Title
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Journal
Brain and Language, 128(1)

ISSN
0093-934X

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Publication Date
2014

DOI
10.1016/j.bandl.2013.11.001

Peer reviewed

Brain & Language 128 (2014) 25–33

Contents lists available at ScienceDirect

Brain & Language

journal homepage: www.elsevier.com/locate/b&l

Structural brain differences in school-age children with residual speech sound errors

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ARTICLE INFO

Article history:
Accepted 3 November 2013
Available online 15 December 2013

Keywords:
Speech sound errors
Speech sound disorders
Structural MRI
Children

ABSTRACT

The purpose of the study was to identify structural brain differences in school-age children with residual speech sound errors. Voxel based morphometry was used to compare gray and white matter volumes for 23 children with speech sound errors, ages 8;6–11;11, and 54 typically speaking children matched on age, oral language, and IQ. We hypothesized that regions associated with production and perception of speech sounds would differ between groups. Results indicated greater gray matter volumes for the speech sound error group relative to typically speaking controls in bilateral superior temporal gyrus. There was greater white matter volume in the corpus callosum for the speech sound error group, but less white matter volume in right lateral occipital gyrus. Results may indicate delays in neuronal pruning in critical speech regions or differences in the development of networks for speech perception and production.

1. Introduction

Speech sound disorders, which involve problems achieving accurate productions of the sounds of the native language, are among the most common type of communication disorder in childhood. In general, speech sound disorders may be associated with reduced speech intelligibility and negative social/interpersonal, academic, and educational outcomes (Crowne Hall, 1991; McCormack, McLeod, McAllister, & Harrison, 2009; Silverman & Paulus, 1989). During typical speech development, phonetically accurate production of speech sounds is usually achieved by about 8–9 years of age (Sax, 1972; Smit, Hand, Freilinger, Bernthal, & Bird, 1990). Residual speech sound errors (SSEs) are a subtype of speech sound disorder marked by speech errors that persist beyond this developmental time window (Shriberg, 2009). Children with residual SSEs typically produce substitutions or distortions of later developing sounds, such as /s, z, r, l, θ, ʃ, ʧ/ (Shriberg, 2009). Whereas decades of research have focused on the cognitive-linguistic and sensorimotor processes that underlie production and/or perception of speech in children with SSEs, this study aims to characterize the structural neurobiology associated with a failure to achieve phonetically accurate speech in school-age children.

There are presently no well-established neurobiological models of childhood speech sound disorders, as neuroimaging has only recently been applied to this population. Cognitive-linguistic theories of speech sound disorders often focus on auditory perceptual influences (Rvachew & Grawburg, 2006; Shuster, 1998), and recent studies investigating the neural bases of speech sound disorders have provided preliminary support for theories of auditory perceptual mechanisms (Gonçalves, Wertzner, Samelli, & Matas, 2011; Preston et al., 2012). Recent models of the neurobiological components of normal speech production and perception also offer brain regions for focusing our exploration of hypothesized differences in the brain structures of children with SSEs. We therefore begin by reviewing brain regions known to play important roles in speech sound production and perception; we then discuss general principles of gray and white matter development; finally, we summarize

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http://dx.doi.org/10.1016/j.bandl.2013.11.001

the existing literature on brain differences associated with developmental speech sound disorders.

1.1. Brain networks for speech sound production

Complex networks are involved in speech sound production, and several of the regions involved in production also play critical roles in the perception of phonetic aspects of speech. One neurobiological model that has attempted to integrate the many years of research on speech production and perception is described by Hickok, Houde, and Rong (2011). They identify dorsal superior temporal gyrus (STG) as a region performing analysis of incoming spectral and temporal information, as well as phonological encoding in the bilateral middle/posterior aspects of superior temporal sulcus. Integration of sensory and motor information is believed to occur primarily at the left posterior Sylvian fissure at the temporal–parietal juncture. Additionally, aspects of speech perception that rely heavily on articulatory encoding are thought to engage the left posterior inferior frontal gyrus/anterior insula, as well as left premotor cortex.

Another neurobiological model, the DIVA model, also outlines feed-forward and feedback processes in speech production centered in various cortical and subcortical regions (Bohland, Bullock, & Guenther, 2010; Terband, Maassen, Guenther, & Brumberg, 2009; Tourville & Guenther, 2011). As described by Tourville and Guenther (2011), feed-forward mechanisms may include a "speech sound map" believed to be centered in the left posterior inferior frontal gyrus. Speech initiation mechanisms reside mainly in the supplementary motor area, and regions controlling articulatory velocity/position are believed to be located in ventral motor cortex. Auditory feedback mechanisms are believed be centered in STG, including Heschl's gyrus (in primary auditory cortex) and somatosensory feedback mechanisms are thought to be centered in supramarginal gyrus and ventral somatosensory cortex. The integration of these feedback mechanisms is believed to involve right ventral premotor cortex and posterior inferior frontal gyrus. It is possible that differences in the structural development of any of these regions could impact speech sound acquisition.

1.2. Gray and white matter development

Gray matter in the brain consists primarily of neuronal cell bodies and glial cells, and it is believed to serve critical functional roles in the brain's processing of information. Gray matter is generally found to decrease throughout development in school-age children, though the trend is non-linear (Wilke, Krägeloh-Mann, & Holland, 2007) and region-dependent (Giedd et al., 1999). The reductions in gray matter volume may be due to synaptic pruning and/or the development of more specialized and more efficient circuits (Alexander-Bloch, Raznahan, Bullmore, & Giedd, 2013). Delays in neural development might therefore lead to larger gray matter in speech-specific regions, which might be the case for children with residual SSEs. An association between structure and function over the course of development has been observed (Alexander-Bloch et al., 2013), and prior work on functional brain differences in children with SSEs may be better understood if there are structural covariances as well.

