, Second Edition Perceptual Reasoning Index, *WRAT-4* Wide Range Achievement Test 4, *Rec* receptive, *Exp* expressive, *NVIQ* non-verbal IQ, *M:F* male:female

[a]Reading data for 14 children is missing (TD $n = 10$; DLD $n = 3$; DSD $n = 1$)

ratings at the time of scanning revealed that children with DSD had speech sound errors consistent with articulation disorder ($n=9$), phonological delay ($n=3$), or both ($n=1$), and more than half of parents reported they had sought assistance from a health professional in relation to concerns with their child's speech. These findings are in line with the longitudinal work by Dodd et al. (2018b) showing different articulation or phonological profiles for the same children over time. Seven children in the DLD group also showed speech sound errors that were consistent with a phonological delay or disorder ($n=5$) or articulation disorder ($n=2$). This is consistent with the high incidence of speech impairment that has previously been reported in children with DLD (Lewis et al. 2015; Shriberg et al. 1999). One-way between-group analysis of variance revealed no significant group differences in total intracranial volume between the groups ($F(2, 69)=1.50$, $p=.23$, $\eta^2=.043$).

Ethics

The Human Research Ethics Committee at the Royal Children's Hospital in Melbourne Australia approved the procedures (HREC31225) and informed consent was obtained from each child's parent/guardian.

Materials

Language assessment

The core language subtests of the CELF-4 (Semel et al. 2006) were administered at the time of scanning to calculate the Core Language Index (CLI), Receptive Language Index (RLI), and Expressive Language Index (ELI).

Speech assessment

The GFTA-2 (Goldman and Fristoe 2000) sound in words subtest was used to elicit the speech sounds of the English language in the initial, medial, and final word positions. Conversation samples of 5 min in duration were also rated to confirm the presence of these errors in connected speech. Sound errors in single words and connected speech were classified according to the DSD subtypes outlined in Dodd et al. (2018a, b) and Morgan et al. (2017).

Reading assessment

The Wide Range Achievement Test, Fourth Edition (WRAT-4; Wilkinson and Robertson 2006) Word Reading was used as a measure of reading level.

Non-verbal intellectual abilities

The Wechsler Abbreviated Scale of Intelligence, Version 2 (WASI-2; Wechsler 2011) Perceptual Reasoning Index (PRI) was used as measure non-verbal intellectual abilities.

Data acquisition

Testing involved both a mock and a real MRI scan, followed by a face-to-face assessment with the child to assess language, speech, and non-verbal intellectual abilities. As part of a larger imaging protocol, high-resolution T1-weighted MRI images were acquired on a Siemens 3 Tesla Skyra scanner (Erlangen, Germany) with 20-channel head coil at the Florey Institute of Neuroscience and Mental Health, Melbourne. Participants watched a DVD during data acquisition via a mirror on the head coil and wore ear-bud headphones. Noise-attenuating headphones were also worn throughout acquisition and padding was inserted around the head to restrict movement. The T1-weighted images were acquired in the sagittal plane using a 3D MP-RAGE sequence with the following parameters: echo time (TE) = 2.49 ms, repetition time (TR) = 1900 ms, inversion time (TI) = 900 ms, flip angle = 9°, matrix = 256 × 256 × 192, and voxel size = 0.9 mm isotropic. Children completed mock scanning training prior to the acquisition of MRI data to familiarize them with the MRI process and minimize head motion artefacts. Images were inspected for motion artefacts at the end of acquisition, and if significant motion was noted, the T1-weighted MP-RAGE sequence was repeated. Prior to analysis, data were visually inspected and scans that contained artefacts such as ghosting or blurring due to head movement were excluded (see section "Participant characteristics" for details).

