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Altered Gray Matter Volumes in Language-Associated Regions in Children with Developmental Language Disorder and Speech Sound Disorder

Short Running Title:

Gray Matter Alterations in DLD and SSD

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Abstract

Developmental language disorder (DLD) and speech sound disorder (SSD) are common, and although scientific evidence for structural and functional alterations in DLD / SSD is accumulating, current neuroimaging studies provide an incongruent picture. Here, we hypothesized that children affected by DLD and SSD present with gray matter (or gray matter asymmetry) aberrations in brain areas associated with language processing compared to typically developing (TD) children. To assess this hypothesis, we enhanced MRI-based information with microscopically defined cytoarchitectonic probabilities of Broca's area (BA 45, BA 44) as well as an auditory area (TE 3.0). We detected a larger rightward gray matter asymmetry in BA 45 in children with DLD (n=13) and with SSD (n=18) compared to TD children (n=18), albeit only on a trend level. Interestingly though, we observed significantly larger gray matter volumes in right BA 45 in DLD compared to SSD children (and also compared to TD children).

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1. Introduction

Developmental language disorder (DLD) and speech sound disorder (SSD) are common, affecting as many as one in twenty preschool children (Eadie et al., 2015; Reilly et al., 2010). Both conditions impact conversational exchanges and have a substantial negative social impact. Later in life, during adolescence and adulthood, poorer outcomes in educational attainment as well as occupational status are frequent compared to unaffected peers (Conti-Ramsden & Botting, 2004; Conti-Ramsden, Durkin, Toseeb, Botting, & Pickles, 2017; Johnson, Beitchman, & Brownlie, 2010; Lewis et al., 2011; Mann & Foy, 2007; Mok, Pickles, Durkin, & Conti-Ramsden, 2014). Both disorders have well characterized, but heterogeneous linguistic phenotypes. That is, children with DLD may show any combination of comprehension and/or expression deficits across semantic, phonological or syntactic domains, while children with SSD present with any combination of articulation or phonological errors.

While the symptomatology of both disorders has been well established from infancy into adulthood (Beitchman et al., 2001; Conti-Ramsden, St Clair, Pickles, & Durkin, 2012; Eadie et al., 2015; Johnson et al., 2010; Morgan et al., 2017), their underlying biology remains poorly understood. As per definition, both DLD and SSD constitute deficits in language perception / expression or speech production that occur in the absence of a frank neurological lesion or known cause (Liegeois, Mayes, & Morgan, 2014; Mayes, Reilly, & Morgan, 2015; Morgan, Bonthrone, & Liegeois, 2016). That is, individual brains do not seem to show any obvious anatomical peculiarities that potentially could explain the existing language / speech symptoms (Morgan et al., 2016). From a neurobiological perspective, however, it would be presumptuous to accept that there are no structural differences, and it seems likely that anatomical aberrations are just subtle enough to evade common neuroradiologic scrutiny. In fact, on a group level, existing studies have revealed cerebral alterations in local gray matter volumes or asymmetry when comparing DLD and SSD brains to typically developing brains (Liegeois et al., 2014; Mayes et al., 2015; Morgan et al., 2016; Njiokiktjien, 1990). However, findings have been extremely inconsistent across publications in terms of the location as well as the direction of the effect (Liegeois et al., 2014; Mayes et al., 2015; Morgan et al., 2016). Nevertheless, at least with respect to DLD, a relatively recent systematic review concluded that structural and functional aberrations seem to be located “within traditionally recognized language regions” (Mayes et al., 2015), an observation that might also be extended to SSD (Kadis et al., 2014; Liegeois et al., 2014; Liegeois, Morgan, Connelly, & Vargha-Khadem, 2011; Tkach et al., 2011).

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Here, we aim to move forward this field by applying a state-of-the-art morphometric method that integrates signal information obtained through high-resolution *in vivo* MRI and region-specific probability information obtained *ex vivo* based on cytoarchitectonic mapping (Kurth, Cherbuin, & Luders, 2015a; Kurth, Jancke, & Luders, 2017b, 2018; Luders, Kurth, Toga, Narr, & Gaser, 2013). We set out to investigate whether regional gray matter tissue is altered in children with DLD and SSD compared to typically developing children. Given the heterogeneity of previous findings as well as the statistical challenges arising when dealing with multiple comparisons, we restricted our investigation to three language regions. More specifically, analyses were aimed at Broca's area defined as BA 44 and BA 45 located within the left inferior frontal gyrus (Amunts et al., 1999) as well as a higher-order auditory processing area (TE 3.0) located within the posterior part of the superior temporal gyrus (Morosan, Schleicher, Amunts, & Zilles, 2005).