White matter consists of myelinated axons, and it serves important roles of connecting functional regions and transmitting messages. During the course of development, there is an increase of white matter from birth through adolescence. In particular, between preschool and adolescence, there is an increase in the white matter of the internal capsule, as well as an increase in white matter in the left arcuate fasciculus (connecting frontal/temporal speech-related regions), which is presumed to reflect the left-hemisphere specialization for speech circuits (Paus et al., 1999). Reduced white matter volume has been reported in some children with developmental delay and has been interpreted to reflect delayed myelination (Pujol et al., 2004). Although there do not appear to be any studies of white matter in children with SSE, reduced white matter in speech-related circuits could indicate under-developed connections. Increased white matter in children with SSE could be indicative of stronger connections among regions.

Structural differences in speech-related regions have been observed in adults learning new (non-native) speech sounds. For example, Golestani and Pallier (2007) compared groups of good and poor learners of a non-native sound. Good learners had greater white matter density in left insula/prefrontal cortex and in bilateral inferior parietal cortex than poor learners. Good learners of speech sounds have also been found to have more asymmetry in white matter volume (left greater than right) in parietal regions just anterior to the parietal–occipital sulcus (Golestani, Paus, & Zatorre, 2002). Although these results come from typically speaking adults, they point to white matter differences that are associated with relatively good and poor speech sound learning mechanisms.

1.3. Neural differences in individuals with developmental speech impairments

The present study is guided by a recent fMRI investigation of school-age children with SSEs who had normal oral language skills. Preston et al. (2012) found greater activation for school-age children with SSEs compared to controls on a speech processing tasks in several regions, including left and right STG, left insula, precuneus, cuneus, right supramarginal gyrus, right precentral gyrus, and right post-central gyrus. Results were interpreted as increased reliance on dorsal speech perception circuits and decreased reliance of ventral speech perception networks, along with increased activation in several right hemisphere speech processing regions. As an extension of these functional results, the current study aims to identify structural differences in this same cohort of school-age children with SSEs, while adding a larger sample.

Much of what is known about the structural brain differences in individuals with SSEs comes from research on the KE family. This family consists of several members with a mutation of the FOXP2 gene resulting in significantly impaired speech and language skills. Among the family members with the mutation, structural differences include reduced gray matter in left inferior frontal gyrus, bilateral caudate nucleus (head), and left supplementary motor area (Watkins, Gadian, & Vargha-Khadem, 1999; Watkins et al., 2002). Affected family members also had more gray matter than unaffected members in left anterior insula, bilateral putamen, right tail of the caudate nucleus, right sensorimotor cortex, and bilateral STG. Additional analyses (Belton, Salmond, Watkins, Vargha-Khadem, & Gadian, 2003) confirmed these findings of reduced gray matter density in bilateral caudate nucleus, cerebellum, and bilateral inferior frontal gyrus. Increased gray matter density was observed in the planum temporale of the STG. Functional magnetic resonance imaging (fMRI) data from affected members of the family during a verb generation task revealed reduced activation in Broca's area and the right hemisphere homologue, right putamen, and left supramarginal gyrus. Increased activation was observed in bilateral posterior STG, middle temporal gyrus, and precentral gyrus (Liegeois et al., 2003; see also Vargha-Khadem, Gadian, Copp, & Mishkin, 2005). Although these data provide strong evidence of disruptions in a variety of speech circuits, the characteristics of this family are unique and relatively severe, and mutation of the FOXP2 gene is not commonly observed in individuals with SSE, making it

difficult to generalize these findings to typical cases of school-age children with SSEs.

Beyond what has been learned from the KE family, there do not appear to be any studies of structural differences in children with SSEs that do not include children with additional diagnoses of language impairment or developmental disorders. Thus, existing studies come primarily from case studies of unique or very severe speech problems, and these studies typically involve identification of gross differences. Plante, Swisher, Vance, and Rapcsak (1991) reported structural MRI differences for eight boys ages 4;2–9;6 with specific language impairment, four of whom also scored at least one standard deviation below the mean on an articulation test. Two of the four participants with low articulation scores had atypical asymmetries of the perisylvian area (with equal right and left perisylvian regions, rather than the typical pattern of left being larger). However, the co-occurring language and speech problems make it difficult to determine which behavioral differences are associated with the structural differences. A recent review by Liégeois and Morgan (2012) surveying the existing literature on childhood apraxia of speech and childhood dysarthria found that most cases of childhood apraxia of speech were characterized by bilateral differences (rather than just left hemisphere); additionally, childhood dysarthria was associated with structural differences in a variety of perisylvian or perirolandic regions, as well as cerebellar and subcortical (basal ganglia) regions. However, these are relatively low-incidence motor speech disorders that do not represent the typical profile of residual SSEs.

A recent fMRI study by Tkach et al. (2011) compared six adolescents with histories of speech sound disorders and seven controls with no history of speech difficulties. When repeating nonsense words, adolescents with histories of speech sound disorders showed reduced bloodflow in right inferior frontal and middle temporal gyri. Increased activation was observed for the children with histories of speech sound disorders in several regions, including left STG, left angular gyrus, left supramarginal gyrus, right middle occipital regions (lingual gyrus, cuneus) and cerebellum. Although these participants had a history of speech sound disorders, only one had speech sound errors at the time of the study. Moreover, whether structural brain differences would also be observed remains an open question.