Data analysis

Pre-processing

Statistical analysis was performed using Statistical Parametric Mapping (SPM8; http://fil.ion.ucl.ac.uk/spm/software/spm8) using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm8/), executed via MATLAB Release 2014a (The MathWorks, Inc., Natick, Massachusetts, United States). The T1-weighted images were pre-processed according to the VBM8 manual for normalizing segmented images to a custom DARTEL template. Customized study-specific templates were created for registration (using all participant data), which has been shown to produce improved results in pediatric samples compared to use of standard adult templates (Yoon et al. 2009). Normalized grey matter tissue classes were modulated using the 'non-linear only' option in VBM8. The resulting images enable the comparisons of

absolute amount of tissue and do not require further correction for differences in brain size in the statistical analysis. The 'check sample homogeneity using covariance' function in VBM8 was used to assist in assessing data quality by identifying outliers that required further assessment. If there were no artefacts and images were identified as of sufficient quality, they were included in the analysis. Modulated grey matter images were smoothed with a 10 mm full-width-half-maximum isotropic Gaussian kernel, with a resultant particular sensitivity to the detection of differences at this spatial scale.

Statistical analysis

Hypotheses were tested using independent sample *t* tests, with an absolute threshold mask of 0.1. Covariates were age, sex, non-verbal intellectual abilities, and handedness. As described, the analysis included non-linear modulation which controls for individual differences in total intracranial volume, and as such this was not included as a covariate. A combination of voxel-wise and cluster-wise corrections was used. Voxel-wise statistics provides an indication of the intensity of the signal within specific locations within the brain. Cluster-level statistics provide an indication of weaker but strongly diffuse signals (Woo et al. 2014). A non-stationarity correction for non-isotropic smoothness in imaging data was applied to enable cluster-level statistics to be used (Hayasaka et al. 2004; Worsley et al. 1999). For whole-brain analyses, t-statistic maps corresponding to volume increases and volume decreases were created for each group comparison. The voxel-level family-wise error (FWE)-corrected significance was set at $p < .05$ (including Bonferroni correction for testing both volume increases and decreases). Cluster-level significance was set at an initial voxel-level cluster defining threshold of $p < .001$ uncorrected, and cluster-level extent threshold of $p < .05$ FWE-corrected (again including Bonferroni correction for testing both volume increases and decreases). For small-volume correction related to specific hypothesis testing (see next section), in addition to correcting for multiple comparisons within each small volume, Bonferroni adjustment was applied to account for the number of specific tests (i.e., the number of regions of interest and/or testing for both volume increases and decreases). This resulted in a threshold of $p < .007$ for the first hypothesis (DLD/typical development) which accounted for a correction for seven comparisons including: reduced volume of left IFG, left pSTG, and caudate, and increased volume of the right IFG, right pSTG, caudate, and putamen (i.e., $p < .05/7$ tests = .007). The threshold for the second hypotheses (DSD/typical development) was .025 which accounted for a correction for two comparisons including increased volume in bilateral pSTG and supramarginal gyrus (see hypotheses in section "Small-volume correction").

Small-volume correction

We had the specific hypotheses that: (1) children with DLD would show (a) reduced volume of the left and/or larger volume of the right IFG and pSTG, (b) atypical caudate volume (i.e., reduced or increased volume), and/or (c) larger putamen volume compared to controls, and (2) children with DSD would show larger grey matter volume in bilateral pSTG and left supramarginal gyrus compared to typically developing controls. To enable small-volume correction for multiple comparisons when addressing these hypotheses, we delineated eight appropriate regions of interest. This included six for the first hypothesis (left IFG, right IFG, left pSTG, right pSTG, bilateral caudate nucleus, and bilateral putamen) and two for the second hypothesis (bilateral pSTG and left supramarginal gyrus; see supplementary information for anatomical definitions).

Results

The results section is structured to include three separate sections. First, we present findings significant at a FWE-corrected threshold of $p < .05$. We then report on the results from the hypothesis-driven small-volume correction, using the appropriate threshold depending on the number of regions of interest for the specific hypothesis (see section "Small-volume correction") and the direction of hypothesis (i.e., increase or decrease in grey matter). Third, highly significant ($p < .001$) uncorrected findings are reported for the purpose of hypotheses generating for future research.

Whole-brain results (family-wise error correction)

Developmental language disorder/typical development

As shown in Table 2 and Fig. 1, whole-brain correction for multiple comparisons revealed that the children with DLD had a cluster of significantly larger grey matter volume in the right cerebellum when compared to the typically developing controls.

