Exploring neural markers of language processing using fNIRS in typically developed children and children with Developmental Language Disorder

Efstratia Papoutselou

BSc (Hons), MRes

Thesis submitted to the University of Nottingham for the degree of Doctor of Philosophy

28th February 2023

Contents

Declaration

I certify that this is my own work, except where indicated by referencing. No part of this thesis has been submitted elsewhere for any other degree or qualification.

E. Papoutselou
28th February 2023

Acknowledgements

I am deeply indebted to all the children, their families and the clinicians who very kindly volunteered in this research! Thank you for giving up your time and driving this work forward!

This endeavour would not have been possible without my supervisors. Ian, thank you for always being calm and patient! Doug, I cannot begin to express how grateful I am to have you as a supervisor. Thank you for all the opportunities and knowledge! Your guidance and support throughout this journey have been truly invaluable! *(Also thank you for reviewing things in the speed of light often from airport lounges.)*

Additionally, thank you to all my PhD "sisters"; Francisca, Sammi, Rachael and Faizah for all their support; emotional and practical! Seeing you all succeed and being as amazing as you are inspired and motivated me to keep going!

I am also grateful to everyone at the gym for being the best most supportive colleagues anyone could have ever asked for! Special thanks to Bas and Beth for all the chats and impromptu trips to fancy Spoons that kept me going this past couple of months!

Also thank you to Guangting for his help with MATLAB and fNIRS analysis, to Polly for her stats advice, to Hattie for lending her voice to all our auditory tasks, to Paige for checking up on recruitment, to Vicenta, Jan and Alison for making sure I get paid and to Louise Sabir for single-handedly keeping the School of Medicine Ethics Committee going.

To the Afasic family for embracing this project and helping me spread the word. Special thanks to Linda for our early morning chats about the gaps in DLD provision and the need for more research!

Lastly, to my family, who (still) does not fully understand what I have been doing all these years but have nonetheless been motivating me with encouraging questions such as “Will you get a job after this?” “Why is this taking so long?” and “Have you written it up yet?”. Whenever I got stressed, I could always count on you to remind me that I’ll be okay and that there were more important things in life. I ‘ll always be grateful for that!

Dedication

To my grandma Theoktisti Sotirchou, the most brilliant, compassionate, and bossy person I have ever met!

4th October 1927 - 23rd May 2022

Abstract

Background: Developmental language disorder (DLD) is a life-long condition with no clear biological causes that affects approximately 8% of the population. The diagnosis currently relies on behavioural testing that is not reliably performed on children younger than school age. Consequently, the diagnosis and treatment of DLD is often delayed until after children enter formal education. Early work in the field suggests that neural markers of language processing could be used to develop an objective diagnostic tool that will allow for accurate and early identification of DLD in preschool years and thus access to early interventions. Here we propose the use of a novel non-invasive neuroimaging technique called functional near infrared spectroscopy (fNIRS) to identify neural markers of language processing in children with DLD. Additionally, we argue that to understand atypical language processing, it is imperative to also investigate typical cortical activations in response to language processing to establish the developmental trajectories of the language network. Parallel to these studies we also investigate patterns of neural synchrony during parent-child interactions. Speech and language development in children is thought to rely on successful parent-child interactions, however, little is known regarding the underlying neural mechanisms from which they arise.

Methods: *Cross-Sectional fNIRS Studies:* A total of 36 participants aged 6–16-year-old (1 participant with DLD) were recruited in two cross-sectional fNIRS studies. Participants underwent a 10-minute resting state imaging session and

completed a series of computer-administered language and cognitive tasks while their brain activity was recorded using fNIRS from the bilateral inferior frontal gyrus (IFG) and the bilateral auditory cortices.

Hyperscanning fNIRS Study: 12 children aged between 3 and 5 years old and their mothers participated in this study. Neural synchrony in mother-child dyads was measured bilaterally over frontal and temporal areas using fNIRS whilst the dyads were asked to play together (interactive condition) and separately (independent condition). Communication patterns were captured via video recordings and conversational turns were coded.

Survey Study: 43 parents of children with DLD and 44 clinicians with DLD expertise completed a qualitative online survey detailing their views, concerns and recommendations regarding the use of neuroimaging-based tool for the diagnosis and monitoring of DLD.

Results: *Cross sectional fNIRS studies:* In typically developed children and adolescents, widespread connections between the language regions and the right IFG appear to continue decreasing as age increases. In contrast connections between temporal regions are well established by late childhood. Increased activity over right auditory regions is associated with decreased language skills. Whilst data from the DLD participant is described, further analysis was not possible due to the limited sample size (n=1).

Hyperscanning fNIRS study: We successfully recorded inter-brain synchrony in bilateral prefrontal and temporal cortices in mother-child dyads while they engaged in cooperative and independent play. Compared to the independent

condition, mother-child dyads showed increased neural synchrony in the interactive condition across the prefrontal cortex and temporo-parietal junction. There was no significant relationship found between neural synchrony and turn-taking, but neural synchrony was negatively correlated with the child's levels of surgency.

Survey study: Clinicians and parents perceived that a potential tool that could diagnose children with DLD earlier would positively impact the children as it would allow them to access interventions earlier. This study offered a unique account of the factors to be considered in the design and implementation of clinical measures for language disorders from the viewpoints of parents and language professionals.

Conclusions: Overall, this research aimed to identify neural markers of language processing in children with DLD and typically developed children to help develop an objective early diagnostic tool. Ultimately, this research might help maximize the benefits of speech and language therapies to improve the quality of life for children with DLD. This can be very impactful translational research in language development given that currently no objective neural-based tools exist for DLD.

Dissemination

Conferences and Presentations

- Biomedical Research Centre Annual Conference, November 2022- Poster Presentation, Nottingham, UK
- Functional Near Infrared Spectroscopy Conference 2022, October 2022, Poster Presentation, Boston, USA
- International Cognitive hearing science for communication conference, June 2022, Poster Presentation, Linkoping, Sweden
- British Cochlear Implant Group Meeting, April 2022, Poster Presentation, Cardiff, UK
- National Association of Professionals concerned with Language Impairment in Children, March 2022, Delegate, Sheffield, UK
- Neuromatch 3.0, November 2021, Oral Presentation, Online
- Sue Watson Event, May 2021, Oral Presentation - 2nd Prize, Online
- British Neuroscience Association Conference, April 2021, Poster Presentation, Online
- National Association of Professionals concerned with Language Impairment in Children, March 2021, Delegate, Online
- Audiological Research Cores in Europe, November 2020, Oral presentation, Online
- Federation for European Neuroscience Societies, July 2020, Poster Presentation, Online

- British Audiology Society 16th Annual Conference, November 2019, Poster Presentation, Liverpool, UK
- International Cognitive hearing science for communication conference, June 2019, Poster Presentation, Linkoping, Sweden
- Nottingham Paediatric Research Showcase, June 2019, Poster Presentation, Nottingham, UK
- M&HS Faculty Postgraduate Research Forum, May 2019, Oral and Poster Presentation, Nottingham, UK
- Language and cognition seminar series, May 2019, Oral Presentation Nottingham, UK
- National Association of Professionals concerned with Language Impairment in Children, March 2019, Delegate, Birmingham, UK
- Neuroscience at Nottingham, January 2019, Poster Presentation, Nottingham, UK

Publications

Papoutselou, E., Harrison, S., Mai, G., Patil, N., Buck, B., Wiggins, I. and Hartley, D., Investigating mother-child inter-brain synchrony in a naturalistic paradigm: A functional near infrared spectroscopy hyperscanning study *Manuscript submitted for publication December 2022, European Journal of Neuroscience.*

Author contributions: EP and DH conceived and designed the study, EP and SH collected the data, GM, BB, and IW contributed the analysis tools, EP, NP and GM performed the analysis, EP wrote the paper, SH, GM, BB, NP, IW and DH revised the paper.

Papoutselou, E., Harrison, S., Wiggins, I. and Hartley, D., under review. Clinicians' and parents' opinions of an objective measure of language processing for the diagnosis and management of developmental language disorder settings. *Manuscript submitted for publication March 2023, International Journal of Language & Communication Disorders*

Author contributions: EP and DH conceived and designed the study, EP collected the data, EP and SH performed the analysis, EP wrote the paper, SH, IW and DH revised the paper.

Harrison, S., Papoutselou, E., Wiggins, I. and Hartley, D., Clinicians' and parents' opinions of an objective measure of speech understanding for use in paediatric cochlear implant settings. *In Preparation*

Author contributions: SH and DH conceived and designed the study, SH collected the data, EP and SH performed the analysis, SH wrote the paper, EP, IW and DH revised the paper.

Financial Support

This PhD was supported by a doctoral award from the National Institute for Health Research (October 2018 – October 2021) and COVID-19 extension funding provided by the University of Nottingham (October 2021 – March 2022). Additional funds were provided by the Ulysses Neuroscience - Minerva Travel award 2020 and a partial registration waiver was provided by the Federation of European Neuroscience Societies for attendance at FENS 2020. The PGR Development Fund was awarded for attendance at FNIRS22, Boston USA.