1.4. Purpose

Much of the research on neurobiological characteristics of children with speech sound disorders has come from individuals with relatively severe speech impairments, which may not be representative of the more common mild-moderate cases of children with SSEs who often have just a few speech sounds in error. Other studies have included children with both speech and language difficulties. The present investigation aims to provide a description of both gray and white matter volume differences in school-age children with residual SSEs who do not have co-occurring language impairments. In particular, this study aims to provide a structural brain comparison to follow our laboratory's recent functional imaging findings (Preston et al., 2012), including participants from the previous study plus additional children who met similar criteria.

If children with residual SSEs show delayed neural pruning in speech-specific regions, we hypothesize greater gray matter volume in speech-related regions. Delayed myelination in speech-related regions would be indicated by reduced white matter in children with SSE, whereas increased myelination might reflect connections that have been made. We anticipate differences primarily in regions associated with canonical speech circuits as well as regions identified in recent fMRI studies of children with SSEs (cf. Preston et al., 2012), particularly in those regions crucial for both perception and production of phonetic aspects of speech.

2. Methods

2.1. Participants

Participants were drawn from a large neuroimaging database of over 300 MRI scans of school-age children primarily from regions throughout the state of Connecticut. Data were collected to assess the neurobiological characteristics of language and literacy development and associated disabilities. Participants were excluded if there was a diagnosis of a developmental disability such as Autism, Down Syndrome or cerebral palsy, if there was known hearing loss, or if they were not native English speakers.

For the present study, we restricted the analysis to include only children who met the following demographic and behavioral criteria: participants were between the ages of 8;6 (yrs; mos) – 11;11, had no known neurological insult, and had standard scores greater than 80 on all of the following: full-scale IQ on the Wechsler Abbreviated Scales of Intelligence (WASI, Wechsler, 1999), the Peabody Picture Vocabulary Test-III (Dunn & Dunn, 1997), and all three language clusters (Oral Language, Oral Expression, and Listening Comprehension) of the Woodcock-Johnson Tests of Achievement-III (Woodcock, McGrew, & Mather, 2001). Descriptive data for these measures are summarized in Table 1.

To identify children with SSEs and typical speech we followed procedures similar to those outlined by Preston et al. (2012). For children who met the above criteria, a screening procedure was first used: a licensed speech-language pathologist with clinical experience with childhood speech sound disorders screened connected speech samples from the Vocabulary subtests of the WASI, in which children provide oral definitions of words. The advantage of this speech sampling procedure is that it allows for similarity in the topics and the structure of the interaction. Based on these speech samples, participants were classified as having obvious misarticulations, questionable speech sound errors, or no apparent speech sound errors. A second listener (a graduate student in speech-language pathology or another speech-language pathologist) also confirmed the group classification. Children with questionable errors were those who produced a distortion of a speech sound (e.g., /r, s/) in a handful of tokens but did not consistently produce errors on the sound(s); the children with questionable errors were therefore excluded from further analysis.

For children who were classified as either having obvious misarticulations (eligible for the SSE group) or as having no obvious speech sound errors (eligible for the Typical Speech [TS] Group), speech samples were analyzed for phonetic accuracy. The participants' responses on the WASI Vocabulary subtests were phonetically transcribed into the LIPP software environment (Oller & Delgado, 2006). Percent Consonants Correct for the "Late-8" speech sounds (PCC-Late 8) was computed for each sample, counting all instances of distortions, substitutions or omissions as errors (Shriberg, Austin, Lewis, McSweeny, & Wilson, 1997). These sampled yielded a minimum of 175 Late-8 consonants per participant (mean 310, SD 80). PCC-Late 8 scores below 85% were used to classify children as having SSEs (range 40–85% PCC-Late 8). This procedure resulted in 23 children in the SSE group (18 male). All 23 of the children with SSEs also achieved less than 70% correct on at least one phoneme; specifically, the number of children with fewer than 70% correct was as follows: 13 for /s/, 12 for /r/, 11 for /z/, 5 for /ʃ/, 4 for /ɻ/, 4 for /θ/, 2 for /ʤ/, 2 for /l/, and 1 for /ð/. The participants could be characterized as mostly intelligible but with noticeable sound errors. Eleven of the 23 children in the SSE group were reported to

Table 1
Participant characteristics for two groups compared on gray and white matter.

	Speech sound error group mean (SD)	Typical speech group mean (SD)	*t*	*p*	Cohen's *d*
Age (yrs; mos)	9;9 (1;0)	9;11 (0;11)	0.80	0.428	0.20
WASI Verbal IQ	114 (14)	117 (15)	1.03	0.307	0.26
WASI Performance IQ	113 (15)	110 (17)	0.691	0.493	0.26
PPVT-III	114 (14)	117 (12)	1.01	0.319	0.17
WJ Oral Language	116 (11)	119 (13)	1.17	0.247	0.29
WJ Listening Comprehension	115 (10)	117 (12)	0.879	0.384	0.22
CTOPP Phonological Awareness Composite	100 (16)	106 (17)	1.52	0.135	0.37
Percent Consonants Correct – Late 8	73.8 (13.2)	99.3 (1.8)	8.69	<0.001	2.7

Notes: WASI = Wechsler Abbreviated Scales of Intelligence; PPVT-III = Peabody Picture Vocabulary Test-III; WJ = Woodcock Johnson; CTOPP = Comprehensive Test of Phonological Processing.

have received speech-language therapy services; one was reported to have a history of childhood apraxia of speech, although the participant's primary errors at the time of the study were residual errors on /r, l/ and his speech sound accuracy was in the mild range (PCC Late-8 score of 80%).