Developmental speech disorder/typical development

Whole-brain correction revealed that the children with DSD had significantly larger peak grey matter volume in the left inferior occipital gyrus compared to typically developing controls (see Table 2 and Fig. 2).

Table 2 Significant group differences in regional grey matter volume for the whole-brain VBM analysis

Contrast	Brain region	*P** (cluster size)	*t*	*z* value	x^a	y^a	z^a
DLD > TD	Right cerebellum	<.000 (5281)	4.60	4.19	26	−48	−20
					18	−38	−29
					38	−57	−20
DSD > TD	Left IOG	.01	5.59	4.87	−26	−87	−9

DLD developmental language disorder, *TD* typically developing, *DSD* developmental speech disorder, *IOG* Inferior occipital gyrus

*p values are whole-brain FWE-corrected (cluster-based statistic for cerebellum, peak-based statistic for inferior occipital gyrus). Cluster-level significance was based on an initial voxel-level cluster defining threshold of $p < .001$ uncorrected, and cluster-level extent threshold of $p < .05$ FWE-corrected. For data reported based on peak-level statistics, peak-level FWE-corrected significance was set at $p < .05$

[a]Co-ordinates are in study-specific template space

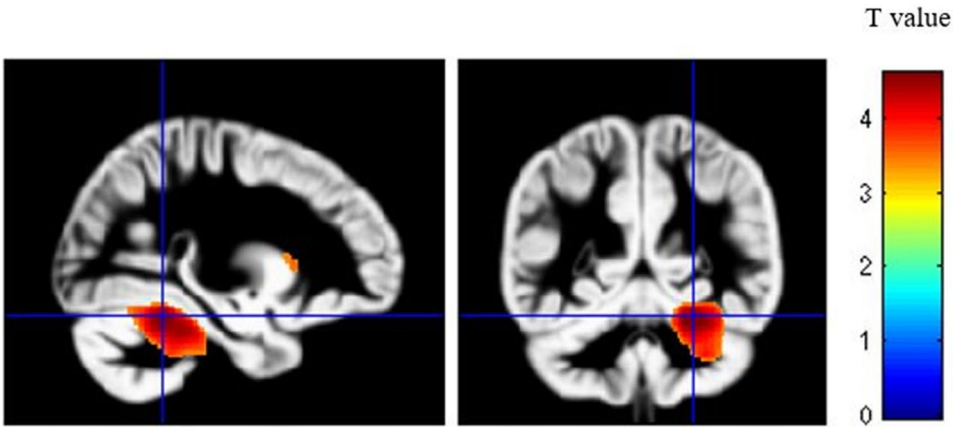

Fig. 1 Statistical parametric maps of regional grey matter volume differences in right cerebellum found between children with DLD and typically developing speech and language (significant at an initial voxel-level cluster defining threshold of $p < .001$ uncorrected and cluster-level threshold of $p < .05$ FWE-corrected; see Table 2). Displayed on coronal and sagittal slices of study-specific grey matter template at peak threshold at $p < .001$ uncorrected. Created in SPM8. Modulated grey matter images were smoothed with a 10 mm full-width-half-maximum isotropic Gaussian kernel