List of figures

List of tables

List of abbreviations

Auditory brainstem response	ABR
Auditory processing disorder	APD
Autism Spectrum Disorder	ASD
Biomedical Research Centre	BRC
Broca's Area	BA
Children's Communication Checklist	CCC-2
Clinical Evaluation of Language Fundamentals	CELF
Continuous wave	CW
Coronavirus	Covid-19
Deoxyhaemoglobin	HbR
Developmental Language Disorder	DLD
Directed Connectivity	DC
Directed Connectivity	DC
Education, health and care plan	EHCP
Electroencephalography	EEG
Emotion Regulation Questionnaire	ERQ
Event Related Potential	ERP
False Discovery Rate	FDR
Frequency Domain	FD
Functional connectivity	FC
Functional Magnetic Resonance Imaging	fMRI
Functional Near Infrared Spectroscopy	fNIRS
General Linear Model	GLM

Haemodynamic modality separation	HMS
Haemodynamic response functions	HRF
High density diffuse optical topography	HD-Dot
High-Definition transcranial Direct Current Stimulation	HD-TDCS
Inferior Frontal Gyrus	IFG
Left Auditory Cortex	LA
Magnetoencephalography	MEG
National Institute for Care Excellence	NICE
National Institute of health Research	NIHR
Near Infrared	NR
Non-Verbal Working memory	NVWM
Oxyhaemoglobin	HbO
Positron emission tomography	PET
Phase Transfer Entropy	PTE
Phonemic Decoding Efficiency	PDE
Positron Emission Tomography	PET
Pre-Frontal Cortex	PFC
Randomised control trial	RCT
Region of Interest	ROI
Resting state connectivity	RSC
Right Auditory Cortex	RA
Right Inferior Frontal Gyrus	RIFG
Scalp-Coupling Index	SCI

Sight Word Efficiency	SWE
Speech and Language Therapist	SLT
Superior Temporal Cortex	STC
Superior Temporal Gyrus	STG
Sylvania fissure between the parietal and temporal lobes	Stp
Temporoparietal junction	TPJ
Test for Reception of Grammar	TROG
Test of Word Reading Efficiency	TOWRE
Total haemoglobin	Thb
Typically Developed	TD
United Kingdom	UK
Very Short form Early Childhood Behaviour Questionnaire	VS-ECBQ
Wechsler Abbreviated Scale of Intelligence	WASI

1 Developmental Language Disorder: an invisible disorder

1.1 Chapter Overview

This chapter is an introduction to developmental language disorder (DLD); its prevalence; risk factors and impact. The current diagnostic and treatment pathways and the challenges associated with them are also described. Neuroimaging is introduced as a potential objective tool for the diagnosis and monitoring of interventions for DLD. Lastly, there is a specific focus on functional Near Infrared Spectroscopy (fNIRS) and how it can be utilised for imaging children with DLD.

1.2 Developmental Language Disorder: an invisible disorder

DLD is defined as developmental language problems that severely impair daily life or educational progress and are associated with poor prognosis that persist into middle childhood and beyond (Bishop et al. 2017). A diagnosis of DLD cannot be given when a language disorder with the characteristics of DLD is observed as part of conditions with more complex patterns of impairments (Bishop et al. 2017). These conditions include brain injury, acquired epileptic aphasia in childhood, certain neurodegenerative conditions, cerebral palsy, and oral language limitations associated with sensory-neural hearing loss (Tomblin et al. 2015), genetic conditions such as Down syndrome and conditions such as autism spectrum disorder (ASD) and/or intellectual disability that are commonly linked to genetic or neurological causes (Bishop et al. 1998, Bishop et al. 2016, Bishop et al. 2017).

Chapter 1

People with DLD present a wide constellation of language difficulties. Signs of DLD are heavily dependent on the age of the child and their dialect. For example, preschool children with DLD typically use short, ungrammatical sentences (e.g. “Me happy.”), they have difficulties understanding what has been said and expressing their thoughts (Rudolph and Leonard 2016). In contrast, primary school children with DLD might struggle to follow complex instructions and produce organised and detailed stories (Rudolph and Leonard 2016). They might also have difficulties using grammatical utterances and reading and writing (Rudolph and Leonard 2016). Later in development, DLD might present with deficiencies in understanding and producing complex grammatical sentences and finding the right words even if they are previously learned (Rudolph and Leonard 2016). Children with DLD might also have language difficulties in social settings (pragmatic language impairment) without presenting a full cluster of deficits related to autism. They appear to have difficulties in forming social relationships with their peers and gaining peer acceptance due to their linguistic and social cognitive problems (Andrés-Roqueta et al. 2016). They are also more likely to experience emotional and behavioural difficulties which correlate with language deficits (Durkin and Conti-Ramsden 2010, Conti-Ramsden et al. 2013), low self-esteem (Wadman et al. 2008) and an increased likelihood of being bullied (Knox and Conti-Ramsden 2003), compared with their typically-developed peers. These psychosocial co-morbidities are more pronounced in adolescents compared with DLD adults (Lewis et al. 2016). Some individuals with DLD also exhibit deficits in cognitive and affective aspects of theory of mind (ToM) (the ability

to recognize mental states and attribute behaviours) (Nilsson and de Lopez 2016, Vissers and Koolen 2016). However, these deficits imply a developmental delay in ToM rather than a disorder (Nilsson and de Lopez 2016). A negative correlation also exists between literacy skills (Boudreau and Hedberg 1999, Catts et al. 2002, Dockrell and Messer 2007, Johnson et al. 2010, Dockrell et al. 2014, Tambyraja et al. 2015, Pentimonti et al. 2016), academic advancement and DLD (Aguilar-Mediavilla et al. 2019) that could impact on employment in adulthood. Lastly, children with DLD appear to be at higher risk of maltreatment (Lum et al. 2015) and engagement with the justice system (Bryan et al. 2015).

People with DLD might exhibit some or all these deficiencies at different stages of their development. For this reason, some researchers have tried to create subtypes of DLD based on the domain predominately affected (expressive, receptive or a mix both) (Conti-Ramsden and Botting 1999). However, even if two people exhibit similar problems in a particular domain, they might differ in the degree to which they are affected. Additionally, some people with DLD might continue to have difficulties in later developmental stages that might have resolved earlier for others (Leonard 2009, Leonard 2010).

It is also important to highlight that the clinical picture and the developmental trajectory of DLD varies widely from person to person and diagnosis mainly relies on exclusionary criteria (Bishop et al. 2017). Thus, it is inappropriate to describe DLD in terms of a particular spectrum of symptoms, as any of the

signs described above could be a result of other conditions (e.g., autism) that have a different aetiology.

1.2.1 Prevalence

DLD has a prevalence ranging from 3% to 7% (Tomblin et al. 1997, Norbury et al. 2016) . Exact estimates of prevalence vary depending on the age of the sample and the definition used for their diagnosis. However, despite its relatively high prevalence, DLD is considerably less researched (figure 1.1) compared to autism (0.65% prevalence) and Attention Deficit Hyperactivity

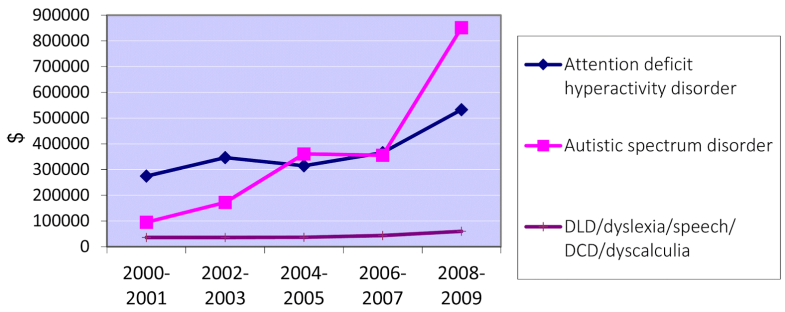


Figure 1.1 Annual spending of the National Institute of Health in the USA over time. Image adapted from Bishop et al 2010.

Disorder (5% prevalence) (Bishop 2010, D'Souza and Karmiloff-Smith 2017).

Indeed, DLD awareness amongst professionals and the public seems to be far less, compared with other developmental disorders such as dyslexia (5-17% prevalence, (Shaywitz and Shaywitz 2004) and ASD (Kamhi 2004)). This also affects real life outcomes for individuals with DLD. A survey of 70 workplace managers in the United Kingdom (UK) reported that less than 30% had ever heard of DLD. In contrast all responders knew of ASD and other developmental disorders (Lemos et al. 2022). This lack of awareness can be partially explained by the high comorbidity of DLD with other conditions such

as reading and auditory processing disorders. In the UK DLD seems to disproportionately affect children from disadvantaged social backgrounds (Gibson 2015) and children of Chinese, Bangladeshi, Black African, Black Caribbean descent (Strand and Lindsay 2009).

Additionally, the lack of objective diagnostic measures for DLD makes its identification particularly difficult. Unfortunately, DLD is also associated with many misconceptions regarding its causes and progression thus making it one of the most poorly understood and seldom recognised of the developmental disorders (Norbury 2017). There has also been a lack of agreement regarding the terminology used within the DLD literature (Ebbels 2014, Reilly et al. 2014). The terms used in the past included developmental dysphasia, developmental aphasia, specific language impairment, language impairment and others (Bishop et al. 2017). The current terminology (DLD) was adopted after a Delphi consensus in 2017 (Bishop et al. 2017).

1.2.2 Risk Factors

The same Delphi consensus mentioned above, identified risk factors for DLD, including i) a family history of language disorders or dyslexia, ii) male gender, iii) being a younger sibling in a large family, and iv) fewer years of parental education (Bishop et al. 2017). Epidemiological studies suggest that the incidence of DLD is almost equitably distributed between the sexes (Tomblin et al. 1997). Furthermore, no associations have been found between language impairments and genes on the sex chromosome (Chilosi et al. 2021): perhaps reflecting underreporting of language impairments in girls compared to boys.

However, in clinical samples and twin studies, DLD is found in boys and girls with a ratio of 3 or 4:1 (Chilosi et al. 2021). Thus, more research is needed to determine whether gender is a true risk factor for DLD.

Family history of language disorders is a strong risk factor for DLD (Bishop 2006). Specifically, using a twin-study design, Bishop and colleagues identified deficiencies in grammatical computation and phonological short-term memory as hereditable but genetically separable deficiencies associated with language impairment (Bishop 2006). However, there are currently no specific genetic markers for DLD that enable identification of the disorder via genetic screening. Some studies have identified potential candidate pathways and genes that might be involved in the aetiology of DLD such as the SETBP1 gene (Kornilov et al. 2015). However, currently these genes cannot be classed as genetic markers of the condition as they appear to influence some, but not all, aspects of DLD. The FOX2P gene was considered to be another promising genetic marker for DLD. Disruptions in this gene appear to affect fine motor control that can have severe consequences for speech development (Newbury and Monaco 2010). However, it seems unlikely that FOX2P is a genetic risk factor for more complex language impairments like DLD (Newbury and Monaco 2010).