Children in the Typical Speech (TS) group met the same requirements as the SSE group for age, IQ, and language scores (listed above). Participants were included in the TS group who had no history of speech or language therapy (as reported by the parent) and who were classified as "no apparent speech errors" based on the initial screening of the recordings. Additionally, once the speech samples were quantified for accuracy, we required that they had PCC-Late 8 scores above 92% (range 92–100% PCC-Late 8) and liquid and sibilant accuracy above 80% (range 80–100%). After the initial screening, one child was excluded from the TS group because of a sibilant score below 80%.[1] The group classification procedures resulted in 54 participants in the TS group (30 male).

As can be seen in Table 1, the groups did not differ in age or in any of the language or IQ variables, but did differ in PCC Late-8 scores. Seventeen participants in each group were part of a previous functional MRI study (Preston et al., 2012). Thus, the present study includes the previous cohort, plus additional participants in each group.

Reliability estimates for PCC Late-8 scores were obtained from a randomly chosen subset of 10 participants in each group by having a second listener score the speech sample (totaling 5869 Late-8 consonant attempts). The two listeners agreed on the accuracy of 95% of the Late-8 phonemes in these 20 speech samples (range 75–100% agreement per subject). The mean agreement was 92% for the 10 SSE participant and 99% for the 10 TS participants.

2.2. Structural MRI data acquisition, processing, and analysis

Structural MRI data were acquired with a 1.5T Siemens Sonata scanner, using a standard 8-channel receiver array head coil. 3D magnetization prepared rapid acquisition gradient echo (MP-RAGE) sequence (TR = 2000 ms, TE = 3.65 ms, flip angle = 8 degrees, 160 slices, matrix 256 × 256, with 1 mm isotropic voxels, total acquisition time 7:30). Structural MRI scans were included in the analysis if they passed visual inspection to identify any movement artifacts and had a final data homogeneity covariance value of at least 0.70 to all other brains in the sample following processing.

[1] The Goldman–Fristoe Test of Articulation-2 (GFTA-2, Goldman & Fristoe, 2000) was added to the test battery part-way through the five-year data collection wave. Because GFTA-2 scores were available only for 23 participants in this sample, it is used only for descriptive purposes. The mean standard score for the 7 children in the SSE group who completed the GFTA-2 was 73.6 (SD = 10.7; range = 56-87). The mean standard score for the 17 children in the TS group who completed the GFTA-2 was 99.5 (SD = 2.2; range = 94–102). Because there was no overlap in the GFTA-2 scores for these groups, this confirms that our speech sampling procedures were identifying children with relatively high and low articulation performance.

Data were processed in SPM8 (Wellcome Department of Imaging Neuroscience Group, London, UK; http://www.fil.ion.ucl.ac.uk/spm), with the voxel-based morphometry (VBM) analyses implemented in VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm.html) using default parameters. Images were bias-corrected (60 mm cutoff), and then segmented into different tissue types (white matter, gray matter, and cerebral spinal fluid) using a Tissue Probability Map included with SPM8 with "very light regularization" (0.0001; Ashburner & Friston, 2005). Each participant's brain was then registered to a version of the MNI152 template using DARTEL, implementing non-linear transform (Ashburner, 2007). A non-linear modulation was applied separately to both gray matter and white matter to account for differences in individual brain size. Finally, the data were smoothed with a 6 mm kernel in AFNI (3dmerge; Cox, 1996). Statistical analyses were performed using AFNI.

Separate statistical models were fit for gray matter and white matter using 3dMVM (Chen, Saad, Britton, Pine, & Cox, 2013) in a 2 (Group: TS vs. SSE) × 2 (Gender: male vs. female) ANOVA. Maps for the group main effects were tested, and group x gender interactions were also explored. These group × gender interactions failed to reach significance in any regions that overlapped with the group main effect map, and were therefore trimmed from the subsequent model. Statistically significant clusters were then identified using the combination of a *p*-value of 0.025 and a cluster-wise correction for multiple comparisons. Significant cluster size for gray and white matter analyses were determined by measuring the smoothness of the individual subject data (3dFWHMx). These smoothness values were then averaged across all subjects for gray and white matter separately and input a monte carlo estimation program (3dClustSim). Using this method, the minimum cluster size for statistical significance was identified as 800 voxels in gray matter or 700 voxels in white matter, with both faces touching [NN = 1]) in the group comparison map. Differences in the minimum cluster size between gray matter and white matter was due to differences in the estimated smoothness of the data. Details on these clusters can be found in Table 2.

3. Results

Gray matter differences are summarized in Table 2 and are shown in Fig. 1. The SSE group was found to have significantly greater gray matter volume than the TS group in two regions: left mid and posterior STG (including Hechl's gyrus and planum temporale, as well as inferior aspect of the supramarginal gyrus) and right STG (planum polare, transverse temporal gyrus [Heschl's gyrus] and planum temporale). A cluster in right lingual gyrus that approached our threshold is also included in Table 2, suggesting a trend for greater gray matter volume in this region for the TS group. The average gray matter volume within these regions was computed for each subject in each group to estimate Cohen's d, a

Table 2
Regions in which the SSE group (n = 23) and TS group (n = 54) differed in gray and white matter volume.

