

Brain basis of childhood speech and language disorders: are we closer to clinically meaningful MRI markers?

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**Abstract**

*Purpose of review:*

Developmental speech and language disorders are common, seen in 1 in 20 preschool children, in the absence of frank neurological deficits or intellectual impairment. They are a key reason parents seek help from paediatricians. Complex neurogenetic and environmental contributions underpin the disorders, yet few specific aetiologies are known. With the advent of quantitative brain imaging, a growing number of studies have investigated neural contributions. Here we discuss current magnetic resonance imaging (MRI) approaches and recent findings (Jan 2014-June 2016) in the field.

*Recent findings:*

Five relevant studies were identified (n=3 speech disorder, n=2 language disorder). Significant variability in MRI approaches and heterogeneity of participant phenotypes were seen. Children with speech disorder had structural and functional anomalies in the left supramarginal gyrus, and functional anomalies in the posterior cerebellum bilaterally; regions critical for sensory-motor integration or feedback. Children with

language disorder showed increased mean and radial diffusivity of the left arcuate fasciculus, although a widespread cortical and subcortical network of regions was implicated.

*Summary:*

Limited evidence exists for specific regional brain anomalies in this population. MRI prognostic markers of speech and language ability are not currently available at an individual level. Further work is required to disentangle neurobiological contributions to speech and language disorders for affected children.

**Keywords:**

3-5 keywords

Speech disorder · Language disorder · Specific language impairment · Childhood apraxia of speech · MRI·

**Abbreviations:**

MRI: magnetic resonance imaging; SLI: specific language impairment; DWI: diffusion weighted imaging; CAS: childhood apraxia of speech

## Introduction

As many as one in twenty preschool children present with developmental speech or language disorders, in the absence of intellectual impairment or frank neurological deficits [1,2], see Table 1. Given the exceptional commonality of these conditions, they are a frequent cause of parents help-seeking with general practitioners and paediatricians [3]. Yet there are currently no robust (i.e., highly replicated) demographic or symptom-based predictors of outcome for childhood communication disorders [1,2]. That is, it is currently challenging to predict who is likely to have persistent speech and language difficulties. This uncertainty is likely because we have focused on surface symptoms and given little attention to the underlying root cause.

‘Insert Table 1 about here’

Aetiology of developmental speech and language disorders is typically described as complex multifactorial in nature, with contributions from genes and environment interacting with the critical lynch pin, the brain. A number of candidate genes have been proposed for these conditions, but none replicated or clearly linked to causation [4]. To date, there is only one monogenic pathway understood in association with any of these developmental disorders, i.e., *FOXP2* mutations explaining a small proportion of cases with the rare speech disorder of childhood apraxia of speech [5,6]. Alongside intensified interest in genetic contributions, there is also greater interest in the neurobiology of these conditions.

Advances in neuroimaging acquisition and analysis methods have resulted in a small but growing number of studies on the neurobiology of child speech and language disorders [12-14]. In particular, new methods have enabled detection of sub-macroscopic functional and structural brain anomalies at the group level. Here we discuss magnetic resonance imaging (MRI) approaches applied to this field and review recent literature on neural correlates for developmental speech or language disorders. We apply a clinical lens to ask whether robust neural fingerprint(s) exist, and whether we can yet employ MRI markers to inform practice at an individual level.

### MRI approaches

MRI has gained the most traction when examining the neural bases of childhood speech and language disorders because it is non-invasive and provides high spatial resolution of images throughout the brain. Clinical brain MRIs are high-resolution scans visually assessed for anomalies by a neuro-radiologist, an effective method of evaluation in populations with known frank abnormalities (e.g., to brain lesions after stroke). Children with developmental speech and language disorders however, do not show frank lesions on MRI. The presence of such a lesion would in fact exclude the child from having a defined developmental impairment. Rather any anomalies or differences in the brains of children with developmental speech or language difficulties are too subtle to be detected at an individual level and can only be detected via group comparisons using

quantitative MRI analyses as explained in the next section (e.g., group with language disorder compared to age and gender matched controls with typical language). MRI approaches most commonly applied to this field are introduced below.

### **Voxel-based morphometry (VBM)**

Voxel-based morphometry (VBM) is an MRI analysis technique using T1-weighted brain scan data to quantify differences in grey or white matter structure or morphology, across groups of individuals. A number of image processing steps ensure that data is optimised for analysis, including normalisation, segmentation and smoothing of voxels [see 15 for detail]. Analysis consists of thousands of voxel-wise parametric statistical tests to compare grey or white matter concentrations between the two or more groups of interest [15].

