A Brain Marker for Developmental Speech Disorders

Angela T. Morgan, BSp, Path (Aud Hons), PhD[1,2], Merina Su, PhD[3], Sheena Reilly, BSpPath, PhD[1,4], Gina Conti-Ramsden, PhD[5], Alan Connelly, PhD[6], and Frédérique J. Liégeois, PhD[3]

Objective To characterize the organization of speech- and language-related white matter tracts in children with developmental speech and/or language disorders.

Study design We collected magnetic resonance diffusion-weighted imaging data from 41 children, ages 9-11 years, with developmental speech and/or language disorders, and compared them with 45 typically developing controls with the same age range. We used probabilistic tractography of diffusion-weighted imaging to map language (3 segments of arcuate fasciculus, extreme capsule system) and speech motor (corticobulbar) tracts bilaterally. The corticospinal and callosal tracts were used as control regions. We compared the mean fractional anisotropy and diffusivity values between atypical and control groups, covarying for nonverbal IQ. We then examined differences between atypical subgroups: developmental speech disorder (DSD), developmental language disorder, and co-occurring developmental speech and language disorder.

Results Fractional anisotropy in the left corticobulbar tract was lower in the DSD than in the control group. Radial and mean diffusivity were higher in the DSD than the developmental language disorder, co-occurring developmental speech and language disorder, or control groups. There were no group differences for any metrics in the language or control tracts.

Conclusions Atypical development of the left corticobulbar tract may be a neural marker for DSD. This finding is in line with reports of speech disorder after left corticobulbar damage in children and adults with brain injury. By contrast, we found no association between diffusion metrics in language-related tracts in developmental language disorder, and changes for language disorders are likely more complex. *(J Pediatr 2018;■■:■■-■■).*

Developmental speech and language disorders are common, seen in 1 in 20 preschool children, in the absence of neurologic deficits, intellectual impairment, or hearing loss.[1-4] These conditions are a leading cause of children presenting to pediatricians. Developmental speech disorders (DSDs; affecting how clearly speech sounds are produced) and developmental language disorders (DLDs; affecting language structure such as grammar and semantics) often coexist, but can occur independently (co-occurring developmental speech and language disorder [DSLD]). DLD was known previously as specific language impairment, but international consensus has since agreed on DLD nomenclature.[2] Despite 100 years of phenotypic investigation, no reliable symptom-based prognostic markers exist. Hence, interest has intensified in examining magnetic resonance imaging (MRI)-based neural markers. Most recently, diffusion-weighted imaging and tractography have become promising tools as measures of white matter organization, allowing us to examine structural brain connectivity in these conditions.

A ventral (extreme capsule system) and dorsal route (arcuate fasciculus) have been implicated in typical child language development, with a "maturational primacy" in the ventral route, present at birth.[5,6] The dorsal pathway matures at a later stage of development and has been suggested to be involved in more complex language functions.[5] Few studies, however, have reported reductions in fractional anisotropy and radial diffusivity (RD) metrics of either stream of this "traditional language tract" in children with DLD.[7-9] Of note, the absence of such findings could be in part because existing studies include highly selected, cross-sectionally recruited, clinical samples,[10-12] with limited generalizability of findings to the broader DLD population. Current studies also fail to examine control tracts outside hypothesized language regions, obscuring whether findings are localized to language tracts or widespread throughout the brain.

ANCOVAS	Analyses of covariance
CBT	Corticobulbar tract
CELF-IV	Clinical Evaluation of Language Fundamentals, 4th edition
DLD	Developmental language disorder
DSD	Developmental speech disorder
DSLD	Co-occurring developmental speech and language disorder
GFTA-II	Goldman Fristoe Test of Articulation, 2nd edition
MD	Mean diffusivity
MRI	Magnetic resonance imaging
RD	Radial diffusivity
WASI-II	Wechsler Abbreviated Scales of Intelligence

From the [1]Murdoch Children's Research Institute and Royal Children's Hospital, Melbourne; [2]University of Melbourne, Australia; [3]UCL Great Ormond Street Institute of Child Health, London, UK; [4]Griffith University, Gold Coast, Australia; [5]School of Health Sciences, The University of Manchester, UK; and [6]Florey Institute of Neuroscience and Mental Health, Melbourne, Australia

Supported by the National Health and Medical Research Council (NHMRC) Centre of Research Excellence (CRE) (1023493 [to S.R., A.M., and A.C.]); NHMRC CRE (1116976 [to A.M., A.C., and S.R.]); NHMRC Career Development Fellowship (607315 [to A.M.]) and NHMRC Practitioner Fellowship (1105008 [to A.M.]); and a Hearing CRC grant (to S.R., A.M.) A.M., S.R., and A.C. are grateful to the Operational Infrastructure Support Program of the State Government of Victoria for their support. The authors declare no conflicts of interest.

https://doi.org10.1016/j.jpeds.2018.02.043

White matter integrity has not been examined in DSD to date, yet left corticobulbar tract (CBT) deficits have been reported in childhood dysarthria after brain injury,[13] childhood stuttering,[14] adult dysarthria,[15] and even in an adult case of neurodegenerative speech disorder in the absence of a language disorder.[16] Furthermore, in relation to the developing system, studies have not directly compared white matter integrity of speech and language disordered groups together, limiting knowledge of shared or distinct neural underpinnings.