Matter	Difference	Region	Volume (mm^3)	p-Value	x	y	z
Gray							
	SSE > TS	Left transverse temporal gyrus (Heschl's gyrus), planum temporale and inferior aspect of the supramarginal gyrus	2065 (6969)	<.01	−48	−43	21
	SSE > TS	Right planum polare, transverse temporal gyrus (Heschl's gyrus) and planum temporale	1518 (5123)	<.01	44	−28	13
	TS > SSE	R Lingual Gyrus	782 (2639)	<.06	23	−92	16
White							
	SSE > TS	Splenium and anterior body of corpus callosum extending into cingulate white matter	1021 (3446)	<.01	0	19	17
	TS > SSE	R lateral occipital gyrus	803 (2710)	<.01	21	−94	13

Note: x, y, z coordinates listed are in MNI space. R = Right, L = Left.

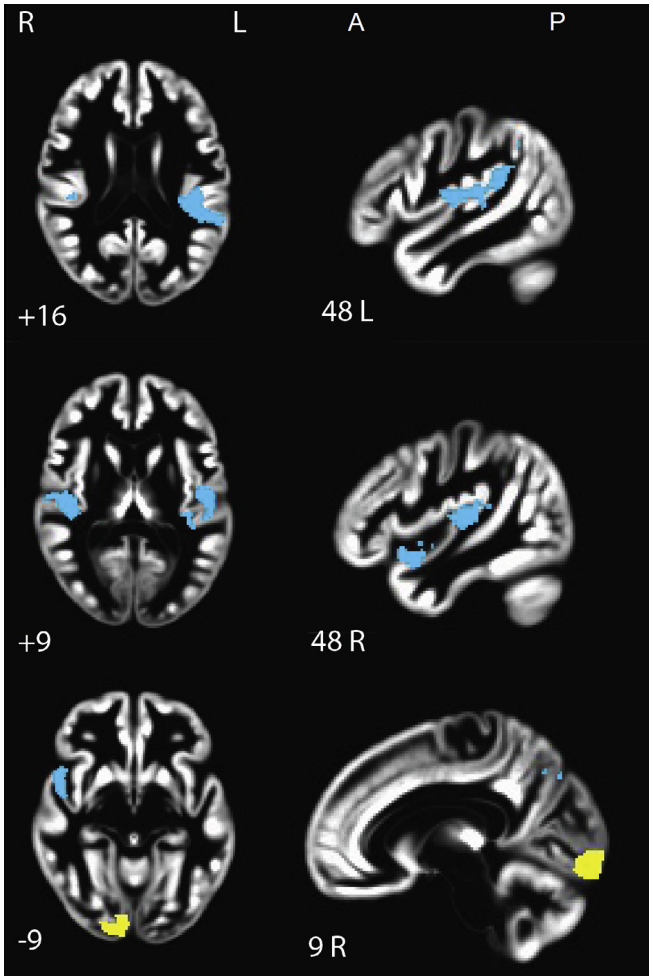

Fig. 1. Axial views (left column) and sagittal views (right column) of clusters in which the Speech Sound Error Group and Typical Speech group differed in gray matter volume. *Note*: Blue represents greater gray matter volume in speech sound error (SSE) group, yellow represents greater gray matter volume in typically speaking (TS) control group. Top panel (z = +16): Left transverse temporal gyrus (Heschl's gyrus), planum temporale and inferior aspect of the supramarginal gyrus. Middle panel (z = +9): Right planum polare, the transverse temporal gyrus and planum temporale. Bottom panel (z = −9): Right lingual gyrus. Axial images are presented in conventional radiological format with the left side of the image reflecting the right side of the brain. R = Right, L = Left, A = Anterior, P = Posterior.

measure of effect size. Large effect sizes were observed between the groups in left STG (d = 1.05), right STG (d = 0.95) and right lingual gyrus (d = 0.86).

There were two regions in which the SSE group and TS groups differed in white matter volume. The SSE group had greater white matter volume than the TS group in the splenium and anterior body of corpus callosum, which extended into cingulate white matter (d = 0.83). The SSE group also had significantly less white matter than the TS group in right lateral occipital gyrus (d = 0.95). These results are summarized in Table 2 and are shown in Fig. 2.

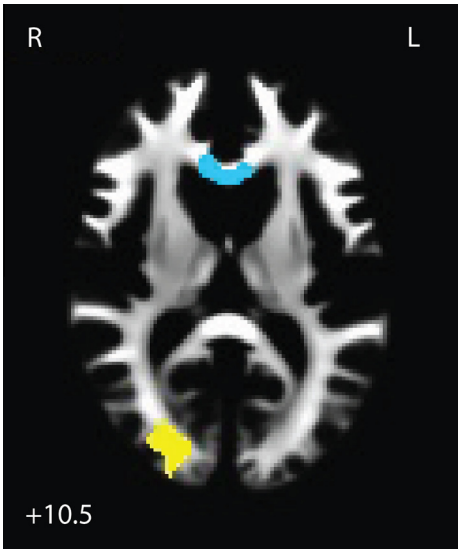

Fig. 2. Axial view of clusters in which the Speech Sound Error Group and Typical Speech group differed in white matter volume. *Note*: Blue represents greater white matter volume in speech sound error (SSE) group in the anterior corpus callosum. Yellow represents greater white matter volume in typically speaking (TS) group in right lateral occipital gyrus. Axial images are presented in conventional radiological format with the left side of the image reflecting the right side of the brain. R = Right, L = Left.

