### **Supplementary Material for**

### Dorsal language stream anomalies in an inherited speech disorder

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# Supplementary Table 1. Speech and cognitive assessment battery

	Domain tested	Task			
	Speech	Goldman Fristoe Test of Articulation (Goldman and Fristoe, 2000) Conversational speech sample			
	Oral motor skills	Verbal Motor Production Assessment for Children (Hayden and Square, 1999) OR Frenchay Dysarthria Assessment, 2 <sup>nd</sup> Edition (Enderby and Palmer, 2008)			
		Up to 5 years of age: Preschool Language Scales, Fourth Edition (Zimmerman <i>et al.</i> , 2011)			
First si si t	I	5 to 21 years: Clinical Evaluation of Language Fundamentals, 4th Edition (Semel <i>et al.</i> , 2006)			
1 list visit	Language	Over 21 years of age:			
		Peabody Picture Vocabulary Test, 4th Edition (Dunn and Dunn, 2007)			
		Expressive Vocabulary Test, 2 <sup>nd</sup> Edition (Williams, 2007)			
		Test For Reception of Grammar, 2 <sup>nd</sup> Edition (Bishop, 2003)			
	Phonological processing	Comprehensive Test of Phonological Processing (Wagner et al., 1999)			
	General intelligence	Kaufman Brief Intelligence Test, 2nd Edition (Kaufman and Kaufman, 2004)			
	Working memory	Digit Span subtest from the Wechsler Intelligence Scale for Children, 4 <sup>th</sup> Edition (Wechsler, 2004) OR Wechsler Adult Intelligence Scale, 4 <sup>th</sup> Edition (Wechsler, 2008)			
Second visit	Literacy	Wide Range Achievement Test, 4th Edition – Reading, Sentence Comprehension and Spelling subtests (Wilkinson and Robertson, 2006)			
		Nonword Memory Test (Gathercole and Baddeley, 1996b) OR			
		Children's Test of Non-Word Repetition (Gathercole and Baddeley, 1996a) AND			
	Creat	Multisyllabic Word Repetition task (Lewis and Freebairn, 1992)			
Third visit	Speech	Diagnostic Evaluation of Articulation and Phonology – Inconsistency assessment (Dodd <i>et al.</i> , 2002)			
		Maximum performance tasks (Duffy, 2013)			

CAS diagnostic criteria	Speech featu	I-1	I-2	II-1	II-2	II-3	II-4	II-5	II-6	II-7	II-8	II-9	II-10	II-11	
Inconsistent	Same word/s	yllable different on repetitions													
errors	Same C/V di	fferent across different words													
Lengthened and		Speech motor behaviors, including													
disrupted		groping during sound production													_
transitions		and disrupted DDK sequence													
between sounds	Any one of	Difficulty sequencing phonemes and													
and/or syllables	these	syllables													
		Difficulty achieving initial													
		articulatory configurations or transitory movement gestures													
		Syllable segregation													
		Intrusive schwa													
		Epenthesis													
		Frequent omission errors													
		Addition errors													
		Repetitions of sounds and syllables													
	Any two or	Voicing errors													
	these	Nonphonemic productions/distorted													
	mese	substitutions													
		Nasality and/or nasal emissions													
		phonological complexity													
		Metathesis													
		Difficulty maintaining syllable													
		integrity													
Inappropriate	Equal stress of	or lexical stress errors													
prosody	Prolongation	errors													
	Vowel distort	tion													
	Altered supra	usegmental characteristics													