1.3 The challenge of Diagnosis and Treatment of DLD

Currently, DLD is identified with a range of exclusionary and inclusionary criteria (Bishop et al. 2017). Children undergo extensive language and behavioural screening (Bishop et al. 2017). If their language skills are below average and there is no other explanation for these deficits, they are

diagnosed with DLD (Bishop et al. 2017). Therefore, children from deprived linguistic environments, with an intellectual disability, or a history of brain injury or a known genetic or neurological cause (such as autism, epileptic aphasia, sensorimotor hearing loss) are not diagnosed with DLD (Bishop et al. 2017). However, since many children have a mixture of problems a diagnosis of DLD can co-occur when a child also exhibits a cognitive, sensory-motor or behavioural disorder that might or might not have a causal relation to the language problems.

Even though advancements have been made in the diagnosis of DLD, it remains nearly impossible to predict outcomes in children under the age of 5 for three reasons. First, many toddlers with limited vocabulary tend to catch up and do not have any long-term problems (Reilly et al. 2010): it has been shown that about 40% of later talkers develop DLD later (Rescorla 2011, Bishop et al. 2017). Secondly, many children that are diagnosed with DLD have typical language development by the age of 3. Lastly DLD is diagnosed with assessments that many toddlers cannot complete as they lack the comprehension and reading skills required. Language problems that persist beyond the age of 5 tend to be better indicators of further language impairments (Stothard et al. 1998, Rice and Hoffman 2015). Therefore, a definitive diagnosis cannot be given before the ages of 5-6 years of age. DLD can be diagnosed after the age of 5, and even into adulthood, as language deficiencies might have gone undetected before then. Additionally, very few diagnostic tools are available for adolescents and/or individuals with English as their second language (Ramos et al. 2022).

A speech and language therapist (SLT) usually provides the diagnosis of DLD, followed by a treatment plan. Most available treatments are behavioural in nature and are divided into different levels, from very universal approaches such as educational packages delivered to all children, to very targeted individualised interventions (Law et al. 2003). However, to date little is known about the clinical efficacy of different treatments as there have been very few randomised controlled trials (Law et al. 2017). It has been reported that individualised approaches yield modest treatment effects (Burgoyne et al. 2018) but the outcomes from these therapies are highly variable (Smith-Lock et al. 2013, Burgoyne et al. 2018). Additionally, interventions that are not delivered and/or monitored by SLTs seem to not be as effective, compared with therapies that are (McCartney et al. 2015). Lastly, it is important to mention that a metanalysis of 15 randomised controlled trials of speech and language therapy as an intervention with DLD showed that even though children had improvements in the short term, the effects of the language therapy did not appear to be long-lasting (Fan et al. 2022). This suggests that until better interventions are available children with DLD potentially need life-long support.

These findings highlight the difficulties in changing language trajectories and the effort and time required to treat the deficiencies associated with DLD (Ebbels et al. 2019). Even though continuous support throughout development and into adulthood is necessary for people with DLD, it is important to mention that early treatment before children enter formal education can mitigate some of the negative effects of DLD and may lead to

better outcomes in the future (Beitchman et al. 2001, Zhang et al. 2008, Norbury et al. 2016). Systematic reviews and meta-analyses examining the effectiveness of interventions for DLD have concluded that the earlier interventions are administered the better the outcomes are for the children (Rinaldi et al. 2021). However, more work needs to be done to establish which treatment options are more effective, the ideal mode of administration, duration and linguistic target (Frizelle et al. 2021, Segura-Pujol and Briones-Rojas 2021). One major challenge in accomplishing that is the lack of consistency in the outcomes measured when assessing the effectiveness of interventions as well as inconsistencies on when these outcomes are measured (Pereira and Lousada 2022). However early intervention requires early identification of children with DLD and currently definitive diagnosis before the age of 5 years of age is not possible. The development of an objective diagnostic and monitoring tool may contribute to the accurate and early identification of DLD in preschool years and as well as facilitate early interventions.

1.4 Neuroimaging: An objective tool for DLD

Neural markers of language processing could be a potential objective tool for the diagnosis and monitoring of DLD. However, to date only a few neuroimaging studies have been conducted in children with DLD and their findings remain inconclusive as different recruitment criteria were used across these few studies, all with small sample sizes. Additionally, activations in the language network vary widely based on specific stimuli and the demands of

the particular task used. These methodological deficiencies, combined with the heterogeneity observed in DLD, render the results across studies difficult to interpret. One of the only consistent findings are abnormalities in the superior temporal gyrus (Review by (Liégeois et al. 2014)). Lastly, functional investigations of DLD are very scarce; most findings to date come from structural neuroimaging studies alone. More than a decade ago, the importance of conducting further functional neuroimaging research was highlighted by Im and colleagues. They suggested that conceivably children with DLD might display functional neuroimaging deficits in the absence of any morphological abnormalities (Im et al. 2007). More specifically, even though all of their subjects with DLD had structurally normal Magnetic Resonance Imaging (MRI) brain imaging, 87.5% of the group had abnormalities in their positron emission tomography (PET) scans in the thalamus, right frontal and temporoparietal regions as well as bilateral occipital regions (Im et al. 2007).

Structural neuroimaging studies measuring grey matter volume and cortical thickness have suggested that both these measures progressively reduce during development, reflecting synaptic pruning in typically developed (TD) children. However, studies of grey and white matter volume in children with DLD report contrasting findings (Girbau-Massana et al. 2014). For example, whilst Badcock and colleagues reported increased grey matter volume within the left inferior frontal gyrus (IFG) in children with DLD compared to controls (Badcock et al. 2012), Soriano-Mas et al. (2009) reported increased grey matter volume in the right hemisphere (Soriano-Mas et al. 2009). Lastly, an MRI study of 33 children showed reduced myelination levels in DLD over

cortical frontal areas and the basal ganglia (Krishnan et al. 2022). Consequently, larger scale structural neuroimaging studies with replicable paradigms are required to help disentangle the structural neural correlates of DLD.

DLD was initially believed to be a result of abnormal lateralization of the language network. Language function exhibits asymmetric lateralization to the left hemisphere in most individuals, even though a small proportion shows right-hemisphere language lateralization or bilateral lateralization. Much of the lateralization literature suggests that atypical language development is associated with reduced language lateralization to the left hemisphere (Crow et al. 1998, Annett 2003, Bishop 2013). This finding has been replicated in other morphological and functional imaging studies, including diffusion tensor imaging tractography (Vydrova et al. 2015, Morgan et al. 2018, Verly et al. 2019), structural MRI (De Fossé et al. 2004, de Guibert et al. 2011, Badcock et al. 2012, Mayes et al. 2015, Pigdon et al. 2019), magnetoencephalography (MEG) (Brown et al. 2014), functional transcranial Doppler ultrasonography (Whitehouse et al. 2008) and functional Electroencephalogram (EEG) (Leppänen and Lyytinen 1997, Shafer et al. 2000).

Even though it appears that some individuals with language impairment have atypical language lateralization, data from a few published studies have concluded that right or bilateral language lateralization is not a risk factor in developing a language impairment (Bishop et al. 2014, Wilson and Bishop 2018, Krishnan et al. 2021, Vansteensel et al. 2021).. Wilson and Bishop

suggested that a causal relationship between DLD and language lateralization might not exist. Instead, they suggested that the same factors contributing to the development of a language impairment might also affect language lateralization, in the absence of a causal relationship between the two (Wilson and Bishop 2018).

Functional results, predominately from EEG studies, report a wide range of deficiencies. An EEG study of 35 children with DLD reported abnormalities in their electroencephalograms particularly in the left language network. Degree of abnormality appeared to correlate with the severity of DLD (Lévy-Rueff et al. 2012). However, a previous review of clinical and electroencephalographic data of 138 children showed abnormal EEG recordings in only 15% of children with DLD, many of whom already had a history of seizures (Nasr et al. 2001). This suggests that using EEG recordings as a tool to diagnose DLD would lack the required sensitivity for a clinical application (Nasr et al. 2001). Other EEG studies have reported atypical event related potentials in phonological processing and early lexical access (Kornilov et al. 2015, Evans et al. 2022), auditory processing (Basu et al. 2010, Shafer et al. 2011, Cheng et al. 2021, Evans et al. 2022, Knowland et al. 2022, Peter et al. 2022), abstract semantic processing (Lorusso et al. 2015), processing of syntactic and grammatic violations (Sabisch et al. 2006, Roa-Rojas et al. 2021), attentional capacities (Shafer et al. 2007), prosodic processing (Sabisch et al. 2009), non-word repetition (McArthur et al. 2009), performance self-monitoring (Arbel and Donchin 2014) and statistical learning (Soares et al. 2022). Auditory brainstem

response (ABR) studies have also confirmed the altered speech processing in children with DLD (Chinn et al. 2022, Elmahallawi et al. 2022)

Only a couple of studies have used functional Magnetic Resonance Imaging (fMRI) and MEG to study functional deficits underlying DLD. A comparison between 8 TD adolescents and 8 DLD children revealed similar brain activity between the groups, in the same brain regions, happening at comparable timeframes, with similar laterality pattern. Nonetheless, children with DLD showed hypo-activation and abnormal patterns of coordination in a few of these regions, compared with TD controls (Ellis Weismer et al. 2005). Specifically, reduced brain activity was found in the left parietal lobe (involved in attentional control), the precentral sulcus (involved in memory processing) and the IFG (involved in language processing, retention of verbal information (Ellis Weismer et al. 2005)). Overall, this study indicates that children with DLD rely on a less functional network, as indicated by regions with reduced activation. Badcock and colleagues reported similar reductions in activation in the frontal and temporal gyri of 8 children with DLD compared to their

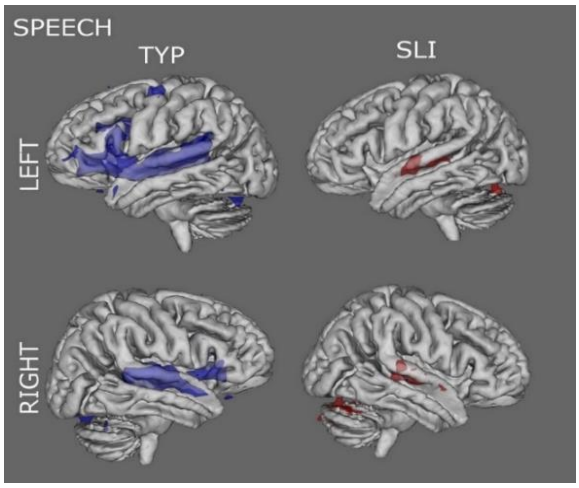


Figure 1.2 Functional brain activations of typically developed children (blue) compared to children with DLD (red) Image adapted by Badcock et al., 2012.

typically developed peers during a covert object naming task (figure 1.2), (Badcock et al. 2012).