Correlations among the gray and white matter volumes are presented in Table 3. There was a moderately strong correlation between the left STG and right STG gray matter volume (r = 0.63, p < 0.01). Fig. 3 demonstrates this relatively strong association between gray matter volume in bilateral STG and the two groups. There was no significant correlation between white matter volume in corpus callosum and gray matter volume in left STG or right STG,

Individual differences in speech sound accuracy (PCC-Late 8) were examined in relation to brain structure. Among the entire sample of 77 participants, the correlations confirmed the group analysis, with PCC-Late 8 scores correlating negatively with left STG, right STG, and corpus callosum white matter. A positive correlation was observed between PCC-Late 8 and right lateral occipital gyrus. However, these correlations are to be expected because the groups were defined on PCC-Late 8 scores. Because this full sample is heavily weighted toward high values (54 participants

Table 3
Correlation coefficients (*p*-values) between speech sound accuracy (Percent Consonants Correct-Late 8) and average gray and white matter values in the regions in which the two groups differed.

	L-STG gray	R-STG gray	CC white	R-LOG white
PCC-Late 8	−.37 (.001)	−.28 (.013)	−.31 (.006)	.449 (<.001)
LSTG gray		.63 (<.001)	.07 (.52)	−.19 (.106)
RSTG gray			.01 (.98)	−.24 (.035)
CC white				−.11 (.331)
Nonparametric correlations for *Speech Sound Error Group only (n = 23):*				
PCC-Late 8	.00 (.98)	.22 (.31)	.08 (.72)	.32 (.14)

Note: Values in the top of the table reflect Pearson correlations based on *n* = 54 TS and n = 23 SSE participants. Values in the bottom row reflect the nonparametric (Spearman's rho) correlation coefficient for PCC-Late 8 values for only the SSE group. *p*-values are listed in parentheses. PCC-Late 8 = Percent consonants correct-late 8; L-STG = Left superior temporal gyrus; R-STG = Right superior temporal gyrus; CC = Corpus callosum; R-LOG = Right lateral occipital gyrus; SSE = Speech sound error.

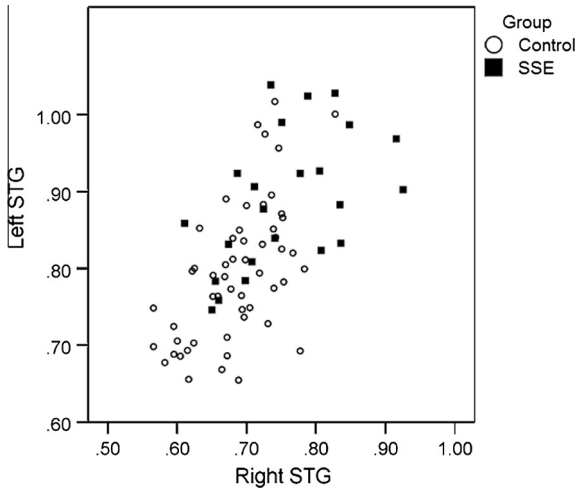

Fig. 3. Correlations between gray matter volume in left and right Superior Temporal Gyrus *Note.* Values greater than 1.0 are occasionally possible in this segmentation due to the use of partial volume estimation (PVE) of gray and white matter, which includes Gray Matter (GM), White Matter (WM), Cerebral Spinal Fluid (CSF), and two mixed classes (GM + WM; GM + CSF). This estimation is also corrected with a non-linear modulation, which adjusts total Gray Matter and white matter percentages per voxel for Total Intracranial Volume.

in the TS group had PCC Late-8 scores near ceiling levels), we also explored correlations between speech sound accuracy and brain structures within the 23 participants in the SSE group (bottom row of Table 3). No significant correlation was observed between PCC Late-8 and any of the gray or white matter volumes. Thus, at the group level, structural differences were observed but gray and white matter measures did not account for significant within-group variance in PCC-Late 8 scores among the children with SSEs.

4. Discussion

The gray and white matter differences we observed provide a complement to recent functional neuroimaging studies of school-age SSEs. The participants in this study were identified based on persisting misarticulations of speech sounds, and children with cognitive impairment or with moderate or severe oral language impairments were excluded. This allowed for a more homogeneous cohort than in previous studies and allowed us to identify differences associated with residual speech (rather than language) impairment. The primary gray matter differences in this study were in bilateral STG (as well as supramarginal gyrus on the left side). A recent fMRI study of adolescents with histories of speech sound disorders found greater activation for children with histories of speech sound disorders in left STG and supramarginal gyrus during a nonword repetition task (Tkach et al., 2011). Studies of the KE family have also revealed structural and functional differences in bilateral STG (Belton et al., 2003; Vargha-Khadem et al., 2005). Furthermore, a recent functional imaging study of children with SSEs from our own lab revealed increased activation of bilateral STG during speech processing tasks (Preston et al., 2012). Thus, bilateral STG involvement appears to have both a structural and functional association with SSEs.