## Supplementary Table 2. Speech features categorised under the three consensus diagnostic criteria for CAS diagnosis.

Iı	ndividu	al	I-1	I-2	II-1*	II-2	II-3*	II-4*	II-5*	II-6*	II-7*	II-8*	II-9	II-10	II-11	
	Sex		М	F	F	F	М	F	F	М	М	М	М	F	М	Normative data
assessmer 1	Age at nt - Cog anguag	nition and	43y	41y	14y2m	12y9m	10y7m	9y3m	9y3m	7y1m	5y3m	5y8m	4y5m	4y8m	2y2m	
T. (. 11')		Non-verbal	109	100	116	90	95	106	111	84	107	95^	NT	NT	n/a	mean 100
Intelligence	e	Verbal	98	106	87	84	87	77	77	94	80	74^	NT	NT	n/a	sd 15
Memory Digit span	Digit	Forward	9	9	13	11	8	10	10	6	NT	NT	NT	NT	n/a	mean 10
	span	Backward	8	10	5	12	5	11	14	5	NT	NT	NT	NT	n/a	sd 3
Language	e	Receptive	PPVT 107 TROG 104	PPVT 106 TROG 105	95	76	94	94	91	88	100	72^	PLS-5 101	PLS-5 98	PLS-5 76	
		Expressive	102	89	104	100	97	95	106	63^	99	<b>49</b> ^	PLS-5 90	PLS-5 83	PLS-5 82	
		Phonological awareness	n/a	n/a	91	106	91	100	115	97	89	unable to score	n/a	n/a	n/a	
Phonologic processing	al g	Phonological memory	n/a	n/a	100	79	79	97	97	70	82	unable to score	n/a	n/a	n/a	mean 100 sd 15
		Rapid Naming	n/a	n/a	100	130	109	133	130	unable to score	unable to score	unable to score	n/a	n/a	n/a	54 15
assess	Age at ment-L	iteracy	45y	42y	15y7m	16y2m	12y	11y6m	11y6m	9y4m	7y5m	n/a	n/a	n/a	n/a	
Literacy		Reading composite	100	92	101	100	95	105	106	89	99	n/a	n/a	n/a	n/a	
Literacy		Spelling	121	101	107	117	87	113	115	96	98	n/a	n/a	n/a	n/a	

Supplementary Table 3. Individual scores on cognitive assessments

*Footnote.* Scores below 80 or 6 are considered in the clinically impaired range and are highlighted in bold. 'Unable to score': too many errors made on practice items and testing discontinued. M = male; F = female; y = years; m = months; sd = standard deviation; r = range; ^external clinical assessment; NT = not tested; Language scores are from the CELF unless specified: PLS-5: Preschool Language Scales, 5<sup>th</sup> Edition; PPVT: Peabody Picture Vocabulary Test; TROG: Test for Reception of Grammar. n/a: test not age appropriate. \*MRI available

**Supplementary Table 4.** Group differences, hemisphere differences, and group by hemisphere interaction effects on FA for each track using analyses of covariance (age as covariate). Significant age effects are indicated with an asterisk. Non-parametric post hoc tests (Mann-Whitney) were used to explore group differences further within each hemisphere. Significant effects are highlighted in bold.

Tract	Group effect	Hemisphere effect	Group by Hemisphere	p by Hemisphere Post hoc group	
			interaction	Left	Right
Corticospinal*	F=1.69, p=0.21	F=0.29, p=0.60	F=1.10, p=0.31	U=31.5, p=0.39	U=28.5, p=0.27
Corticobulbar	F=0.91, p=.35	F=1.23, p=.28	F=0.41, p=.53	U=22.5, p=0.11	U=32.5, p=0.58
Arcuate-direct	F=6.37, p=0.023	F=0.97, p=0.34	F=0.28, p=0.61	U=5, p=0.001	U=15, p=0.07
Arcuate-anterior	F=6.77, P=0.019	F=1.21, P=0.29	F=0.02, P=0.90	U=12, P=0.012	U=13, P=0.015
IFOF*	F=0.79, P=0.39	F=0.26, P=0.62	F=0.30, P=0.59	U=33, p=0.49	U=33, p=0.49

FA, fractional anisotropy; IFOF, inferior fronto-occipital fasciculus

Anatomical region	BA nomenclature	С	oordinates (x y z	z)	T Value
L Precentral gyrus extending into postcentral gyrus	6/4	-46	-14	38	8.49
		-50	-10	32	8.14
		-56	-10	44	8.08
R Precentral gyrus extending into postcentral gyrus	6/4	50	-8	32	8.32
		56	-4	46	8.27
		64	-2	8	6.56
R cerebellum		20	-66	-18	7.15
L cerebellum		-14	-70	-16	6.54
L occipital lobe		-6	-70	-10	6.24
R medial frontal gyrus, extending into cingulate cortex	6/24	2	0	62	6.56
L medial frontal gyrus, extending into cingulate cortex	6/24	-2	4	46	5.76
L Thalamus		-6	-22	10	6.34
R Thalamus		2	-18	10	6.23
		12	-26	-8	6.05
L Cuneus	7	-6	-86	38	5.22
R Cuneus	7	10	-80	40	4.61
R posterior STG, extending into planum temporale and supramarginal gyrus	22/41/40	48	-28	0	4.58
L posterior STG, extending into planum temporale and supramarginal gyrus	22/41/40	-52	-42	8	4.58
		-64	-38	8	4.54
R globus pallidus *		14	-6	14	4.41
L globus pallidus *		-14	-8	14	4.84

**Supplementary Table 5.** Regions of decreased activation in the family relative to the control group for the Speak vs. Listen contrast. Results are presented in MNI coordinates at p=0.05 (family wise error correction).