Existing theories suggest an altered hemispheric processing of language in affected children (Badcock, Bishop, Hardiman, Barry, & Watkins, 2012; De Fosse et al., 2004; de Guibert et al., 2011; Fabbro, Libera, & Tavano, 2002; Herbert et al., 2005; Mayes et al., 2015; Njiokiktjien, 1990; Plante, Swisher, & Vance, 1989; Witelson & Rabinovitch, 1972), which may be accompanied by functional and structural deviations from the usual degree of hemispheric dominance (Dubois et al., 2009). Thus, we hypothesized altered gray matter volumes in affected children, with less left-hemispheric gray matter (or more right-hemispheric gray matter), compared to typically developing children. Moreover, we examined whether such potential hemisphere-specific gray matter alterations would also manifest as significant gray matter *asymmetry* differences across groups. More specifically, we tested the hypothesis of a decreased leftward asymmetry (or increased rightward asymmetry) in affected children (Fabbro et al., 2002; Mayes et al., 2015; Njiokiktjien, 1990).

2. Methods

2.1 Sample Source and Inclusion Criteria

The current study included 18 typically developing (TD) children, 13 children with DLD, and 18 children with SSD, aged between 9;3 years and 11;3 years. These children were selected from a large pool of participants recruited for the Early Language in Victoria Study; ELVS (Reilly et al., 2007; Reilly et al., 2010). ELVS is a longitudinal epidemiological community cohort study of 1,910 children enrolled at 8 months of age in 2003/2004. With language development being tracked almost annually, language trajectories are well-known from infancy to time of scanning when children were between

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9;3 years and 11;3 years old. Ethics approval (HREC31225) was obtained from the Human Research Ethics Committee at the Royal Children's Hospital, Melbourne (Australia). At least one parent provided informed consent and children provided oral assent.

Inclusion criteria for the current study for all children were a non-verbal IQ of≥ 80 on the Kaufman Brief Intelligence Test; KBIT (Kaufman & Kaufman, 2004) at age 4 and the Wechsler Abbreviated Scales of Intelligence; WASI (Wechsler, 1999) at age 7. Moreover, all children were required to be English native speakers and, aside from the presence of SSD or DLD in the respective groups, to have no history of other neurodevelopmental disorders (e.g., attention-deficit / hyperactivity disorder, autism spectrum disorder, developmental coordination disorder) or any other significant medical or developmental issues. Importantly, TD and SSD children were required to show normal language performance, whereas TD and DLD children were required to have normal speech performance, as based on the assessment tools described below and in conversation.

2.2 Study-specific Assessments and Group Characteristics

Each child underwent a 90-minute assessment to confirm language, speech, and non-verbal cognitive abilities as well as handedness. Language was examined using four subtests of the Clinical Evaluation of Language Fundamentals assessment tool (CELF Preeschool-II and CELF-IV, Semel, Wiig, & Secord, 2006; Wiig, Secord, & Semel, 2006). The subtests – Concepts and Following Directions, Recalling Sentences, Formulating Sentences, and Word Classes Total – provide an overall language estimate (Core language score) as well as summary scores for receptive and expressive language[1] (for review of diagnostic criteria in DLD, see Bishop, Snowling, Thompson, & Greenhalgh, 2017; Reilly et al., 2014). Speech was examined using the Goldman-Fristoe Test of Articulation (GFTA-II, Goldman & Fristoe, 2005) eliciting the speech sounds of English language in initial, medial and final positions in single words, which were analyzed for persistent articulation and/or phonological errors to confirm a diagnosis of SSD[2] (Dodd, Ttofari Eecen, Brommeyer, Reilly, & Morgan, 2017; Morgan et al., 2017). Non-verbal intelligence, hereafter referred to as performance IQ (PIQ), was measured with the Block design and Matrix reasoning subtests of the WASI-II (Wechsler, 2011). Handedness was determined using a modified version of the Edinburgh Handedness Inventory (Oldfield, 1971). Last but not least,

[1] CELV-IV standard scores (total, receptive, expressive) were also used as regressors in the statistical model for Analysis II.
[2] GFTA-II standard scores were also used as a regressor in the statistical model for Analysis II.

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total intracranial volume (TIV) was calculated using the CAT12 toolbox (http://dbm.neuro.uni-jena.de/vbm.html).

Overall, there was no significant difference with respect to age, sex, handedness, or TIV between the three groups (see **Table 1**). Children with DLD exhibited consistently impaired language, defined as a total language score of ≤ 81 at two time points (either at ages 4 and 7, or at ages 5 and 7) as per the CELF Preschool-II (Wiig, Secord, & Semel, 2006) at age 4 and the CELF-IV (Semel, Wiig, & Secord, 2006) at ages 5 and 7. **Supplementary Table 1** provides detailed information on the language phenotypes in the DLD group. DLD children had significantly lower CELF-IV scores (total, receptive, and expressive) than the other two groups (see **Table 1**). Children with SSD showed impaired speech, as previously described (Luders et al., 2017). **Supplementary Table 2** provides detailed information on the speech phenotypes in the SSD group. As expected, SSD children had significantly lower GFTA-II scores than the other two groups (see **Table 1**). Finally, a significant group difference was also revealed for PIQ, which – although within the typical range – was lower in DLD children than in the other two groups (see **Table 1**), similar as has been previously reported (Conti-Ramsden et al., 2012).