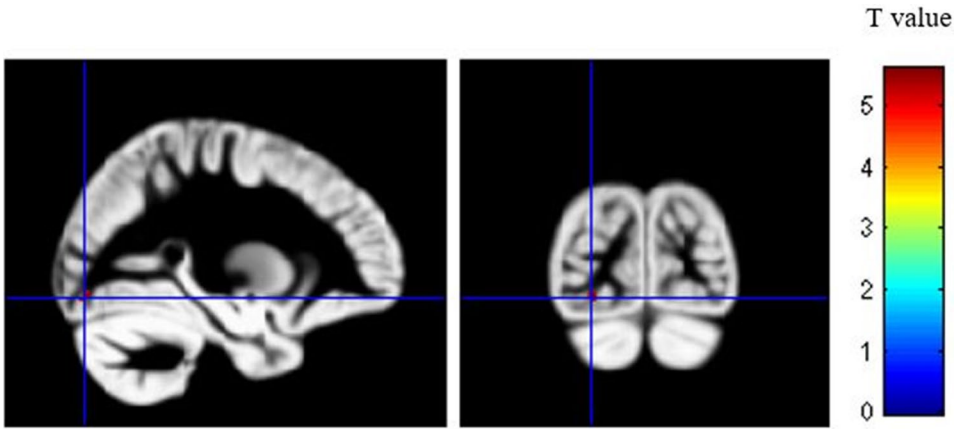

Fig. 2 Statistical parametric maps of regional grey matter volume differences in left inferior occipital gyrus found between children with DSD and typically developing speech and language. Displayed on coronal and sagittal slices of study-specific grey matter template voxel-level significance $p < .05$ FWE-corrected (see Table 2). Created in SPM8. Modulated grey matter images were smoothed with a 10 mm full-width-half-maximum isotropic Gaussian kernel

Table 3 Significant group differences in regional grey matter volume following small-volume correction

Contrast	Brain region	p*	t	z value	x^a	y^a	z^a
DLD > TD	Right IFG	.03	3.58	3.36	57	26	−5
	Right pSTG	.02	3.86	3.60	45	−14	3
	Right putamen	.04	3.61	3.39	32	6	8

DLD developmental language disorder, *TD* typically developing, *IFG* inferior frontal gyrus, *pSTG* posterior superior temporal gyrus

*p values are peak voxels after small-volume correction (family-wise error $p < .05$). Note: These findings were no longer significant after applying a Bonferroni correction for the number of specific tests (i.e., the number of regions of interest and/or testing for both volume increases and decreases; see section "Statistical analysis")

[a]Co-ordinates are in study-specific template space

Developmental language disorder/development speech disorder

No significant differences between the DLD and DSD groups were detected after whole-brain correction.

Small-volume correction

Developmental language disorder/typical development

As shown in Table 3, small-volume correction for each of the six regions for the first hypothesis (outlined in section "Small-volume correction") revealed the DLD group had significantly larger grey matter volume compared to the typically developing control group in the right IFG and pSTG, as well as the putamen (right side only) at a threshold of $p < .05$ (FWE-corrected); however, these findings were not significant after applying a Bonferroni correction for the number of specific tests (i.e., the number of regions of interest and/or testing for both volume increases and decreases; see section "Statistical analysis").

Developmental speech disorder/typical development

Small-volume correction of the (a) bilateral pSTG and (b) left supramarginal gyrus revealed no significant differences between the DSD group and typically developing controls.

Uncorrected findings within regions of interest

Developmental language disorder/typical development

There were no additional regions of increased or decreased grey matter volume at an uncorrected level between the DLD and typical development group that has not already been reported in previous section.

Developmental speech disorder/typical development

The DSD group showed increased peak grey matter volume within the left supramarginal gyrus region at uncorrected levels ($p < .001$).

Developmental language disorder/development speech disorder

Further exploration of uncorrected comparisons at a threshold of $p < .001$ revealed differences across the right hemisphere. For example, the DLD group had larger peak grey matter volume in the transverse temporal gyrus, IFG (pars triangularis), parahippocampal gyrus, and caudate tail, and less peak grey matter volume in the right cuneus and inferior occipital lobe.

Discussion

This study revealed evidence suggesting that different neural systems may be involved in the specific deficits that manifest in DLD and DSD. The study compared regional grey matter volumes in 9–11 year old children with developmental language or speech difficulties to that of typically developing controls. It was hypothesised that children with DLD would show reduced volume in the left and/or larger volume in the right key language regions (i.e., IFG and pSTG), as well as larger putamen volume and atypical (either larger or smaller) caudate volume when compared to controls. Children with DSD were predicted to have larger volume, compared to controls in the pSTG bilaterally and left supramarginal gyrus. Contrary to predictions, children with DLD had larger grey matter volume in the right cerebellum compared to controls, whereas children with DSD had larger grey matter volume in the left inferior occipital lobe compared to controls, after whole-brain correction for multiple comparisons. The DLD group also displayed larger volume compared to controls that approached significance in the right putamen, IFG and

pSTG (i.e., significant differences following small-volume correction, but not following a Bonferroni correction for the number of specific tests including regions of interest and prediction of either increase or decrease of grey matter). This suggests a trend for the DLD group to have larger volume within these brain regions, which provides some support for the hypothesis. Finally, the results showed no significant differences in grey matter volume between the DLD and DSD groups (when directly compared).