Although an fMRI study investigating shifting attentional control in 6 children with DLD failed to report significant differences in task performance between children with TD and DLD, it demonstrated abnormal pattern of activations that indicated recruitment of compensatory mechanisms (Dibbets et al. 2006). Also, abnormal patterns of brain activity were reported in members of a Finnish family with DLD, compared with responses from aged-matched controls (Hugdahl et al. 2004). Specifically, this family showed hypo-activation in Broca's areas (BA 44) and an area in the middle temporal gyrus bordering the superior temporal sulcus (Hugdahl et al. 2004). Vansteesel and colleagues also demonstrated that DLD might be characterised by reduced activations in temporal regions during a story listening task (Vansteensel et al. 2021).

Furthermore, a MEG study reported that receptive impairments in children with DLD might originate from abnormalities in early auditory processing in the right posterior areas of the superior temporal gyrus (STG) (Cardy et al. 2010). Another MEG study of 11 children with DLD reported activations of equal strength in the left hemisphere for words and non-words and defective short-term maintenance of the linguistic input (Helenius et al. 2014). TD children showed stronger activations only for non-words (Helenius et al. 2014). However, an fMRI study of 19 children with DLD did not reveal any statistically significant differences in brain activations between the DLD and the TD group indicating that non-word repetition might not be a sensitive

enough marker for DLD (Pigdon et al. 2020). The largest functional neuroimaging study of adolescents with DLD to date (N=50) also showed that they had similar neural responses to TD children in hemispheric lateralisation of frontal regions during an overt verb generation task. Task performance was not significantly different between the two groups, thus potentially, the task was too simple to elicit differences in cortical activations (Krishnan et al. 2021).

To our knowledge only one study of resting state connectivity has been conducted with participants with DLD. Hwang and colleagues (2006) compared single-photon emission computerized tomography images of 21 children with DLD to TD children and reported function defects in the inferior parietal lobe and the basal ganglia (Hwang et al. 2006).

Lastly to date only two studies have recorded functional Near Infrared Spectroscopy (fNIRS) brain responses in individuals with DLD (Fu et al. 2016, Berglund-Barraza et al. 2020). Fu and colleagues investigated syntactic processing in 15 children with DLD using an agent assignment task (Fu et al. 2016). They reported abnormal hemodynamic responses in the DLD group in the bilateral inferior frontal and bilateral inferior posterior parietal brain regions and left temporal parietal junction (Fu et al. 2016). Berglund-Bazzara and colleagues used fNIRS to measure prefrontal brain activations in response to a n-back working memory task in two adults with DLD. Participants completed a non-word repetition task whilst receiving High-Definition transcranial Direct Current Stimulation (HD tDCS) (Berglund-Barraza et al.

2020). Results showed different brain patterns both between the TD and the DLD group as well within the two participants in the DLD group. After receiving the stimulation, brain activity in the DLD group resembled that of the TD group (Berglund-Barraza et al. 2020). Even though the sample size in this study was very small, it demonstrated the feasibility of using fNIRS to differentiate between individuals with and without DLD as well as measure the impact of interventions (Berglund-Barraza et al. 2020).

1.5 Functional Near Infrared Spectroscopy

FNIRS is a neuroimaging technique used for the functional mapping of the human cortex (Wolf et al. 2007). fNIRS is a non-invasive, safe technique that uses optic fibres to transfer light to and from the brain (Wolf et al. 2007). Because of the flexibility of the fibres, fNIRS can be used for any position or posture allowing for more naturalistic experimental environment without restraint or sedation and is quite robust to movement artefacts (Wolf et al. 2007). fNIRS has been used to create brain maps based on the hypothesis of neurovascular coupling where a specific stimulus can cause cortical neuronal activation which is followed by an increase in metabolic demand and an increase in blood flow. This hemodynamic response is characterised by an increase in oxyhaemoglobin and total haemoglobin and often, a simultaneous decrease in deoxyhaemoglobin (Hu et al. 2012).

Near-infrared spectroscopy relies on a few facts:

- Brain human tissues are relatively transparent to near infrared (NR) light (650–1000 nm). NR is about 100 times more likely to scatter rather than being absorbed.
- NR light is either absorbed by pigmented elements (chromophores) or scattered in the tissues. One of these chromophores is haemoglobin.
- Haemoglobin can absorb NR depending on its oxygenation status, meaning that the oxygenated and deoxygenated forms of haemoglobin have distinctly different absorption spectra and can be differentiated when light attenuation is measured at two or more wavelengths.
- Given the fact that 70–80% of the blood in the brain is in the venous compartment, the fNIRS technique offers information mainly about the oxygenation changes occurring at the venous blood level. (Ferrari and Quaresima 2012, Harrison and Hartley 2019, Pinti et al. 2020).

fNIRS can thus measure oxyhemoglobin (HbO), deoxyhemoglobin (HbR), and total haemoglobin (tHb, tHb = HbO + HbR) (Saager and Berger 2008, Sitaram et al. 2009, Kopton and Kenning 2014). However, it is not always the case that the haemodynamic response will be characterized by an increase in HbO and a decrease in HbR (Ferrari and Quaresima 2012, Kamran et al. 2016, Quaresima and Ferrari 2019). In that case, when an HbO decrease is found, it is speculated that the signal corresponds to a deactivation of the corresponding brain region. There is an ongoing debate regarding which measurement better reflects changes in brain activation in response to a stimulus (Ferrari and Quaresima 2012, Quaresima and Ferrari 2019). Some studies have shown an increase in HbO without a corresponding decrease in

HbR. Thus, it seems reasonable to report all three measurements when analysing the fNIRS signal (Ferrari and Quaresima 2012), (Nishiyori 2016). However, it is worth mentioning that during the analysis of fNIRS data, the haemodynamic modality separation (HMS) algorithm is commonly used to report cortical activations (Yamada et al. 2012). The HMS assumes that changes in HbO and HbR are negatively correlated in the functional responses but positively correlated in the motion and physiological noises, rendering the HbR signal redundant.

Haemodynamic responses last for 16s (Ferrari and Quaresima 2012, Nishiyori 2016, Quaresima and Ferrari 2019). They typically peak around 5-6 second after the stimulus presentation that triggers the underlying neuronal activity and take approximately a further 10s to fully return to baseline (figure 1.3) (Ferrari and Quaresima 2012, Nishiyori 2016, Quaresima and Ferrari 2019).

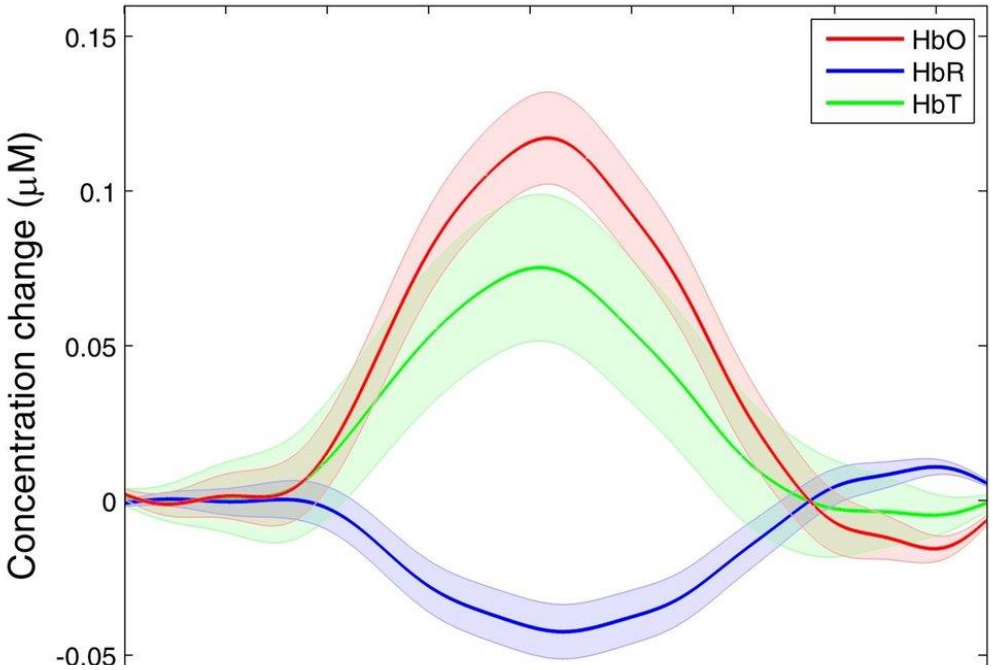


Figure 1.3 Graphical representation of the haemodynamic response. The haemodynamic response reaches its peak approximately 6sec after stimulus presentation and returns to the baseline after about 16sec. Image adapted from Ferrari and Quaresima, 2012.