- Table 1 -

2.3 Image Data Acquisition and Preprocessing

Participants were scanned at the Florey Institute of Neuroscience and Mental Health in Melbourne, Australia (https://www.florey.edu.au/). All brain images were acquired on a Siemens 3 Tesla Skyra system with a 20-channel head coil using the following parameters: TR = 1900 ms, TE = 2.49 ms, flip angle = 9°, matrix size = 256 x 256, field of view: 240 x 240 mm^2, voxel size = 0.9 × 0.9 × 0.9 mm^3. For each participant, the acquired brain images were immediately inspected for motion artifacts and the scan was repeated if necessary. The images were analyzed using the SPM12 software (http://www.fil.ion.ucl.ac.uk/spm; version 6685) and the CAT12 toolbox (http://dbm.neuro.uni-jena.de/vbm.html; version 1004), as previously described (Kurth et al., 2015a; Kurth et al., 2017b, 2018; Luders et al., 2013), which resulted in segments of gray matter, white matter, and cerebrospinal fluid (CSF) in native space. TIV was derived by adding those tissue volumes in native space (TIV = GM + WM + CSF).

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2.4 Combining Gray Matter Information with Cytoarchitectonic Tissue Probabilities

The aforementioned gray matter partitions were spatially normalized to the DARTEL template provided by the CAT12 toolbox using 12-parameter affine transformations and high-dimensional warping (Ashburner, 2007). The normalized gray matter segments were divided by the Jacobian determinant derived from the normalization matrix (to preserve the actual voxel-wise gray matter content) and then integrated with cytoarchitectonic probability maps (that also had been spatially normalized to the DARTEL template), as detailed elsewhere (Kurth et al., 2015a; Kurth, Cherbuin, & Luders, 2017a; Kurth et al., 2017b, 2018; Luders et al., 2013). In order to investigate possible structural aberrations in DLD and SSD in language-associated regions, we used the cytoarchitectonic probability maps of left and right[3] BA 45, BA 44, and TE 3.0 (see **Figure 1**)**.** Those maps were originally created using cell-body stained histological sections of 10 *post mortem* brains through cytoarchitectonic mapping (Amunts et al., 1999; Amunts, Schleicher, & Zilles, 2007; Eickhoff et al., 2005; Morosan et al., 2005; Schleicher et al., 2000; Schleicher et al., 2005; Zilles & Amunts, 2010; Zilles, Schleicher, Palomero-Gallagher, & Amunts, 2002). The aforementioned integration resulted in voxel-wise measures of region-specific gray matter content. Multiplying this content with the volume of each voxel and then adding it across the entire image yielded the gray matter volume (in mm^3) for each language-associated region of interest: left / right BA 45, left / right BA 44, and left / right TE 3.0. **Table 2** summarizes the region-specific means and standard deviations of these volumes within each group (TD, DLD, and SSD).

As discussed in detail elsewhere (Kurth et al., 2015a, 2017a; Kurth et al., 2017b, 2018; Luders et al., 2013), combining MRI-based gray matter information with cytoarchitectonic tissue probabilities has several advantages over defining regions of interest (ROIs) the conventional way. For example, conventional approaches rely on visible and/or automatically detectable macro-anatomic landmarks (gyri, sulci, etc.), which are not always present or unambiguously identifiable. Furthermore, even if macro-anatomic landmarks exist, they do not necessarily match the actual cytoarchitectonic (and functionally relevant) boundaries. Moreover, those boundaries may vary substantially between individuals, even after spatial normalization to a template (Amunts et al., 1999; Caspers et al., 2006; Choi et al., 2006; Kujovic et al., 2013; Kurth et al., 2010; Morosan et al., 2005; Palomero-Gallagher et

[3] Since language/speech disorders might be associated with an altered hemispheric processing, the three regions were assessed within both hemispheres.

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al., 2015; Rottschy et al., 2007; Scheperjans et al., 2008). The integration of MRI-based signal intensities with cytoarchitectonic probabilities solves these problems as this approach does not rely on macroscopic landmarks, but on microscopically defined cytoarchitectonic boundaries, while accounting for inter-individual variability in the location and extent of functionally relevant areas.

– Figure 1 –

– Table 2 –

2.5 Statistical Analyses

Statistical procedures pertaining to analysis I and II (see below) were conducted using a general linear model, with the volumetric measures for left and right BA 45, BA 44, and TE 3.0 as dependent variables, and age, sex, TIV, and PIQ as variables of no interest. Significance was assessed at $p \leq 0.05$ corrected for multiple comparisons using a Monte-Carlo simulation with 10,000 permutations to control the family-wise error (Nichols & Holmes, 2007).

Analysis I: Differences in the region-specific gray matter volumes (BA 45, BA 44, TE 3.0) between DLD, SSD, and TD were investigated by including group as the independent variable in the aforementioned model. Significant omnibus effects were assessed using F-tests and, if indicated, followed by between-group comparisons using T-tests. Given that sex differences in language are well known (Bauer, Goldfield, & Reznick, 2002; Halpern, 1992; Hyde & Linn, 1988; Kimura, 1999; Leaper & Smith, 2004; Morisset, Barnard, & Booth, 1995) and have previously been observed with respect to gray matter in BA 44 and 45 (Kurth et al., 2017b), interactions between group and sex were additionally tested.