### **Functional MRI**

Functional MRI (fMRI) is an indirect measure of brain activation that measures the blood oxygenation level dependent (BOLD) response. This method encompasses both (1) task-related and (2) resting-state fMRI. Task related fMRI examines which regions are associated with performing a speech or language task. To record changes in blood flow during a task, fMRI experiments require a baseline condition. The nature of these experiments means fMRI is only possible when the participant has the cognitive ability to understand the task instructions. Even in the case of developmental speech and language disorders where the child has typical non-verbal IQ, fMRI is still challenging in children younger than 5 years of age due to the requirement of lying still and systematically following instructions. A recent development able to overcome this limitation of task-dependent fMRI is resting-state fMRI.

### **Diffusion weighted imaging (DWI) and fibre tractography**

Diffusion weighted imaging enables mapping of the diffusion of water molecules in the white matter pathways of the brain. Using software packages (e.g., MRTrix [16]), the analysis method of fibre tractography is then used to delineate these pathways and measure properties of the tracts including volume and fractional anisotropy (FA). FA describes the degree of 'restrictedness' (anisotropy) of diffusion, with values ranging between 0 (diffusion is unrestricted or equally restricted in all direction) and 1 (diffusion occurs along 1 axis and is fully restricted in other directions). As such, FA is viewed as a marker of fibre density or myelination of the white matter tract, yet the direct link between FA and the anatomical or microstructural properties of the tracts remain unclear.

In summary, a range of functional and structural MRI approaches can shed light on regions of the brain most critical for subserving speech and language function. The most informed view on the neural bases of a condition comes however, from considering both structural and functional data together. To date there has been no examination of both brain structure and function on the same individual group of children applied in this field. Existing findings are reviewed in the following section.

## **Neural correlates of developmental speech and language disorders**

Here we conducted a systematic search and review of relevant studies on MRI neural correlates from Jan 2014 to June 2016. Studies were included if they reported results of individuals with either a developmental (i.e., also known as ‘specific’) speech or language disorder (i.e., in the absence of intellectual impairment, frank neurological deficits, or neurodevelopmental disorders), together with a MRI method to investigate brain structure or function. Studies of pragmatic or social language deficits were excluded. As regards speech disorder, we considered studies of subtypes outlined in Table 1, as well as studies using less explicit diagnostic terms of ‘speech errors’ and ‘speech delay’. Full text articles were required to be published in English. EMBASE, OVID MEDLINE and PubMed databases were searched (see Supplemental digital content for explicit MeSH terms utilized). This review methodology was adapted from a prior review by Liegeois et al. [13].

Titles were independently reviewed by AB to remove any duplicates and a total of 846 abstracts were identified (838 from electronic databases, 8 from manual search). Authors AM and FL reviewed titles and abstracts independently and excluded articles based on: participant selection criteria (e.g., excluding children with frank neurological disorders or co-morbidities); imaging methods (e.g., excluding studies without MR imaging); and analysis methods (e.g., excluding studies with no quantitative MR analysis).

‘Insert Table 2 about here’

Five papers met criterion and were included (Table 2), three on speech disorder [17-19] and two on language disorder [20,21]. All five were case-control studies, rated as only level III-2 evidence on the National Health and Medical Research observational study rating scale [22]. Effect sizes for group comparisons were only available for 1 study (Table 2) and could not be calculated for the remainder as standard deviations were not provided. Children were examined from as young as four and a half years [18] up to 11 years [17,20].

## **MRI findings in developmental speech disorder**

As regards developmental speech disorder diagnosis, two studies examined children with persistent articulation (phonetic level) disorder [17,19<sup>1</sup>]. The former study examined structural morphometry across the whole brain and the latter a motor tapping fMRI task. The third speech disorder focused study, on children with CAS, examined cortical thickness in regions of interest bilaterally in the inferior frontal gyrus, supramarginal gyrus (SMG), posterior superior temporal gyrus (pSTG) and inferior pre-

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<sup>1</sup>No phonetic vs phonemic analysis was reported for Redle et al. [19] to clarify phonological vs articulatory involvement, hence a phonetic deficit is presumed based on reported test scores on the Goldman Fristoe Test of *Articulation*.

and post-central gyri [18].

Despite studying distinct phenotypes, both Preston et al. [17] and Kadis et al. [18] reported statistically significant increases in the left SMG for the affected groups. With Preston et al., also reporting increases in the *right* SMG and bilaterally in the planum temporale and Heschl's gyrus in the speech disordered group. Apparent anomalies of the SMG seen here are in line with data showing the importance of this region for learning and adapting sensorimotor patterns for speech [23].