Depending on the illumination pattern used, three different fNIRS techniques can be described. First, in the continuous wave (CW) technique, the tissue is constantly illuminated and the attenuation of light through the head is measured. The CW method provides information regarding concentration changes in HbO and HbR. CW measurements are more spatially resolved due to the lower cost photon detectors (Scholkmann et al. 2014). In the frequency-domain (FD) method, the tissue is illuminated with intensity-modulated light allowing for the measurement of both the attenuation and the phase shift of the emerging light (Schroeter et al. 2004). Lastly in the time-domain technique, the tissue is illuminated with short pulses of light and the shape of the pulse after propagation through the tissue can be measured (Torricelli et al. 2014). The FD and time-domain methods provide information regarding the absorption and reduced scattering coefficients from which it is possible to retrieve absolute concentration values of HbO and HbR. The FD and time-domain techniques allow for sampling rates of up to 100 Hz, whereas the CW instruments have a sampling rate of around 5 Hz (Nishiyori 2016, Davies et al. 2017). In the present work the Hitachi ETG-4000 system that utilises the continuous wave technique will be used.

One of major limitation of fNIRS is its poor spatial resolution relatively to fMRI and PET, that is limited to centimetres. Spatial resolution in fNIRS is limited by the physical principles of light propagation restricting to the cortical surface and provide no information on subcortical signal changes or activations in medial cortical areas, which are distant from the brain's surface (Ferrari and Quaresima 2012, Quaresima and Ferrari 2019, Pinti et al. 2020).However,

even though channel distances on the scalp are as sparse as EEG, fNIRS has a much higher spatial resolution and more reliable signal propagation compared to EEG, (Hu et al. 2012, Pinti et al. 2020). Lastly when analysing fNIRS, factors such as hair density and colour, scalp and muscle blood flow and physiological noise from the cardiac pulse and breathing need to be considered (Ferrari and Quaresima 2012, Quaresima and Ferrari 2019, Pinti et al. 2020).

1.5.1 Comparison of fNIRS to other neuroimaging techniques

Traditionally linguistic and auditory studies have utilized electrophysiology techniques, and predominately electroencephalograms (EEG) because of two of its characteristics: high temporal resolution that allows for construction of models of hierarchical and parallel processing steps, and low experimental constraints (Besle et al. 2009, Beres 2017). But EEG has low spatial resolution; the assignment of a language-specific component to a cortical area is somewhat arbitrary – in some instances even with respect to lateralization (Besle et al. 2009, Beres 2017). Analysis is less robust when examining longer timeframes than 10-1000ms. Event related potential (ERP) studies also have very low spatial resolution (the N400 has been located in various location across the temporal lobe). On the other hand, fNIRS provides a spatial resolution of about 1cm (figure 1.4) (Review by (Obrig 2014)).

Vascular-based techniques such as fMRI revitalized neurolinguistics research as they offered better localization of the activation and the integration over longer time frames (Logothetis 2008, Silver et al. 2021). fMRI allowed for the detection of the exact functional–anatomical relations in the language

network as it has great spatial resolution and depth penetration (Logothetis 2008, Silver et al. 2021). However, auditory tasks are very challenging due to the instrumental noise of the scanner. Whilst speech perception remains relatively robust to these effects, under certain conditions, noise remains a critical factor with detrimental effects on task performance, particularly in research examining the differentiation of subtle acoustic features, such as phoneme discrimination (Dietrich et al. 2006, Szameitat et al. 2009). It is worth mentioning that PET is also acoustically quiet but is invasive compared to fNIRS.

Additionally, an fMRI experimental set-up is not child-friendly, as it is challenging to "convince" children to stay still for a long time. Furthermore, it can be quite a claustrophobic environment for anyone, not least a young child (Obrig 2014).

The BOLD signal of the fMRI provides information regarding changes in oxygenation (Logothetis 2008). However, many fNIRS studies have shown increases in HbO without corresponding decreases in HbR, therefore fMRI may not be able to detect these kinds of activations (Gallagher et al. 2012). Even though both fMRI and fNIRS measure haemodynamic responses, fNIRS has a greater sampling rate (Ferrari and Quaresima 2012). Thus, the latter provides a better resolution of the hemodynamic onset, and, potentially direct measurement of fast neuronal signals (Gallagher et al. 2012). In fact, fMRI appears to be less sensitive in detecting bilateral speech patterns

compared to fNIRS (Benke et al. 2006, Gallagher et al. 2012) (figure 1.4, (Mehta and Parasuraman 2013)).

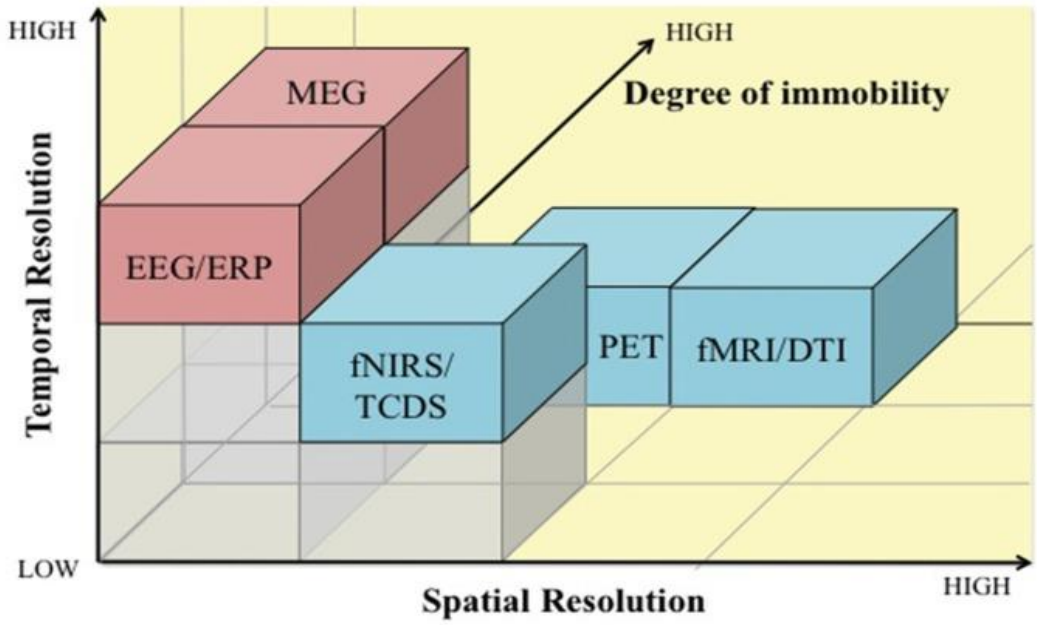


Figure 1.4 Graphical representation of comparison between different neuroimaging techniques. FNIRS has a better temporal resolution compared to fMRI (y-axis) and a better spatial resolution compared to EGG (x-axis) as well as allowing for a great degree of mobility (z-axis). Image adapted from Mehta and Parasuraman, 2013.

1.5.2 FNIRS in Language Research

FNIRS has been widely used in language and speech research (Minagawa-Kawai et al. 2008, Ferrari and Quaresima 2012, Quaresima et al. 2012, Vanderwert and Nelson 2014, Soltanlou et al. 2018, Tassi et al. 2022). FNIRS is non-invasive posing no risks for participants thus allowing for long testing runs. Traditional neuroimaging techniques are very sensitive to motion artefacts caused by head and mouth movements during overt speech (Zhang et al. 2017). Thus, most neuroimaging investigations of speech production use covert speech or sparse sampling to avoid effects of blood pressure and

respiratory changes (Zhang et al. 2017). However, studies have reported that systemic artefact removal on fNIRS signals can be used to process overt speech successfully accounting for motion artefacts (Zhang et al. 2017). fNIRS has also been used successfully in studies of speech production in stuttering individuals (Walsh et al. 2017). Additionally, it has been used in bilingual studies in both children and adults (Groba et al. 2019, Sun et al. 2022). It has also been ideal for hearing loss research particularly in populations with hearing aids and cochlear implants (Anderson et al. 2017, Anderson et al. 2019, Bortfeld 2019). fNIRS has been shown to be effective in identifying language laterality and language specific areas such as Broca's area independently of task used (Kennan et al. 2002, Cui et al. 2011, Ota et al. 2011, Arun et al. 2018).

Group-level fNIRS reliability has been investigated in a phonological verbal fluency task and a finger tapping task, where high reliability was reported but only based on small sample sizes (Sato et al. 2006). Since then, investigations with larger samples have shown acceptable group-level reliability in visual stimulation, finger tapping, verbal fluency tasks, prefrontal activations and social perception in infants, (Plichta et al. 2006, Plichta et al. 2007, Schecklmann et al. 2008, Blasi et al. 2014, Huang et al. 2017). Recently, Wiggins and colleagues demonstrated the test-retest reliability of fNIRS for auditory stimulation (Wiggins et al. 2016).

Quantitative comparisons between fNIRS and fMRI also support fNIRS validity for creating resting state connectivity maps (RSC) (Zhang et al. 2011, Duan et

al. 2012). RSC maps are particularly important in language research as they allow for investigations of the language network in populations unable to perform task-based neuroimaging. Studies comparing the laterality index of the language network between resting state fMRI and task-based fMRI have found strong correlations between the two (Tanaka and Stufflebeam 2016, Sair et al. 2017, Smitha et al. 2017). Gallagher and colleagues have demonstrated that RSC patterns of the language network measured with fNIRS are highly correlated with task-based measures of fNIRS, both for language localization as well as for hemispheric language dominance (Gallagher et al. 2016). These results validate the use of RSC analysis using fNIRS for evaluating language function.

An emerging field of research on language development in children is hyperscanning. Hyperscanning is the simultaneous recording of brain activities of two or more individuals (Dumas et al. 2010). The importance of measuring brain activity concurrently during human interactions has been recognised for a long time. In 2002 the first hyperscanning experiment was conducted using fMRI (Montague et al. 2002) and since then EEG is the most commonly neuroimaging modality used (Czeszumski et al. 2020). However, the evolution of fNIRS has revolutionised the field. The portability of fNIRS and its robustness to participant movements has allowed for designing naturalistic experiments that can be particularly suitable for imaging paediatric populations and investigating language and communication patterns. Indeed, a series of studies has validated its use for exploring parent-child interactions

(Reindl et al. 2018, Miller et al. 2019, Nguyen et al. 2020, Wang et al. 2020, Hoyniak et al. 2021, Kruppa et al. 2021, Nguyen et al. 2021).