Grey matter volume anomalies in developmental language disorder

The children with DLD in the present study showed significant clusters of increased grey matter volume in the right cerebellum when compared to typically developing controls. When we used peak-wise statistics, we did not detect significant group differences in the cerebellum, which is consistent with the previous reports in individuals with DLD using VBM (Badcock et al. 2012; Girbau-Massana et al. 2014; Soriano-Mas et al. 2009). However, none of these past studies included cluster-wise statistics, which detect statistically significant clusters on the basis of the number of contiguous voxels whose voxel-wise statistic values lie above a cluster defining threshold, in combination with a predefined cluster extent threshold. Taking into consideration, both peak and cluster statistics can increase sensitivity by detecting weaker but widespread group differences (Woo et al. 2014).

It is now well accepted that the cerebellum plays an important role in language function (Mariën et al. 2014). Research shows that the right cerebellar hemisphere is anatomically and functionally connected to cortical language regions in the left frontal and parietal lobes (Jissendi et al. 2008; Krienen and Buckner 2009), is engaged during fMRI language tasks (Stoodley and Schmahmann 2009), and that damage to this region, particularly during childhood, is associated with language deficits (Riva and Giorgi 2000). It also plays an important role in the automatization of skills via implicit or procedural learning (Nicolson and Fawcett 1990) which has been proposed as an underlying deficit in DLD (Ullman and Pierpont 2005). The cerebellum also supports various functions via its role in timing, sequencing, sensorimotor integration, and prediction (Mariën et al. 2014), all of which are essential in language acquisition and function. Therefore, the cerebellar anomalies in the DLD group, especially given they are on the right side, are consistent with previous research indicating the crucial role the cerebellum plays in supporting skill acquisition and language function. Cerebellar volume abnormalities, albeit reduced, have also been described in several other neurodevelopmental disorders (e.g., ADHD and dyslexia), both of which show deficits in procedural learning (Stoodley 2016). It is possible, therefore, that the cerebellar anomalies in the DLD group may relate to deficits associated with implicit/procedural skill learning, as opposed to language-specific functions.

We found no evidence to support the hypothesis that children with DLD would have atypical caudate volume compared to controls. Previous research has shown inconsistent results, with both increased (Soriano-Mas et al. 2009) and decreased (Badcock et al. 2012; Herbert et al. 2003) caudate volume being reported. The DLD group in our study did, however, show a trend towards larger volume in the right putamen, as well as the right IFG and pSTG (i.e., significant differences compared to controls following small-volume correction, but not after the appropriate additional Bonferroni correction). The larger volume of the right IFG and pSTG reported here is consistent with the previous work reporting increased volume in the right and/or reduced volume in the left hemisphere for these brain regions, in contrast to controls (De Fossé et al. 2004; Herbert et al. 2005; Soriano-Mas et al. 2009; Kurth et al. 2018). In regards to the putamen, whole-brain VBM studies in DLD have not previously reported volume anomalies in the putamen (Badcock et al. 2012; Soriano-Mas et al. 2009). However, larger volume has been reported in this population when the putamen has been examined in region of interest analysis (Lee et al. 2013), a technique that greatly increases the sensitivity compared to whole-brain VBM. The findings from the current study in the context of previous work suggest that volume anomalies of the putamen in DLD may be too subtle to be detected using whole-brain VBM.