We examined white matter connectivity in children with DSD, DLD, and typically developing controls. Participants were recruited from a longitudinal community cohort study of speech and language. We hypothesized that developmental speech and language disorders would be associated with atypical development of speech-motor (corticobulbar) and language (dorsal and ventral streams) tracts, respectively.

Methods

Participants (n = 86; age range, 9.25-11.25 years) were recruited from the Early Language in Victoria Study (ELVS), a longitudinal community-based study of 1900 children.[3] Communication status was collected almost annually from 8 to 10 months of age[3] up to the age at the current study (ie, 9-11 years). Age of scanning was carefully chosen to reflect a time when communication trajectories are relatively stable.[17] Ethics approval was granted by the Royal Children's Hospital Human Research Ethics Committee (Reference number HREC31225).

Participants were recruited to 4 groups based on longitudinal data: controls (n = 45), DLD (n = 13), DSD (n = 17), and DSLD (n = 11). The DLD, DSD, and DSLD groups were combined into an "atypical" group for the first stage of analyses, followed by subgroup analyses.

Inclusion criteria for all 4 groups included a nonverbal IQ of ≥80 on the Kaufman Brief Intelligence Test[18] administered at age 4 years and the Wechsler Abbreviated Scales of Intelligence (WASI-II)[19] at age 7 years. DLD and control groups were required to have typical speech as assessed via the Goldman Fristoe Test of Articulation, 2nd edition (GFTA-II)[20] at ages 4 and 7 years. The DLD group was also required to have impaired language, defined as a total language score of ≤81 (1.25 SD below the mean)[3] on the Clinical Evaluation of Language Fundamentals, 4th edition (CELF-IV) at 2 time points at ages 4 and 7 years, or 5 and 7 years. Some attrition occurred across the 4- and 5-year-old waves of the ELVS, and expanding the DLD inclusion criteria across 2 data waves provided a larger pool for recruitment. In contrast, children with DSD had articulation or phonological speech errors consistent with DSD at ages 4 and 7 years.[21] To assess speech performance, the GFTA-II was administered as a single-word test that elicits all the speech sounds of English in initial, medial, and final positions. All sounds were transcribed and assessed for the presence of articulation and phonological errors to confirm a diagnosis of DSD.[21,22] Articulation disorder was denoted as phonetic-based distortions (eg, lisps, de-rhotacism) in which the occurrence of the distortion was more frequent than correct production of that phone. Articulation disorder could also include an omission error when the phone was absent in the child's inventory, but appeared in the phonetic inventory of >90% of peers in normative data.[22-24] Phonological delay was use of a phonological process that occurs in speech, but used beyond an age when it is typically resolved in >90% of peers.[23] Phonological disorder was use of a phonological process that is atypical and seen in <10% the normative sample population at any age.[23] Conversational samples were also rated to confirm the presence of errors noted in single-word stimuli in connected speech to provide further evidence of persistence. In addition, the DSD and control groups were required to have normal language scores (≥85) as per the CELF–preschool[25] at age 4 years, and CELF-IV[26] at ages 5 and 7 years. Exclusion criteria were a history of neurologic, hearing, genetic, or neurodevelopmental disorders (eg, autistic spectrum disorder) and a non–English-speaking background.

Procedure

At the time of scanning, participants were assessed with the same speech, language, and nonverbal IQ tests reported above for participant group selection (**Table I**). Standardized scores were used for the CELF-IV[26] and WASI.[19] Clinical diagnosis of DSD was made based on phonetic transcription and phonological process analysis.[21,22]

T1-weighted images were acquired with an isotropic resolution of 0.9 mm (inversion time = 900 milliseconds; repetition time = 1900 milliseconds; echo time = 2.6 milliseconds; flip angle = 9°; matrix size 256 × 256; 160 partitions) on a 3-Tesla Tim Trio MRI scanner (Siemens Medical Solutions, Erlangen, Germany). A conventional T2-weighted scan was also

Table I. Characteristics for controls, DSD, DLD, and DSLD groups

			Group		Test statistics			Effect size
	Control (n = 45)	DSD (n = 17)	DLD (n = 13)	DSLD (n = 11)	Df	Statistic	*P*	η^2
Age at testing (mo)	123.47 ± 6.59	123.06 ± 3.51	123.23 ± 2.68	125.18 ± 3.52	3	$H = 1.55$	.671	.02
Nonverbal IQ	102.09 ± 9.76	106.06 ± 11.22	94.46 ± 9.71	96.91 ± 10.09	3	$H = 11.13$	.011	.10
CELF-IV Core Language	107.20 ± 8.78	102.88 ± 8.45	85.31 ± 9.32	83.27 ± 10.71	3	$F = 33.99$	<.001	.55
CELF-IV Receptive	105.40 ± 8.74	102.12 ± 6.69	86.46 ± 7.63	84.45 ± 14.62	3	$H = 38.90$	<.001	.44
CELF-IV Expressive	109.02 ± 9.76	104.12 ± 9.30	87.77 ± 10.89	83.09 ± 11.47	3	$F = 29.07$	<.001	.52
GFTA-II	103.29 ± 2.06	99.59 ± 4.49	103.15 ± 2.15	100.27 ± 4.73	3	$H = 12.89$	.005	.12

Df, Degrees of freedom.
Values are means ± SD.

FLA 5.5.0 DTD ■ YMPD9827_proof ■ April 25, 2018