1.6 Summary

This chapter underscores the pressing clinical requirement for the advancement of novel assessments tailored to Developmental Language Disorder (DLD), aiming to enhance the diagnostic and monitoring processes. It outlines the viability of leveraging language processing brain activations to detect distinct neural indicators of DLD, which can subsequently be integrated into an objective neural-based assessment tool for DLD. A significant portion of the existing neuroimaging research has lent support to investigations focused on the language network to uncover distinct processes affected within the brains of individuals with DLD. Consequently, our present study will centre on the examination of brain activations within the language network using fNIRS. In the next chapter, we will delve into behavioural tasks capable of eliciting activations within the language network, particularly targeting the linguistic domains known to be impacted in individuals with DLD. The meticulous selection of appropriate tasks, tailored to address deficiencies present in individuals with DLD, holds paramount importance as it paves the way for the identification of pertinent neural markers.

2 Potential Neural Markers for DLD

2.1 Chapter Overview

This chapter focuses on potential neural markers that can be measured with fNIRS and possibly be used clinically for the diagnosis and monitoring of interventions in children with DLD. The overall aims of the PhD are discussed, and an overview of the research conducted is summarised at the end.

2.2 Potential Neural Markers for DLD

2.2.1 Language Processing

Children with DLD exhibit deficits in phonological awareness, grammatical and semantic processing and memory and control systems (Boudreau and Hedberg 1999, Rice et al. 2004, Leonard 2009, Schulz 2010, Vandewalle et al. 2012, Claessen et al. 2013, Farquharson et al. 2014, Pavelko et al. 2018, Aguilar-Mediavilla et al. 2019, Gillam et al. 2021).

2.2.1.1 Phonological awareness

Phonological awareness refers to the ability to categorise and manipulate the sounds of language (Bishop et al. 2017). Children with DLD tend to fail to recognise a phoneme when it is presented with another auditory event (Factor and Goffman 2022), particularly during the earliest stages of development. A phoneme is "*the smallest distinct sound unit in a given language*" (Matthews 2014). Additionally, children with DLD can have difficulties segregating words into phonemes (Mengisidou and Marshall 2019, Cheng et al. 2022). These difficulties can have negative consequences on language acquisition, word learning and literacy (Vandewalle et al. 2012).

It has been argued that the phonological deficits observed in DLD are underlined by an auditory processing disorder (APD), which would impair successful phonemic awareness and perception of speech. As a result, children with DLD would fail to develop phonological, syntactic and semantic skills like their typically developed peers (Rosen 2003). Some researchers have suggested that a subgroup of children with DLD experience difficulties in discriminating speech from non-speech sounds when they occur rapidly (Tallal 1980, McArthur and Hogben 2001) and when they vary in spectral frequency (McArthur and Bishop 2005, Mengler et al. 2005). Event related potential (ERP) studies also support these behavioural findings by demonstrating abnormal brain responses to sounds by about one third to one half of children with DLD (McArthur and Bishop 2004, Bishop et al. 2007, McArthur et al. 2009). Since auditory deficits are not found in all cases of DLD, and some studies have failed to replicate the above findings, it has been argued that an auditory deficit could compromise phonological skills but is not sufficient to cause DLD (Bishop et al. 1999, Briscoe et al. 2001, Rosen 2003, Dawes and Bishop 2009). Additionally, others have argued that the apparent auditory processing deficits seen in children with DLD are a result of a more global processing deficit (Hartley et al. 2003). Thus, it can be concluded that APD and DLD might share common pathological causes, which would explain their high comorbidity but that does not indicate a causal relationship between the two (Rota-Donahue et al. 2016).

Neuroimaging investigations of auditory processing in children with DLD have predominantly been conducted using EEG as described in section 1.4.

2.2.1.2 Grammar

The prevalence of grammatical deficits in DLD has led many to describe a specific grammatical subtype of DLD (Heather and Jackie 2003, Rice et al. 2006). Difficulties have been identified both in morphology as well as syntax (Rice et al. 2006, Leonard 2009). Syntax refers to the relationship between words and other units within a sentence, and morphology refers to the grammatical structure of words (Matthews 2014). In terms of their expressive morpho-syntactic skills, children with DLD persistently omit morphological inflections leading to the formation of the extended optional infinitive hypothesis (Rice et al. 1995, Wexler 2003, Rice et al. 2004, Lin 2006). An inflection is "*any form or change of form which distinguishes different grammatical forms of the same lexical unit*" (Matthews 2014). In typical language development, there is an optional infinitive stage where children use tense markings (e.g., "–ed" in a past tense verb) optionally. However, they move past that stage around the age of 5 years old, whereas children with DLD do not (Bishop 2014, Calder et al. 2022). Morphological errors persist throughout early stages of language development in children with DLD but become less prominent later in adolescence (Miller et al. 2008, Duinmeijer 2013).

Children with DLD also have prominent difficulties in decoding complex syntactic structures (Duinmeijer 2013, Hsu and Bishop 2014). They struggle to interpret the grammatical relationships between elements of a sentence (e.g., determine agent), especially in complex structures (passive sentences, relative clauses) (Dick et al. 2004, Montgomery and Evans 2009, Fu et al. 2016).

Difficulties with complex syntactic structures persist well into adolescence. Teenagers with DLD tend to either avoid using them when producing language (Marinellie 2004, Tuller et al. 2012) or make more errors when doing so (Avram et al. 2013, Delage and Frauenfelder 2020). Thus, in the investigations of neural markers of syntactic processing in children with DLD it is not appropriate to use a spontaneous speech production task (Nippold et al. 2008) since children with DLD avoid using complex syntax altogether.

2.2.1.3 Semantics

Whilst the domain of semantics has not received as much attention in DLD investigations (Schulz 2010), it is important that neural signatures of semantic processing are explored. Children with DLD display well-documented word finding difficulties and poorer naming of objects, arising potentially from poor semantic representations and weak mental lexicon connections (Marinellie and Johnson 2002, Messer and Dockrell 2006, Sheng and McGregor 2010). Children with DLD also might struggle forming mental representations of verbs (Sheng and McGregor 2010, Andreu et al. 2012) and abstract concepts (Leroy et al. 2012, Vigliocco et al. 2018). Also, they might have difficulties retrieving meaning for already known words (Katsos et al. 2011).

Children with DLD struggle with decoding meaning from word combinations (Katsos et al. 2011). This difficulty is more pronounced when general all-purpose verbs are used (e.g., “get wet” vs “get the joke”) (Rice and Bode 1993, Kambanaros and Grohmann 2015). They have pronounced difficulties in processing the meaning of a sentence and deciding which nouns can be plausible in the context of particular sentence (e.g. in the sentence “The rock

bleeds." the noun "rock" is implausible) (Thordardottir and Weismer 2002, Ebbels 2007, Andreu et al. 2012, Pijnacker et al. 2017).

2.2.1.4 Memory and control systems

Language deficits especially morpho-syntactic and phonological processing in children in DLD have been associated with reduced working memory capacities (Ellis Weismer et al. 2017), (Conti-Ramsden et al. 2015). That prevents children from forming mental representations of sound sequences and encoding them in their short-term storage (Baddeley et al. 1998, Ellis Weismer et al. 2000, Ellis Weismer et al. 2005, Leonard et al. 2007). Difficulties in working memory impair attention and perception and may account for the observed difficulties to follow directions and complete tasks (Gathercole and Baddeley 1990, Archibald and Gathercole 2006, Leonard et al. 2007, Montgomery and Evans 2009).

Short-term phonological working memory has received particular attention. Deficiencies in that modality are well-documented in children with DLD (Alt 2011, Conti-Ramsden et al. 2015, Lum et al. 2015), highly heritable and some consider it to be a phenotypic marker of DLD (Bishop et al. 1995). On the other hand, findings are inconclusive in the case of non-verbal working memory (NVWM). Some behavioural studies have reported NVWM deficits in children with DLD (Bavin et al. 2005, Im-Bolter et al. 2006, Marton 2008, Henry et al. 2012, Vugs et al. 2014) while others have not (Archibald and Gathercole 2006, Archibald and Gathercole 2007, Ellis Weismer et al. 2017).

It is also worth mentioning that some studies have suggested that children with DLD exhibit deficits in procedural learning (autonomous learning).

However, the results of these studies remain inconclusive, and do not provide insights into the developmental trajectories of procedural learning in DLD (Ullman and Pierpont 2005, Lum and Bleses 2012, Mayor-Dubois et al. 2014, Desmottes et al. 2016, West et al. 2018). A metanalysis of 18 studies investigating procedural learning in children with DLD between the ages of 9 and 11 concluded that procedural learning appears to be present but delayed in DLD compared to typically developed children (Zwart et al. 2019). Deficits in procedural learning are in agreement with the observed deficiencies in motor skills in DLD (Sanjeevan and Mainela-Arnold 2019). Lastly children with DLD seem to also have impaired executive control functions such as shifting attention and inhibition (Im-Bolter et al. 2006, Henry et al. 2012, Engel de Abreu et al. 2014, Vissers et al. 2015, Sikora et al. 2019). However, it has not been established whether these difficulties are causally related to DLD and if so what the direction of that relationship is. Identifying neural markers of DLD may shed some light on the relationship between cognition and language development, not only in children with DLD, but also in typically developing children.

2.2.1.5 Sentence Repetition

A task that allows for examination of all linguistic characteristics (i.e. phonological awareness, grammar and semantics) as well testing memory demands during language processing is sentence repetition (Levelt 2001). Sentence repetition of semantically and syntactically plausible sentences has been well described in previous literature as a potential screening tool for DLD in English as well as other languages (Stokes et al. 2006, Archibald and

Joanisse 2009, Hesketh and Conti-Ramsden 2013, Leclercq et al. 2014, Theodorou et al. 2017, Fitton et al. 2019, Vang Christensen 2019, Pham and Ebert 2020, Taha et al. 2021, Wang et al. 2022). Ability to repeat sentences accurately has been used as a measure of grammatical proficiency and it also reflects short-term phonological memory (Klem et al. 2015, Polišenská et al. 2015) Additionally, language processing and consequently sentence repetition also involve executive control (Smith and Jonides 1999, Novick et al. 2005, Badre and Wagner 2007).