Analysis II: Correlations between the region-specific gray matter volumes (BA 45, BA 44, TE 3.0) and language/speech skills were investigated by including the CELF-IV scores (total, receptive, expressive) and the GFTA-II scores as independent variables in the aforementioned model. Due to the high inter-correlation between these scores, separate models for each score were used (Poline, Kherif, Pallier, & Penny, 2007). In addition, interactions between group and CELF-IV scores (total, receptive, expressive) as well as GFTA-II scores were tested.

Analysis III: To compare groups with respect to region-specific gray matter *asymmetry*, the asymmetry index (AI) was calculated for each region (BA 45, BA 44, TE 3.0) as previously established (Kurth, Gaser, & Luders, 2015b): AI = (Right - Left) / (0.5 x (Right + Left)). The region-specific

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asymmetry indices were then used as the dependent variable in the statistical model, while group was the independent variable of interest, and age, sex, and PIQ the variables of no interest. As the asymmetry index corrects for global and local differences in brain size (Kurth et al., 2015b), it was not necessary to include TIV as a covariate of no interest (as done in analysis I and II). Significance was assessed at $p \leq 0.05$. Given the exploratory nature of this analysis, we abstained from correcting for multiple comparisons.

3. Results

3.1 Group Differences – Left and Right Gray Matter Volumes

Group-specific boxplots for each region of interest are shown in **Figure 2**. The main effect of group was significant for right BA 45 (p = .041). Follow-up T-tests revealed that this omnibus effect was driven by significantly larger gray matter volumes in DLD compared to TD (p = .008) and to SSD (p = .035). No other region than right BA 45 showed a significant group difference, even if the corrections for multiple comparisons were omitted. There was no significant interaction between group and sex for any of the regions of interest.

– Figure 2 –

3.2 Correlations – Left and Right Gray Matter Volumes

Significant negative correlations were observed in right BA 45 between the region-specific gray matter and all three CELF-IV scores (total: p = .007; receptive: p = .003; expressive: p = .025). For correlation coefficients and regression slopes, please refer to **Figure 3**. No other region than right BA 45 showed a significant negative correlation with the language / speech scores, and significant positive correlations were absent altogether. There was no interaction between group and CELF-IV scores (total, receptive, expressive) or the GFTA-II scores.

– Figure 3 –

3.3 Group Differences – Gray Matter Volume Asymmetry Indices

Group-specific boxplots for each region of interest are shown in **Figure 4**. The main effect of group was significant for BA 45, but only on a trend level (p = .090). Given our *a priori* hypothesis, follow-up

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T-tests were applied revealing significant group differences in rightward asymmetry between TD and DLD (p = .041) as well as between TD and SSD (p = .026) with increased rightward asymmetries in DLD / SSD children compared to TD children. No other region than right BA 45 showed a significant group difference.

– Figure 4 –

4. Discussion

Despite their relatively high prevalence in the population, DLD and SSD have been the subject of few neuroimaging analyses, and reported findings from available studies are incongruent (for review see Liegeois et al., 2014; Mayes et al., 2015; Morgan et al., 2016). Here, we detected increased gray matter volumes within right BA 45 in children with DLD compared to TD children. We also observed a stronger rightward asymmetry in this region, both in DLD children and in SSD children compared to TD children. These findings confirm and extend previously reported DLD-/SSD-related aberrations in brain structure and function, such as observed in the inferior frontal gyrus (which contains Broca's area) or associated with a reduced leftward lateralization (Badcock et al., 2012; de Guibert et al., 2011; Fabbro et al., 2002; Liegeois et al., 2014; Mayes et al., 2015; Njiokiktjien, 1990; Plante et al., 1989).

4.1 Effects in BA 45 (right hemisphere): A case for Procedural Deficits?

The laterality of the effect is thought-provoking as previous neuroimaging studies in healthy young adults have reported right BA 45 to be involved in episodic memory retrieval as well as sustained attention, while left and right BA 45 are active during working memory tasks (Cabeza & Nyberg, 2000). In contrast, mainly left BA 45 has been implicated in language and semantic memory retrieval (Cabeza & Nyberg, 2000; Dubois et al., 2009). It is therefore possible that the current effects in right BA 45 point to faulty memory and/or attention networks in affected children, rather than to impaired language networks *per se*. Indeed, broader deficits in cognitive processing have been proposed to accompany or underlie DLD (Mayes et al., 2015; Ullman & Pierpont, 2005). An influential theory, the 'procedural deficit' hypothesis, proposes that DLD for example is not exclusively a language disorder, but rather results from abnormalities in a network subserving the learning and execution of cognitive and motor skills (Ullman & Pierpont, 2005). In support of this assumption, altered activation patterns