By contrast, Redle et al., [19] who also examined children with persistent speech disorder, revealed significant increases in activation in the posterior cerebellum, bilaterally, for children with PSD compared to controls. This finding is not at odds with the SMG findings of the other two speech studies discussed [17,18] however, given known interconnections of the SMG with the inferior frontal cortex, cerebellum and primary sensory areas all forming part of a key sensorimotor system in the brain [23]. Previous studies have also highlighted the importance of the cerebellum for the fine motor control of speech articulation [24]. Further to the cerebellar findings, Redle and colleagues also reported positive correlations between brain activation in multiple cortical and subcortical regions with Purdue Pegboard scores across different conditions [19]. Yet it is challenging to interpret the meaning of these multiple fine motor brain-behaviour correlations in the context of speech function.

Overall, findings could be argued to be consistent as regards involvement of the SMG in childhood speech disorder, with the caveat that a widespread sensorimotor network is also involved beyond this region, and without clear evidence for a left-lateralised system.

### **MRI findings in developmental language disorder**

Diffusion weighted imaging and tractography was conducted in both language-focused studies reviewed here. As for speech disorder, inclusion criteria and diagnoses were highly varied for the participant groups with more comprehensive reporting of the phenotype with standardized assessment in Roberts et al. [20] (Table 2). Authors of this study found an increase in mean and radial diffusivity metrics in the left arcuate fasciculus for children with LI [20]. Only diffusion metrics of the AF were recorded, in the absence of whole brain measures or use of a 'control tract' for comparison. Hence it is not possible to determine whether changes in AF metrics across groups were specific to that tract. In line with these findings, Vydrova et al. [21] also reported increases in mean diffusivity in the AF for children with language disorder, but bilaterally. Increases in MD were also seen in the left inferior fronto-occipital fasciculus and left inferior longitudinal fasciculus in this study [21]. Increased RD was also seen bilaterally in the AF and uncinata fasciculus, and again in the left inferior frontal-occipital fasciculus and left inferior longitudinal fasciculus [21].

Hence a consistent finding for the language disorder field appears to be increases in mean and radial diffusivity metrics of the left AF. Yet Vydrova et al. [21] also revealed

anomalies in a more widespread network of cortical white motor tracts. This finding is in line with past reviews where children with language disorders show widespread structural and functional cortical and also subcortical anomalies [13]. Overall we have little evidence for specific regional anomalies in developmental language disorder.

## **CONCLUSION**

Despite the high prevalence and impact of speech and language disorders in childhood, surprisingly few neuroimaging studies exist in this area. Evidence is particularly lacking for children under 7 years of age, the very period when speech and language disorders are at their most obvious and prevalent. The dearth of literature results in part from the challenge of scanning young children. The recent availability of techniques requiring less child participation, such as resting state-fMRI and DWI, may intensify interest in the area.

As well documented in past reviews [11,12], literature is challenging to compare and interpret in this field due to the small number of studies focused on different phenotypes and use of variable MRI approaches. As a result robust neural correlates are not yet confirmed. Whilst MRI methods have become more sophisticated, allowing statistical comparison at a group level, current methods cannot provide paediatric clinicians with a prognostic marker of an *individual's* speech and language. It is still too early to disentangle the genetic, environmental, compensatory and neurobiological contributions to speech and language disorders an individual level.

## **Key points:**

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- Children with developmental forms of developmental speech and language disorders show no frank brain lesions on clinical MRI.
  - Aetiology of developmental speech and language disorders remains poorly understood but research is intensifying into genetic and neural contributions.
  - Current MRI studies show no specific or repeatable neural correlates of these conditions.
  - Current approaches not sensitive for detection of brain markers at an individual level to inform practice.

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### **Conflicts of interest**

Authors have no conflicts of interest to declare.

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Table 1. Subtypes of childhood speech and language disorders