Therefore, it allows for a thorough examination of multiple facets of language processing, which is particularly important in children with DLD as they have highly variable phenotypes. Additionally, sentence repetition is an easy-to-follow verbal task thus ensuring that younger children can be tested and accounts for the high comorbidity between DLD and reading disorders, since it does not require reading stimuli. Thus, it is an appropriate task to identify neural markers of language processing that are unique to children with DLD.

Currently, there has only been a handful of neuroimaging studies of language repetition in DLD. Rinker and colleagues studied electrophysiological responses in preschool children with DLD vs typically developed children using a non-word repetition task and found no group differences in brain activity (Rinker et al. 2014). Berglund-Bazzara and colleagues measured overt non-word repetition in two young adults with DLD compared to 21 controls and reported that activity over frontal lobes was significantly different both between the two groups as well as between the two participants with DLD

(Berglund-Barraza et al. 2020). This work, as mentioned above, demonstrates the feasibility of using language repetition to detect differences in neural activations between people with and without DLD. However, the small sample size and the lack of recordings over language processing areas prevent us from making any conclusions about the potential differences in the language network.

It is also worth mentioning that no neuroimaging work has explored the neural signatures of sentence-level repetition in children with DLD.

In typically developed individuals, neuroimaging literature from both functional investigations as well as tractography studies has shown that sentence repetition is supported by a complex neural network across the peri-Sylvanian cortex that engages both language comprehension and language production mechanisms (Leonard et al. 2011, Majerus 2013, Moritz-Gasser and Duffau 2013). Bilateral temporal regions covering the auditory cortices are tasked with processing the auditory stimuli (Kovelman et al. 2014) i.e. the sentence to be repeated. Structures supporting the ventral stream for language in the temporoparietal lobe such as Wernicke's area are recruited to decode the semantic and syntactic information of the stimuli which are then stored in the phonological working memory at the Sylvania fissure at the boundary of the parietal and temporal lobes (Stp) (Hickok et al. 2003, Rogalsky et al. 2015). Sentence reconstruction engages the dorsal language stream including frontal regions such the IFG and Broca's area as well as motor cortex areas that support articulation (Hickok and Poeppel 2004,

Hickok and Poeppel 2007, Saur et al. 2008, Majerus 2013). Subcortical regions such as the putamen which is involved in motor responses and single word selection processes are also recruited (Argyropoulos et al. 2013) (van Heuven et al. 2008, Ali et al. 2010, Tremblay and Small 2011). Investigations of brain lesions in patients with aphasia are in line with these findings as they have shown that impaired sentence repetition performance is associated with reduced connectivity between the IFG and middle temporal gyrus and damage to the arcuate fasciculus i.e., the fibre tracks that connect them. Lesions to the posterior superior temporal gyrus as well as the anterior insula, a subcortical area beneath the IFG are also thought to lead to sentence repetition deficits (Berthier et al. 2012, Northam et al. 2018).

Language repetition activates mainly the left hemisphere however functional investigations have shown that increased task demands lead to activations in right hemispheric regions. A study showed that when presented with sentences with more complex word order, participants showed activations in right temporal regions (Segaert et al. 2013). Additionally, Melzer and colleagues reported brain activations in right temporal and frontal regions due to increased phonological demands were associated with poorly recalled sentences (Meltzer et al. 2017).

Some studies have shown that repeating syllables, words or non-words, or short sentences might be relying more heavily on the dorsal language stream without engaging the ventral stream (Liégeois et al. 2016). Repeating those utterances requires auditory and phonological processing in the temporal

lobes, access to working memory in the left IFG and motor processes for language production (Suh et al. 2007, Sierpowska et al. 2017). However, it does not tap into semantic and syntactic processing as short stimuli like single words can be reproduced from memory alone. For instance, activity in the left IFG is reduced when recalling sentences consisting of 6 words compared to producing original sentences of the same length reflecting decreased demands on semantic processing (Tremblay and Small 2011). It is worth noting that the authors did not compare repetition and production of longer sentences. On the contrary, other work has shown that repeating longer sentences especially ones that are semantically coherent and/or have complex syntactic structure requires processing of the conceptual relationships between the words (McDaniel et al. 1998). Recreating that stimuli recruits processes that support standard language planning and production processes such as retrieving the semantic message from phonological working memory and regenerating its grammatical and syntactic structure (Mascelloni et al. 2019). Thus, sentence repetition is a valuable index of language proficiency that engages the entire language network.

To date there have been very few investigations of sentence repetition in children. In late childhood non-word repetition engages similar patterns to adults namely bilateral posterior temporal regions involved in auditory, phonological and semantic processing, left temporoparietal junction involved in phonological working memory and bilateral frontal regions involved in speech production and motor areas involved in articulation control (Buchsbaum et al. 2005). Lum and colleagues demonstrated that sentence

repetition performance in an off-line behavioural task was negatively correlated with resting state power in the theta frequency band (Lum et al. 2022). Power in that band declines from late childhood to adolescence as part of typical development thus indicating that resting state oscillatory activity is related to language proficiency as measured by sentence repetition skills (Lum et al. 2022). However, the neural network supporting repetition in younger children is unknown. To our knowledge there are no investigations of on-line overt sentence-level repetition processing in children of any age.

2.2.2 Resting State Connectivity Patterns

Cortical connectivity complements task-related investigations of language processing by providing information on the underlying mechanisms of cognitive processes. Resting state connectivity (RSC) refers to low-frequency regional brain activity that occurs spontaneously in the absence of stimuli (Tomasi and Volkow 2012). Investigation of RSC in language processing brain regions have identified an underlying network that spreads across both hemispheres and includes the inferior frontal gyrus, the middle frontal gyrus, and inferior temporal and temporo-parietal areas (such as the supramarginal gyrus, planum temporale, Sylvian parieto-temporal, superior temporal gyrus, and inferior parietal cortex) (Price 2010, Tomasi and Volkow 2012, Yin et al. 2019). The RSC language network appears to be left lateralised very early in life (Liu et al. 2022) and the degree of left lateralisation increases with age (Holland et al. 2007, Reynolds et al. 2019, Bruchhage et al. 2020). For instance, a study investigating RSC patterns in 3- and 5-year-old children

reported higher degree of left lateralisation in RSC of the IFG and the STG in the older children (Xiao et al. 2016). The same group also showed that children appear to have stronger interhemispheric RSC between the right and left IFG whereas adults showed increased RSC between the IFG and STS in the left hemisphere (Xiao et al. 2016). Similarly, findings from task-dependant studies of language processing indicate that connectivity also increases intra-hemispherically within the left hemisphere whereas decrease or no change are observed in the connectivity within the right hemisphere (Gaudet et al. 2020). This increase in left connectivity asymmetry also reflects a shift from inter-hemispheric to intra-hemispheric connectivity with age (Yamada et al. 2010, Perani et al. 2011, Youssofzadeh et al. 2017) and potentially an automation of language skills.

Investigations of RSC offer practical advantages to task-dependant explorations of language processing. Namely, participants are not required to understand or perform a specific task, allowing us to study the RSC in the language network in prelingual children, and or children with cognitive and communication needs that prevent them from completing language tasks. Additionally, the language networks detected by fNIRS RSC analysis show good test-retest group-level reliability with activations found in the language network in response to language processing tasks (Gallagher et al. 2016). Thus, validating RSC as a way of exploring the language network.

To date there have not been any investigation into the RSC patterns of children with DLD. However, based on studies of typically developed children

as well as children with other developmental disorders, RSC could potentially be a great neural marker for diagnosing and monitoring DLD.

In a longitudinal study from 5 to 6 years old Xiao et al demonstrated that increased RSC in the language network positively correlated with advancements in sentence comprehension ability (Xiao et al. 2016). Another longitudinal study followed up children from infancy to school age (mean age 6.5 ± 0.96 years) and found that RSC patterns in infancy could predict language and literacy skills in childhood (Yu et al. 2021). Alcauter et al also demonstrated that RSC within left regions and subcortical regions of the language network could predict reading speed in 6-9 year old children (Alcauter et al. 2017). These findings indicate that RSC could potentially also be used to predict outcomes for children with DLD.

Similar findings have been reported in older children in studies exploring the relationship between RSC and reading ability (Koyama et al. 2011, Li et al. 2017, Benischek et al. 2020). Namely, RSC patterns between areas typically associated with reading (i.e., fusiform gyrus, motor areas, IFG and STG) and were positively associated with reading performance (Koyama et al. 2011, Li et al. 2017, Benischek et al. 2020). Qi et al demonstrated that higher RSC across the language network were correlated with better language skills in a sentence comprehension task and an increase in connectivity between the left IFG and left temporoparietal regions was observed in relation to increased age from 4 to 9 years old (Qi et al. 2021). Higher connectivity and integration of the language resting state networks have also been found to be positively

correlated with academic attainment across a variety of school subjects in 7- to 9-year-old children (Chaddock-Heyman et al. 2018).