It is well established that left posterior STG is involved in perception of acoustic–phonetic aspects of speech sounds (Buchsbaum, Hickok, & Humphries, 2001; Hickok et al., 2011; Myers, 2007). The co-occurrence of perception and production differences in children with speech sound disorders (Cohen & Diehl, 1963; Rvachew & Grawburg, 2006; Shuster, 1998) suggests that differences in left hemisphere dominant auditory perceptual networks could conceivably lead to speech sound production difficulties. Thus, a possible underlying mechanism associated with residual SSEs might involve reduced synaptic pruning of regions that are responsible for fine-grained phonetic perception and production (particularly in superior temporal regions and supramarginal gyrus), which could lead to less efficient brain networks for speech processing. A potential psycholinguistic consequence of disrupted STG development might be disrupted auditory perception (impacting perception of others' speech as well as one's own speech), which has been observed in several studies of speech sound disorders (Cohen & Diehl, 1963; Rvachew, Ohberg, Grawburg, & Heyding, 2003; Shuster, 1998). Specifically, posterior STG is known to have topographically distinct regions associated with phonetic categories (Cheng et al., 2010). We speculate that reduced pruning in posterior STG might result in broad speech-related regions of that are not finely-tuned for phonetic categories. Additionally, an increased bilateral engagement for speech perception/production (cf. Preston et al., 2012; Tkach et al., 2011) could lead to stronger cross-hemispheric connections and result in more white matter volume in the corpus callosum.

It is noteworthy that we observed increased gray matter volume in regions that involve the integration of auditory and somatosensory information for speech, rather than feed-forward speech production regions per se. That is, bilateral STG and supramarginal gyrus are part of the auditory and somatosensory feedback loops and are important for error detection and correction during both phonetic learning and online-monitoring of speech (Tourville & Guenther, 2011; Tourville, Reilly, & Guenther, 2008). This suggests differences in regions that are responsible for fine-tuning production, rather than primary differences in the "speech sound" map thought to reside in inferior frontal gyrus (Tourville & Guenther, 2011). One area for further exploration could include how children with SSEs use these regions as part of the feedback mechanisms for speech sound learning and monitoring of their speech production.

Another possible interpretation of the differences observed in this study is that children with SSEs simply show a "delay" in brain

development across these networks, as several of these regions showing group differences have been found to co-develop. Alexander-Bloch et al. (2013) recently studied the association between brain structure, function and maturation in a large dataset encompassing a wide age range (9–22 years). They observed a set of regions with strong covariance in function and structure over the course of development, which included the bilateral superior temporal cortex, supplementary motor area, inferior frontal and medial cortex, supramarginal gyrus and precuneus. Thus, the larger gray matter volume in children with SSEs observed in STG and supramarginal gyrus might be indicative of delays in associated structure–function-maturation. If this were the case, one might expect these children to eventually "catch up" in their brain maturation and in their speech sound development. However, existing literature suggests that residual SSEs do not necessarily spontaneously resolve (Irwin, Knight, & Oltman, 1974; Sax, 1972) and that there can be residual behavioral and neurobiological effects of speech sound disorders into adolescence and adulthood (e.g. Felsenfeld, Broen, & McGue, 1994; Lewis & Freebairn, 1992; Tkach et al., 2011).

The biological correlates for gray and white matter volumes are only partially known, and gray matter and white matter volumes are not the consequence of a single neurobiological process. For example, gray and white matter volumes may be influenced by genetic factors controlling neurodevelopment, episodes of environmental exposure to particular stimuli, and neuroplastic response to environmental events (Tau & Peterson, 2010). Gray matter volume may be influenced by the number of synapses, which may be accounted for by reduced synaptic pruning in the SSE group and/or an increase in functional use of those regions; however, gray matter volume is also influenced by the degree of intra-cortical myelination (Paus, Keshavan, & Giedd, 2008; Tau & Peterson, 2010). White matter volume may reflect both myelin and axonal caliber (Paus et al., 2008) and it may be associated with both genetic factors and functional factors such as inter-hemispheric signaling and functional use of a non-dominant hemisphere (Fields, 2008; Kanai & Rees, 2011; Putnam, Wig, Grafton, Kelley, & Gazzaniga, 2008). For example, individuals with SSE show increased functional activation of both hemispheres during phonological tasks (including STG, Preston et al., 2012) and it is possible that the increased white matter volume in the corpus callosum could signal differences in functional use. Finally, it remains to be determined whether the gray and white matter volume differences are associated with causal mechanisms for speech sound errors (e.g., genetic influences) or are a consequence of differences in functional organization of the brain for speech-related tasks. Longitudinal research on younger children with speech sound disorders may help to adjudicate among the possible mechanisms underlying these structural differences.

It is important to point out that the gray and white matter differences observed are not necessarily causal mechanisms. At least two possibilities exist: (a) that these regions might differ in early stages of development, perhaps even before a speech disorder is apparent, or (b) that these regions might begin with normal structure (and function) and structural differences may emerge over time. The age of these participants places them at or beyond the typical window of speech sound acquisition; thus, the structural differences observed may be a consequence of genetic and environmental factors that have influenced brain development during a critical period for speech sound learning (i.e., the first eight or more years of life). The role of specific genetic vs. environmental factors that contribute to the differences in brain structure remains to be explained. For example, the type, frequency, timing, and duration of language stimulation and/or deprivation (e.g., through recurring otitis media) could mediate the quality of language input and subsequently influence neurodevelopment. Whether the regions identified here might change in structure and/or function (e.g., with speech therapy) is an open question best addressed by prospective longitudinal research.