Grey matter volume anomalies in developmental speech disorder

The children with DSD in the current study showed larger grey matter volume compared to typically developing controls in the left inferior occipital gyrus. The only other reported whole-brain VBM study comparing children with and without speech sound errors (to our knowledge) found atypical grey and white matter within the occipital lobe (Preston et al. 2014). However, that study reported reduced grey matter volume in the right occipital lobe rather than increased volume on the left as in the present study, and those differences were not quite significant. Functional anomalies in the occipital lobe have previously been reported in DSD groups using task-based fMRI (Preston et al. 2012; Tkach et al. 2011). While the visual cortex is not typically considered part of the neural network for speech production, it does play a role in speech perception via its role in processing the visual aspects of speech (Hickok and Poeppel 2007; Nath and Beauchamp 2011; Pulvermüller and Fadiga

2010). Previous work has shown that visual speech information (i.e., observed articulations) supports early speech development, as it enhances phoneme discrimination and assists phonetic category learning (Teinonen et al. 2008). It has also been reported that the visual cortex is especially important for speech perception when the auditory processing of speech is compromised (Bergeson et al. 2005; Schepers et al. 2015). Furthermore, larger grey matter volume in the visual cortex has been associated with greater reliance on the visual, compared to auditory, aspects of speech in individuals with hearing impairment (Allen et al. 2013). Given that DSD has been associated with deficits in auditory speech perception (Edwards et al. 2002; Kenney et al. 2006), our finding of larger volume in the occipital lobe could reflect greater reliance on the brain regions involved in the visual aspects of speech perception as a compensatory mechanism for inefficiencies in the auditory-perceptual networks, as previously proposed by Preston et al. (2014). The visual cortex also plays an important role in reading; however, the children with DSD in this study did not show significantly reduced reading scores compared to controls, and thus, this finding is unlikely to be explained by an underlying problem with the network sub-serving reading skills.

Differences between DLD and DSD

We found no significant differences in grey matter volume between these groups after correcting for whole-brain multiple comparisons. Uncorrected results revealed several right-sided differences between the groups. For example, the children with DLD showed larger grey matter volume in the transverse temporal gyrus, IFG, parahippocampal gyrus, and caudate tail, as well as smaller volume in the right cuneus and inferior occipital lobe. While these results are not corrected for multiple comparisons and thus should be interpreted with caution, it is interesting that differences, albeit subtle, are detected in these brain regions given their role in speech, language or learning. In particular, the transverse temporal gyrus and the IFG are fundamental components of the speech language network, important in the early processing of incoming auditory information and speech/language production, respectively (Darby and Walsh 2005). While further testing in future cohorts is required, the above subtle differences could provide potential targets for focused hypotheses in future research.

Strengths and limitations

Some characteristics and limitations of this study should be considered when interpreting the results. Strengths include the narrow age range designed to enhance sample homogeneity and the well-documented developmental history of participants, confirmed by longitudinal data. In particular, the detailed developmental histories enabled confirmation of persistence (or absence) of language/speech difficulties from preschool to early adolescence, and verified the absence of a history of other developmental difficulties. The concomitant caveat of the age range being purposely restricted to children between 9 and 11 years is that these findings do not necessarily generalize to children outside this age range. An additional strength of the current study was that we used a whole-brain VBM analysis protocol (http://dbm.neuro.uni-jena.de/vbm8/) which is less biased than region of interest analysis and enables easier replication in future research. Despite attempts to maximize group homogeneity, the DLD and DSD groups did nonetheless show heterogeneity in their respective phenotypes. The DSD group included children with errors consistent with articulation disorder, phonological disorder, or both, while the DLD group included children with primary receptive, primary expressive, and mixed receptive/expressive language impairments.

Summary and conclusion

The results from this study provide an important piece of the puzzle regarding how the brains of 9–11 years of children with DLD and DSD differ structurally from typical controls. We found evidence to suggest an association between cerebellar anomalies and DLD which is consistent with the important role that the cerebellum plays in language and skill acquisition during development, and may be associated with the procedural learning deficit proposed in DLD. In addition, we found a relationship between DSD and regional grey matter volume in the left inferior occipital gyrus, possibly indicating a compensatory role of the visual processing regions due to sub-optimal auditory-perceptual processes.

Future directions

Given that underlying neurobiology is influenced by a complex interaction between genes and environmental experiences, research in DLD and DSD would likely benefit from a more holistic approach. Future research in individuals with and without DLD and DSD that incorporates genetic, imaging, cognitive-behavioural, and environmental data is warranted. In particular, large-scale studies that examine these factors longitudinally would likely lead to better understanding of the relationship between neurobiology and developmental language and developmental speech disorder at various stages of development.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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