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have been observed in functional imaging studies in DLD, regardless of whether a classic language task or a more executive functioning focused paradigm was used (Badcock et al., 2012; de Guibert et al., 2011; Mayes et al., 2015; Weismer, Plante, Jones, & Tomblin, 2005). Moreover, it has been demonstrated that DLD is often accompanied by additional non-linguistic deficits (Lum, Conti-Ramsden, Page, & Ullman, 2012; Ullman & Pierpont, 2005). Future research may therefore specifically target brain regions underlying the learning and execution of cognitive and motor skills, such as frontal-basal ganglia circuits, etc. (Ullman & Pierpont, 2005). Indeed, some studies seem to suggest that DLD is associated with aberrations of the caudate nucleus (which is part of the basal ganglia), but reports differ with respect to the direction of that effect (Badcock et al., 2012; Liegeois et al., 2014; Mayes et al., 2015; Soriano-Mas et al., 2009).

Whether these assumptions can be extended to SSD remains to be explored. Of note, there were no significant differences between SSD and TD in the gray matter volume of right BA 45, but perhaps this constitutes a false negative finding due to limited statistical power, although the number of individuals in the SSD sample (n=18) was already larger than in the DLD sample (n=13). Interestingly, there were no significant correlations between GFTA-II scores (which quantify symptom severity in SSD) and gray matter volumes in the regions of interest examined. Thus, SSD-specific alterations may, indeed, be located outside the traditionally recognized language regions. In fact, two previous studies have reported increased gray matter in SSD in the left supramarginal gyrus (Kadis et al., 2014; Preston et al., 2014), which is thought to play a role in auditory-sensorimotor integration as well as in learning and adapting sensorimotor patterns for speech (Gow, 2012; Shum, Shiller, Baum, & Gracco, 2011). Furthermore, functional alterations have been observed in SSD in the portions of the primary motor and somatosensory areas involved in the sensorimotor coordination of speech (Liegeois et al., 2011; Tkach et al., 2011).

4.2 Effects in BA 45 (asymmetry): Altered Hemispheric Processing?

The observed effects in right BA 45, together with the asymmetry effect, may reflect a shift of hemispheric involvement and mobilization of language/speech reserves in DLD and SSD. However, rather than assuming a completely reversed direction of asymmetry (e.g., from left to right), the findings of this study point to a more subtle alteration in the degree of the asymmetry (e.g., from rightward to even more rightward). More specifically, as shown in **Figure 4** (top panel), region BA 45 is lateralized to the right in all three groups, but to an even larger degree in DLD and SSD children than

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in TD children. Interestingly, the seemingly altered asymmetry across groups (omnibus effect) was only significant on a trend level. This may either indicate that the current study lacks the necessary statistical power or, alternatively, that the overall asymmetry effect may constitute a false positive finding. Future studies involving larger samples will need to resolve this question. Importantly, prior reports of a decreased leftward asymmetry in DLD and in SSD (Badcock et al., 2012; de Guibert et al., 2011; Fabbro et al., 2002; Liegeois et al., 2014; Mayes et al., 2015; Njiokiktjien, 1990; Plante et al., 1989) are not necessarily in conflict with our present findings suggesting an increased rightward asymmetry. Those prior analyses included a much larger region of the inferior frontal gyrus than our current analysis aimed at discriminating between two subregions of Broca's area (BA 44 and BA 45). In fact, when we combined BA 44 and BA 45 into a single region in a supplemental analysis, we observed a leftward lateralization across all three groups, but with significantly less leftward asymmetry in DLD and SSD than TD children (see **Supplemental Figure** 1), which is in agreement with those previous reports.

4.3 Conclusions and Outlook

DLD presented with significant aberrations in gray matter volumes in BA 45. Moreover, both DLD and SSD were associated with an altered gray matter asymmetry in BA 45 on a trend level. Sufficiently powered follow-up studies are necessary not only to replicate the current findings, but also to conduct DLD- and SSD-specific analyses while expanding the number of regions investigated. Including areas outside the traditionally recognized language (or language-relevant) regions seems to be especially advisable with respect to SSD. Furthermore, future studies, preferably longitudinal in nature, will have to test existing theories about the etiology of DLD as well as SSD to foster our understanding of the heterogeneity of these disorders and also to aid in the development of suitable diagnostic tools (Morgan et al., 2016; Morgan et al., 2017). On this note, the observed negative correlations between gray matter of right BA 45 and CELF-IV scores indicate that larger tissue volumes are associated with worse language performance. Importantly, this relationship was evident across all groups (DLD, SSD, and TD). Thus, increased gray matter in right BA 45 – as observed here in DLD – seems to be linked to stronger negative impacts. If this association could be confirmed in studies involving larger samples, the gray matter volume within BA 45 – and potentially also the magnitude of its gray matter asymmetry – might serve as a marker for the severity of either (or both) language disorder(s).

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Disclosure Statement

There are no actual or potential conflicts of interest.