Speech or language diagnosis	Sub-type	Definition	Prevalence	Aetiology	Natural history
Speech disorder	Articulation disorder	Inability to produce a perceptually acceptable pronunciation of one or more speech sounds, in words or in isolation, and at every attempt. Disorder exists in absence of any explainable cause (e.g. No hearing impairment, no orofacial structural deficits).	1 in 20 preschool children [1,3]	Complex multifactorial.	Highly tractable. Majority 'resolve' by 7 years unless structural.
	Phonological delay	The child is delayed, relative to peers, in understanding and correctly using the speech sounds of their language to contrast meaning.	1 in 20 preschool children [1,3]	Complex multifactorial.	Highly tractable, responds to therapy or may resolve 'naturally'.
	Phonological disorder	Child fails to understand and correctly use speech sounds of their language to contrast meaning. Child uses atypical speech errors not used in typical development (e.g. a sound preference substitution where a favourite sound is used in place of the correct phoneme, e.g. 'd' for 'k' in cup, 'd' for 'n' in knife, and 'd' for 'sh' in shoe).	1 in 20 preschool children [1,3]	Complex multifactorial.	Highly tractable, responds to therapy, unlikely to resolve 'naturally'.
	Childhood Apraxia of Speech	Disorder of speech motor programming/planning that affects a child's ability to perform the spatiotemporal parameters of movement sequences, resulting in errors in speech production and prosody [4].	1 to 2/1,000 [5]	Monogenic, metabolic, complex multifactorial, acquired.	Highly intractable. Responds to therapy but arguably never resolves.
Language disorder	Specific Language Impairment	Condition of language impairment where cognitive skills are within normal limits and there is no identifiable cause for the impairment. SLI is determined by applying exclusionary criteria [6].	1 in 14 preschool children [7]	Complex multifactorial.	Expressive SLI more tractable than receptive SLI [8]

Table 2.

Article	Speech/Language impairment*	Sample size	Mean age [range]	Methods	Brain-behaviour correlations	Decreases in study group	Increases in study group
Kadis et al., [18]	CAS	CAS (n=11, 8 M) TD (n=11, 5 M)	CAS: 4.7y TD: 4.8y	Cortical thickness ROIs in both hemispheres: IFG-PO; pSMG; pSTG; inferior pre- and post-central gyri	No correlation between LSMG & any speech performance measures	None	Increased cortical thickness: LSMG
Preston et al., [17]	SSE	SSE (n=23, 18 M) TD (n=54, 30 M)	SSE (9y9m), TD (9y11m) [8 y6m to 11y11m]	VBM (whole brain)	No significant correlations between speech accuracy & gray & white matter in SSE group alone	Reduced grey matter: R lingual gyrus (d=0.86) Reduced white matter: R lateral occipital gyrus (effect size d=0.95)	Increased grey matter: L Heschl's gyrus, L planum temporale, inferior LSMG, LSTG (d=1.05), R planum polare, R Heschl's gyrus, R planum temporale (d=0.95) Increased white matter: Splenium & anterior CC extending to

							cingulate (d=0.83) Increased cortical thickness: LSMG
Redle et al., [19]	PSD	PSD (n=12, 4F) TD (n=12, 4F)	7.42 (SD 1.25) 7.44 (SD 1.25)	fMRI cued finger tapping task vs. passive listening	Positive correlations between fine motor praxis performance and activation of multiple cortical regions noted in PSD group.	Decreased activation for task vs baseline in the parahippocampal gyrus, posterior cingulate cortex and cuneus/precuneus (components of the "default-mode" network, Figure 1B).	Increased activation in posterior cerebellum bilaterally for PSD during finger tapping, compared to controls
Roberts et al., [20]	SLI	SLI (n=14, 8M) ASD+LI (n=16, 14M) TD (n=25, 16M)	9.73 9.8 11.4	DTI	CELF scores and AF diffusion measures: None significant within groups.  Trend (p=0.08) for	No FA differences LI  No group differences in	Increase MD and RD in LAF for children with LI

					correlation between MD and CELF-core in combined SLI and ASD+LI groups	right AF	
Vydrova et al., [21]	SLI	SLI (n=37, 25M) TD (n=34, 18M)	8.4y (6.3-11.9) 8.9y (6.3-11.9y)	DTI	Not examined	Reduced FA bilaterally in AF, IFOF, UF, ILF	Increased volume bilaterally in ILF Increased MD bilaterally in AF, LIFOF, LILF. Increased RD in bilateral AF and UF, LIFOF, LILF More rightward asymmetry of IFOF

\*Diagnostic terminology used in original study.

Abbreviations: CAS: childhood apraxia of speech; SSE: speech sound errors; PSD: persistent speech disorder; SLI: specific language impairment; M: males; TD: typical development; ASD: autism spectrum disorder; LI: language impairment; ROI: region of interest; p: posterior; inferior frontal gyrus –pars operculari; SMG: supramarginal gyrus; STG: superior temporal gyrus; VBM: voxel-based morphometry; DTI: diffusion tensor imaging; fMRI: functional MRI; L left, R right; CELF: clinical evaluation of language fundamentals test; AF: arcuate fasciculus; FA: fractional anisotropy; MD: mean diffusivity; RD: radial diffusivity; IFOF: inferior fronto-occipital fasciculus; Inferior longitudinal fasciculus; UF: uncinate fasciculus.