Differences were also observed in occipital regions: the SSE group had significantly less white matter than controls in right lateral occipital gyrus; there was also a trend for less gray matter than controls in right lingual gyrus. The specific role of these regions in SSEs is uncertain; however, it may be that occipital regions might play a role in the detection of fine-grained phonetic detail (Golestani, Molko, Dehaene, LeBihan, & Pallier, 2007; Myers, 2007). Additionally, lateral occipital regions have been observed to participate in visual perception of speech (Fridriksson et al., 2008), and it is possible that the group differences observed in white matter volume in right lateral occipital gyrus could also reflect differences in the organization of tracts that aid visual perception of speech. An alternate interpretation could be that these occipital regions are often associated with the development of reading circuits (Pugh et al., 2013), and group differences might therefore reflect differences in brain specialization for reading (Preston et al., 2012).

Finally, the lack of correlation between these structural measures and PCC-Late 8 within the 23 participants in the SSE group indicates that measures of gray and white matter volume fail to explain individual differences among children with SSEs, as measured by PCC-Late 8. However, it should be noted that PCC-Late 8 can be relatively low for a variety of reasons, including errors on any of the late developing speech sounds (e.g., sibilants, liquids, interdental fricatives). Our participants were relatively homogeneous, primarily representing the mild to moderate clinical cases of children with misarticulations; hence, we did not select the participants to have a wide range of within-group variance. Clinically, individualized measures of articulatory accuracy are often used to quantify errors, as no one-dimensional speech production measure will be appropriate for comparing all children with SSEs. It is possible that future studies that employ subtyping analyses (e.g., based on well documented developmental histories, specific speech sound errors, or etiologies) might identify within-group variables associated with brain structure.

4.1. Caveats and limitations

One potential limitation of the current study is that we did not sub-type participants in the SSE group. Although the groups were well matched on cognitive and language skills, it is possible that differences within the SSE group in previous developmental trajectories might play a role in structural development. For example, some children with residual SSEs might show speech delays from preschool ages, whereas others may show typical speech development until approximately the age of 6, then plateau in speech development (Shriberg, Kwiatkowski, & Gruber, 1994). Although differences in developmental histories likely exist, the association between subtypes of speech sound disorders and brain structure requires exploration.

Perhaps one unexpected finding that emerged from the study was the absence of a group differences in left inferior frontal gyrus. This region has classically been associated with articulation in lesion studies and in functional MRI studies of speech production. One conceivable explanation is that the underlying difficulties for many children with SSEs are primarily representational (i.e., having well-defined perceptual categories for the sensorimotor features of speech sounds, centered primarily in STG), rather than problems in regions associated with formulating and executing an articulatory plan per se. Prior structural imaging studies of the KE family, which includes several members with severe speech sound disorders and language impairment associated with FOXP2 gene mutation, also revealed greater gray matter in bilateral

superior temporal regions (Belton et al., 2003). This result, in concert with the aforementioned functional neuroimaging studies, provides confirmation of consistent differences in STG in individuals with SSEs. Studies of the KE family have observed more widespread structural involvement (Belton et al., 2003; Watkins et al., 1999, 2002), although the neural phenotype of severe speech problems associated with FOXP2 mutation might differ from the less severe but more common cases of childhood SSEs described here. Thus, it is possible that differences in STG are associated with SSEs in general, and that more widespread structural differences are present in more severe cases of speech sound disorders (or the developmental apraxia of speech subtype) seen in the KE family.

When considering the entire dataset (54 TS and 23 SSE), small correlations were observed between gray matter volumes and our measure of speech sound accuracy, PCC-Late 8. However, within the SSE group, there was no apparent relationship between severity in PCC-Late 8 scores and gray or white matter. Thus, at present, these structural differences appear to be sensitive to group-level differences but not to individual differences among children with SSEs. It is possible that measures beside speech sound accuracy, such as developmental history, speech sound disorder subtype, or etiological factors might contribute to within-group variance in brain structure.

A final caveat to note is that the structural differences observed here can be viewed as an extension of our previous functional MRI findings (Preston et al., 2012). The advantage is that we now have structural confirmation of differences in regions that showed functional differences as well. However, because there is overlap in the participants from the two studies, these results reported here are not entirely independent of the functional findings.

5. Conclusions

In summary, the primary hypotheses of gray matter differences in speech-related regions were confirmed by our finding of greater gray matter volume for the SSE group in bilateral STG and in left supramarginal gyrus. Greater white matter was observed in the corpus callosum for the SSE group; these white matter tracts might develop to support increased bilateral engagement in speech perception-production regions (Preston et al., 2012; Tkach et al., 2011), though the time course of these structural differences is clearly a topic in need of further study. The reduced white matter volume in right lateral occipital gyrus is contrary to our predictions, as this is not canonically associated with perception or production of speech sounds. The mechanisms responsible for these differences remain speculative, but the present study provides a foundation for future studies of brain differences in younger children with speech sound disorders.

This study provides the first quantitative report of gray and white matter differences in school-age children with SSEs who have typical language skills. In particular, the data may provide support for theories of speech sound disorders that point to differences in speech perception and processing of phonetic detail (Rvachew & Grawburg, 2006; Rvachew et al., 2003; Shuster, 1998), skills which rely heavily on superior temporal regions. The data offer targeted brain regions to guide genetic studies of speech sound disorders and extend theories of causal mechanisms (Shriberg, 2009). Future longitudinal work investing whether similar structural brain differences are evident at younger ages would be of value.

Acknowledgments

Funding was provided by NIH Grants P01HD001994, R01HD048830, and R01HD065794. Author F. Hoeft was supported by K23HD054720.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bandl.2013.11.001.

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