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Figure Legends

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Figure 1. Probabilistic Regions of Interest. Displayed are the cytoarchitectonically derived probability maps of BA 45 (top panel) and BA 44 (middle panel), both constituting Broca's region within the left inferior frontal gyrus, as well as the auditory region TE 3.0 (bottom panel) within the posterior part of the superior temporal gyrus. All regions are presented on renderings of the MNI single subject template. The color bar encodes the region-specific probability.

Figure 2. Region- and group-specific gray matter volumes. The boxplots depict each group's median, quartile, and 1.5 interquartile range per hemisphere for BA 45 (top panel), BA 44 (middle panel) and TE 3.0 (bottom panel). All volumes are adjusted for age, sex, TIV, and PIQ. Groups are coded in color (TD=gray; DLD=blue; SSD=green) and the red asterisks mark the significant group differences (DLD>TD; DLD>SSD) at $p \leq 0.05$, corrected.

Figure 3. Significant correlations between region-specific gray matter and language skills. The scatterplots depict the association between the gray matter volume in right BA 45 and the CELF-IV *total* language scores (left panel), the CELF-IV *receptive* language scores (middle panel), and the CELF-IV *expressive* language scores (right panel). All volumes are adjusted for age, sex, TIV, and PIQ.

Figure 4. Region- and group-specific gray matter asymmetries. The boxplots depict each group's median, quartile, and 1.5 interquartile range for BA 45 (top panel), BA 44 (middle panel) and TE 3.0 (bottom panel). Positive values indicate a rightward asymmetry. All asymmetry indices are adjusted for age, sex, and PIQ. Groups are coded in color (TD=gray; DLD=blue; SSD=green) and the red asterisks mark the significant group differences (DLD>TD; SSD>TD) at $p \leq 0.05$, uncorrected.

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Table 1: Sample Characteristics

	Typically Developing (TD)	Developmental Language Disorder (DLD)	Speech Sound Disorder (SSD)
Sex (boys / girls)	10 / 8	6 / 7	7 / 11
Age in months (mean ± SD)	122.44 ± 3.71	122.46 ± 2.73	123.22 ± 3.90
TIV in ml (mean ± SD)	1,578.18 ± 129.73	1,502.78 ± 128.53	1,586.87 ± 123.44
CELF-total (mean ± SD)*	107.28 ± 8.55	85.31 ± 9.32	101.39 ± 10.36
CELF-expressive (mean ± SD)*	109.00 ± 9.88	87.77 ± 10.89	102.78 ± 10.66
CELF-receptive (mean ± SD)*	105.83 ± 8.39	86.46 ± 7.63	100.83 ± 8.47
GFTA (mean ± SD)*	103.00 ± 2.54	103.15 ± 2.15	99.72 ± 4.39
WASI-PIQ (mean ± SD)*	101.76 ± 12.25	94.46 ± 9.71	106.00 ± 10.89

The asterisks denote where the ANOVA revealed a significant group effect.

TIV = Total Intracranial Volume; CELF = Clinical Evaluation of Language Fundamentals; GFTA = Goldman-Fristoe Test of Articulation; WASI-PIQ = Wechsler Abbreviated Scales of Intelligence - Performance IQ

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Table 2: Group-specific regional gray matter volumes (mean ± SD) in ml