BA, Brodmann's area; STG, superior temporal gyrus. \* detected using small volume correction

Anatomical region	BA nomenclature	Peak Coordinates	(x y z)	T Value	
L Precentral gyrus	6	-46	-14	38	13.57
		-52	-12	44	13.29
L Precentral gyrus	4	-18	-28	60	6.93
R Precentral gyrus	6	50	-8	34	13.06
R Precentral gyrus	4	26	-26	72	6.23
		20	-28	62	5.96
R medial frontal gyrus	6	2	0	64	10.59
		2	10	38	8.08
L middle frontal gyrus		-22	34	2	4.70
Right cingulate gyrus		16	-32	46	6.01
L cuneus	19	-8	-84	34	6.52
L precuneus		-16	-68	40	4.90
R precuneus	19	12	-80	40	5.95
		12	-52	64	5.65
R paracentral lobule	7	16	-44	52	4.66
L postcentral gyrus	2	-64	-26	38	4.75
R SPL	7	20	-54	62	6.27
L IPL	40	-64	-30	40	4.61
R Middle temporal gyrus		40	-52	4	4.84
R temporal lobe		28	-54	16	4.70
R parahippocampal gyrus	30	28	-58	6	4.84
R cerebellum		50	-60	-30	4.72

**Supplementary Table 6.** Activated regions for the control group for the Speak > Listen contrast. Results are presented in MNI coordinates at the threshold of FWE corrected 0.05 significance level.

NB. No suprathreshold voxels for the family at the FWE corrected p<.05 level. BA, Brodmann's area.

Measure	Bayes factor	Interpretation in relation to null (H0) and alternative (H1) hypotheses
Corticospinal tract FA		
Left	BF01=2.094	Anecdotal evidence for H0 or data insensitivity
Right	BF01=1.501	Anecdotal evidence for H0 or data insensitivity
Corticobulbar tract FA		
Left	BF01=0.883	Anecdotal evidence for H0 or data insensitivity
Right	BF01=2.170	Anecdotal evidence for H0 or data insensitivity
Arcuate direct FA		
Left	BF10=13.580	Strong evidence for H1
Right	BF10=1.434	Anecdotal evidence for H1 or data insensitivity
Arcuate anterior FA		
Left	BF10=6.901	Moderate evidence for H1
Right	BF10=5.949	Moderate evidence for H1
IFOF FA		
Left	BF01=1.909	Anecdotal evidence for H0 or data insensitivity
Right	BF01=1.868	Anecdotal evidence for H0 or data insensitivity
IFOF volume		
Left	BF10=4.513	Moderate evidence for H1
Right	BF10=2.832	Anecdotal evidence for H0 or data insensitivity

**Supplementary Table 7**. Factors for Bayesian Mann-Whitney U tests of group differences (family vs. control group) in diffusion metrics.



**Supplementary Figure 1.** Subcortical volumes in family members and controls, expressed as percentage of total grey matter volume. Filled symbols, left hemisphere; empty symbols, right hemisphere.



**Supplementary Figure 2.** Relationship between age and mean FA in the left (a) and right (b) corticospinal tract and in the left (c) and right (d) inferior fronto-occipital fasciculus. Age was positively correlated with FA within the corticospinal tracts (left: r=.75, p=0.0002; right, r=.69, p=0.001) and IFOF (left: r=.52, p=0.018; right, r=.55, p=0.012), but not the other tracts (r<.41, p>.08).











**Supplementary Figure 3.** Enlarged illustrations of tractography reconstruction displayed in Figure 3.

A Speak > Listen





0

-2

-4

1



**Supplementary Figure 4.A**. Mean parameter estimates (arbitrary units) for the Speak > Listen contrast for family members and controls (n=7 in each) in the three main cortical regions where underactivity was detected in the family. Means are derived from 3-mm spheres centred around peak voxels (see Supplementary Table 5) of the left precentral (-46, -14, 38), right precentral (50, -8, 32) and left posterior temporal (-52, -42, 8) clusters.

4

■ Left precentral ■ Right precentral ■ Left posterior superior temporal

7

Error bars indicate  $\pm 1$  SEM. **B.** Group activation for the control group (n=7), displayed at p=0.05 (FWE corrected. **C** . Mean parameter estimates in individual family members (1 to 7) in the same regions as in 4A.

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