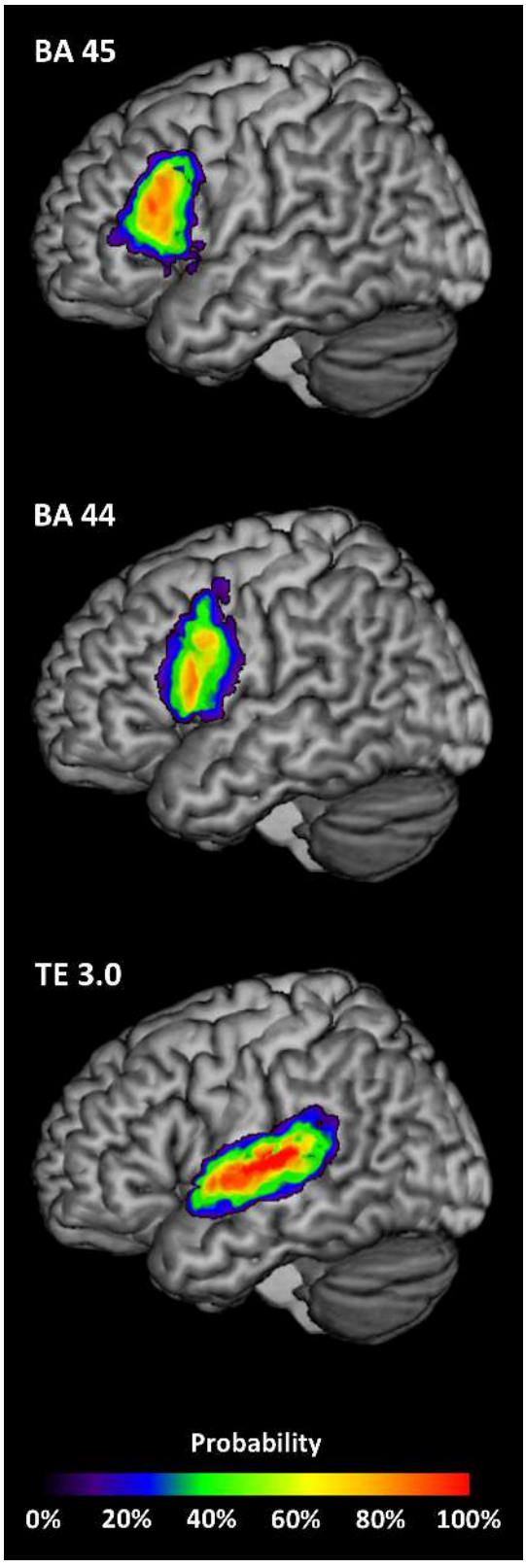
	Typically Developing (TD)	Developmental Language Disorder (DLD)	Speech Sound Disorder (SSD)
Left BA 45	2.73 ± 0.37	2.68 ± 0.34	2.67 ± 0.27
[adjusted][1]	$[2.70 \pm 0.25]$	$[2.81 \pm 0.27]$	$[2.60 \pm 0.18]$
Right BA 45	3.30 ± 0.31	3.44 + 0.43	3.39 ± 0.26
[adjusted]	$[3.29 \pm 0.27]$	$[3.58 \pm 0.26]$	$[3.35 \pm 0.20]$
Left BA 44	3.81 ± 0.31	3.79 ± 0.47	3.91 ± 0.30
[adjusted]	$[3.79 \pm 0.24]$	$[3.90 \pm 0.34]$	$[3.88 \pm 0.22]$
Right BA 44	2.45 ± 0.22	2.50 ± 0.24	2.58 ± 0.27
[adjusted]	$[2.45 \pm 0.20]$	$[2.58 \pm 0.16]$	$[2.56 \pm 0.20]$
Left TE 3.0	4.34 ± 0.34	4.35 ± 0.58	4.41 ± 0.47
[adjusted]	$[4.37 \pm 0.29]$	$[4.59 \pm 0.32]$	$[4.39 \pm 0.27]$
Right TE 3.0	3.70 ± 0.31	3.73 ± 0.52	3.83 ± 0.48
[adjusted]	$[3.69 \pm 0.30]$	$[3.90 \pm 0.32]$	$[3.80 \pm 0.32]$

[1] after removing the variance associated with age, sex, total intracranial volume (TIV), and performance IQ (PIQ)

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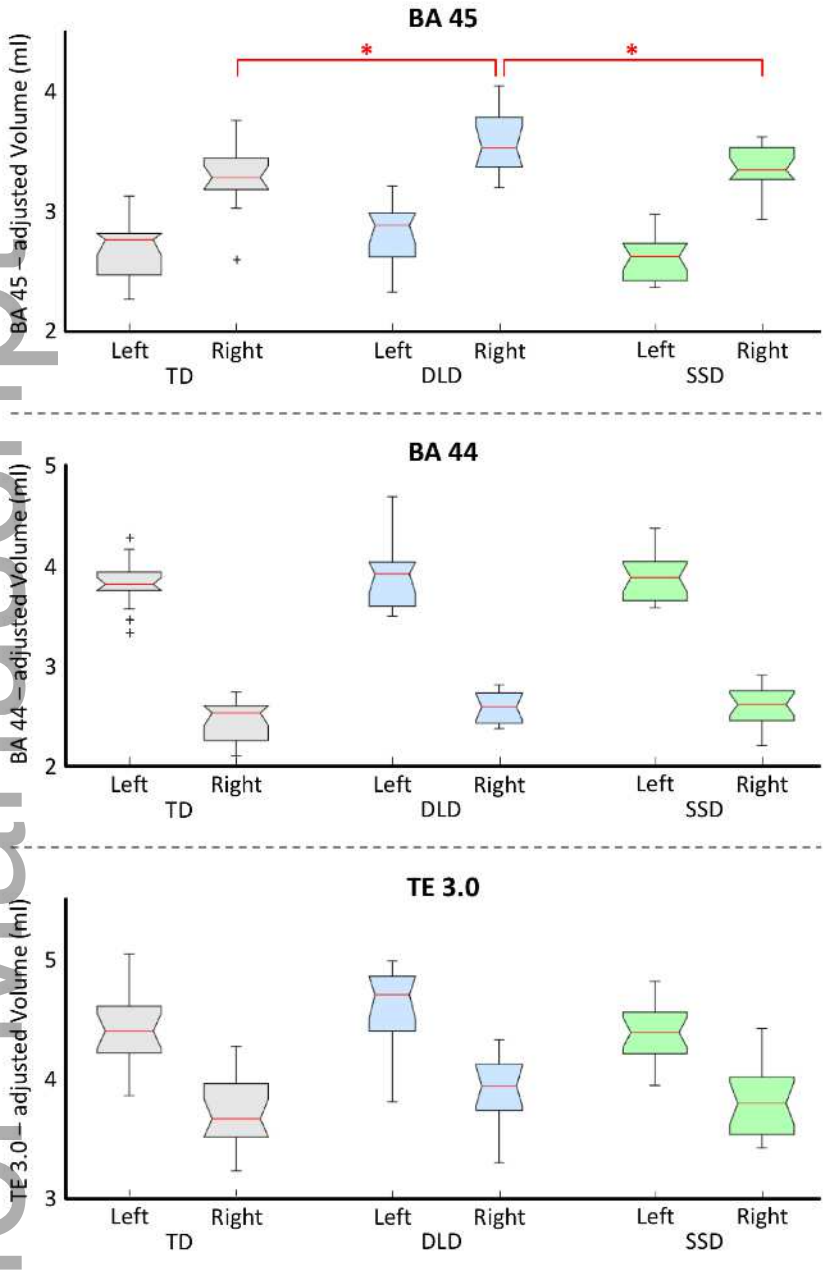
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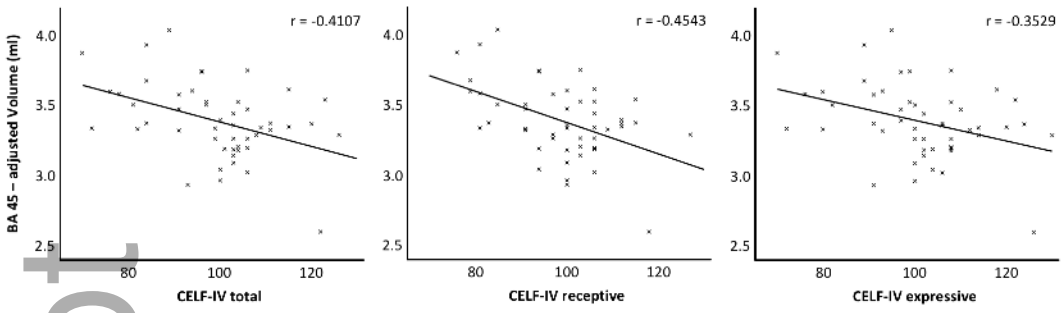
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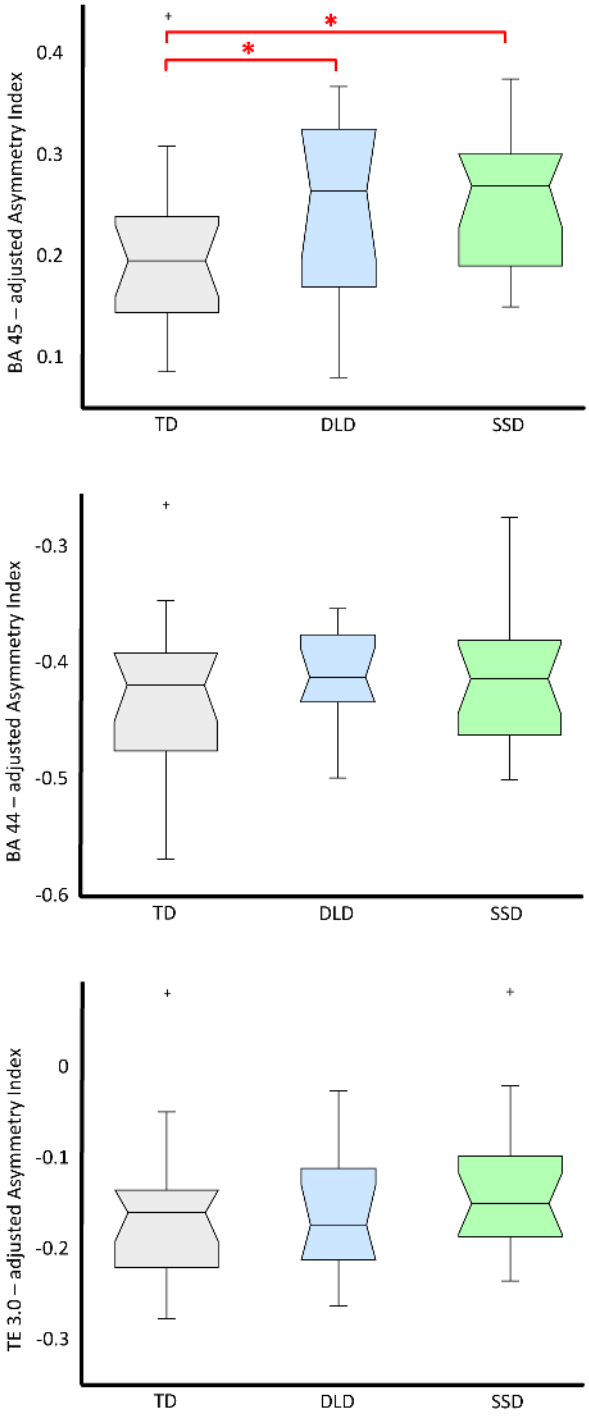


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