Another reason why RSC patterns could be a potential neural marker for DLD is the fact that abnormal RSC patterns have been identified in children with other developmental disorders such as autism (Gabrielsen et al. 2018) and epilepsy (Ailion et al. 2022). For example, a study showed that children who stuttered had reduced RSC in areas associated with rhythmic discrimination compared children who did not stutter (Chang et al. 2016). Furthermore, Haghighat et al demonstrated that RSC in language processing areas in young children and adolescents were different not only when compared to typically developed age-matched controls but also between the two ASD age groups (Haghighat et al. 2021). This finding highlights the possibility to identify not only differences in RSC between typically developed children and children with DLD but to also track maturational changes in children with DLD. Finally, resting state connectivity patterns have been used for the early diagnosis of Tourette syndrome in children from 3 to 16 years old (Wen et al. 2018). The authors described a set of disrupted regions that were used to differentiate between typically developed children and children with Tourette's with an accuracy of 88.79%. (Wen et al. 2018)

Lastly, measuring RSC patterns in children with DLD could be an ideal tool to monitor the effectiveness of interventions developed for DLD. Currently there is no published work on the potential neural changes of resting and active networks of children with DLD after treatment. However, studies on other

clinical populations have shown successfully that RFSC can detect changes in pre and post intervention. Two randomised control trials (RCTs) in autistic children receiving music therapy and a reading training program vs no intervention both showed that participants in the intervention group not only had significant higher RSC in the relevant brain regions compared to the control group but also higher RSC from pre to post-intervention (Maximo et al. 2017, Sharda et al. 2018). Zhu et al reported similar findings where in deaf children receiving exercise intervention vs control RSC between subcortical regions and the frontal gyrus was significantly different both between groups as well as pre and post intervention (Zhu et al. 2021). Resting state connectivity patterns of children with autism were also used to quantify brain network changes after transcranial direct current stimulation therapy (Zhu et al. 2021). Finally, changes in RSC were also detected in children with reading difficulties after receiving a reading training program (Horowitz-Kraus et al. 2014, Horowitz-Kraus and Holland 2015).

The findings discussed above refer to investigations of cortical connectivity between brain regions have used functional connectivity (FC) analysis. FC describes the correlations across neurophysiological events that occur in spatial remote brain regions. FC analyses provide a wealth of information on statistical dependencies of neural activations patterns; however, it does not offer any insights into the causal relationships between neural systems (Babaeeghazvini et al. 2021). On the other hand, directed connectivity (DC) analysis overcomes this limitation by using the data to produce a model of the causal influences between different brain regions. DC is typically quantified

using Granger Causality (Granger 1969) and dynamic causal modelling (Friston et al. 2013). However, in this project, DC will be assessed using Phase Transfer Entropy (PTE). PTE addresses some of the limitations imposed by Granger Causality and dynamic causal modelling as it is not sensitive to signal noise and does not require a preconceived model of underlying neural patterns (Lobier et al. 2014).

2.2.3 Neural Synchrony Patterns

A child's social, emotional, and cognitive development has been shown to be directly influenced by the quality of parent-child interactions in early childhood. Indeed, behavioural studies have shown a strong correlation between parent-child interactions and children's emotional regulation, language, and social competence outcomes (Osterling et al. 2002, Cartmill et al. 2013, Hollenstein et al. 2017, Romeo et al. 2018, Cooke et al. 2019, Justice et al. 2019). For these reasons, parent-child interactions have been the target of numerous treatment plans for children (Jeong et al. 2021). A global systematic review and meta-analysis showed that interventions that targeted parent-child interactions improved the child's cognitive, language, and motor development (Jeong et al. 2021).

Particularly for DLD, a recent longitudinal study of 73 children of DLD followed them up from the age of 4 until the age of 6-7 years old and assessed the association between language development and quality of parent child interactions. The findings suggest parental behaviour alone was not predictive of language outcomes, instead the level of behavioural attachment between

parents and children was related to future language skills (Jokihaka et al. 2022). Additionally, parent implemented therapies are shown to be effective tools to stimulate language acquisition for children with DLD (Alpert and Kaiser 1992, Crowe et al. 2004, Justice et al. 2005, Allen and Marshall 2011, Law et al. 2019). Additionally, a non-randomised control trial showed that a parent-based shared book reading therapy improved mother-child communication styles and enhanced the child's expressive language skills (Lavelli et al. 2019). Another control trial of 30 children at risk of developing DLD showed that after receiving parent-implemented language intervention, they showed vocabulary scores within the normal ranges for their age (Law et al. 2019). Lastly a metanalysis of 76 studies showed that children with DLD showed significant improvements in social communication after receiving parent implement interventions (Roberts et al. 2019). However, it is worth noting that many of the studies reviewed above included relatively small sample sizes and were not randomised. Additionally, different outcomes to track language development were used making it hard to draw definitive conclusions regarding the effectiveness of these therapies. What is more, it is still unclear what are the mechanisms behavioural and neural that drive their effects on language development for children with DLD.

In typically developed children, successful mother-child interactions are thought to rely on behavioural, physiological, and neural synchrony (Harrist and Waugh 2002, Feldman 2007, Leclère et al. 2014, Davis et al. 2017). In this context, synchrony describes the phenomenon where interacting partners mutually adapt their behaviour in real time in response to one another

(Delaherche et al. 2012). Behavioural synchrony refers to the coordination of verbal and non-verbal communication (e.g., eye gaze, posture etc) whereas physiological synchrony encompasses coordination of biological rhythms such as heart rate and breathing patterns (Feldman 2007, Miles et al. 2009, Valdesolo and DeSteno 2011, Hoehl et al. 2020). Neural synchrony is defined as the temporal alignment of concurrent brain activity between interacting partners (Dumas et al. 2010). Neural synchrony between pairs can be measured using hyperscanning.

Even though, currently, there are no studies of neural synchrony between parents and children with DLD, a wealth of evidence exists already demonstrating the relationship between behavioural and physiological synchrony and parent-child interactions for typically developed children (Carollo et al. 2021). This body of work has proven first and foremost the presence of neural synchrony between parent-child dyads as well as its significance with regards to child development. Neural synchrony is associated with interactions of parents and children, and might be a neural marker of behavioural coordination, in cooperation tasks (Atzil and Gendron 2017, Leong et al. 2017, Miller et al. 2019). Thus, a positive feedback loop is created, whereby interaction leads to neural synchrony and neural synchrony could potentially underlie better interactions. Neural synchrony between parents and children appears to be supported by nonverbal behavioural reciprocity cues such as joint attention and mutual eye gaze, as well as the participants' current mental states and personality characteristics (Hasson et

al. 2012, Reindl et al. 2018, Azhari et al. 2019, Azhari et al. 2020, Nguyen et al. 2020).

To sum up, the section above highlight that the constellation of difficulties found in DLD leads to an array of potentially useful neural markers. Having reviewed the literature, we identify a need for exploring these markers in more ecologically valid task scenarios.

2.3 Aims of the thesis

The aim of this thesis was to investigate neural markers of language processing in typically developed children and children with DLD using fNIRS. As described above diagnostic and monitoring tools for DLD are currently lacking. Additionally, the maturational trajectory of the language network in both typically developed individuals, as well as children with DLD remains elusive. Furthermore, the relationship between standardised measures of language proficiency and brain activity are not well understood. Thus, identifying cortical patterns of language processing in typically developed children and children with DLD could not only shed light on the neural basis of DLD but also might lay the groundwork for the development of clinical tools for DLD. These clinical tools could enable the identification of DLD and access to interventions at an earlier stage than currently possible leading to better language outcomes. To successfully design and implement clinical measures for language disorder the unique account of the factors to be considered from the viewpoints of parents and language professionals are essential. Lastly, technological developments have allowed for the neuroimaging of two or more individuals simultaneously. The clinical applications of that are just

beginning to be explored and as part of this thesis we aimed to investigate it between mothers and their children.

The key aims of this thesis are as follows:

i. Characterise cortical patterns of language processing in typically developed children and adolescents.
ii. Characterise cortical patterns of language processing in children and adolescents with DLD.
iii. Explore cortical patterns of resting state connectivity in typically developed children and adolescents.
iv. Examine the feasibility of a free-play hyperscanning paradigm to measure mother-child neural synchrony.
v. Explore the opinions of end users of neuroimaging-based tool for the diagnosis and monitoring of DLD.

2.4 Thesis Structure

The aims described above were accomplished by conducting two cross-sectional fNIRS studies of typically developed children and children with DLD, a resting state connectivity fNIRS study, a hyperscanning fNIRS study and a survey of parents and clinicians. More specifically:

Chapter 3 describes the patterns of cortical activation during overt and covert language processing in typically developed children and adolescents. Maturational trajectories and the use of fNIRS as a predictive tool of language performance are explored.

Chapter 4 investigates the validity of using a sentence repetition paradigm to measure neural markers of language processing in TD children and children with DLD.

Chapter 5 details the patterns of resting state connectivity and their relationship with standardised language assessments in TD children.

Chapter 6 assesses the feasibility of a free play paradigm for the measurement of inter-brain synchrony between mothers and children.

Chapter 7 presents the views of clinicians with DLD experience and families of children with DLD regarding the use of a neuroimaging-based tool for the diagnosis and monitoring of DLD.

Chapter 8 summarises the main findings of each experiment and provides an overall discussion of the project aims. The limitations, impact and future direction of this work is presented.

2.5 The impact of Covid-19

On the 20th of January 2020 the Director General of the World Health Organisation declared the outbreak of the 2019 novel Coronavirus (Covid-19) as a Public Health Emergency of International Concern. Following that, on the 26th of March 2020 the British government announced an order to "stay at home" marking the first national lockdown (26/3/20 to 13/05/20). Since then, the country entered two more national lockdowns (5/11/20-2/12/20 and 6/1/21-06/03/21) and Covid-19 related restrictions remained until the 24th of

February 2022 when the government announced the “Living with Covid” plan (UKHSA 2022).

As a result of the above all research activities that required face to face contact were postponed and all laboratory facilities were inaccessible from March 2020 until November 2020. That was a time of great uncertainty as it could not be predicted when research activities would resume. That made it nearly impossible to create a contingency plan and we were unsure regarding the degree to which we needed to change the initial aims and scope of this thesis. Nonetheless an online survey querying the opinions of parents and clinicians regarding a neuroimaging-based clinical tool for DLD was launched in the summer of 2020. The survey was extremely valuable not only because it offered insightful guidance on the development of fNIRS as a clinical tool from the perspective of its potential end users but also because it allowed me to delve into a different field of research and develop qualitative research skills.

Research activity was allowed to resume from November 2020. We worked very hard to ensure that all possible safety measures were in place and competed risk assessments that were approved by both the University of Nottingham as well as by the Nottingham University Hospitals Trust. However, the continuous lockdowns and restrictions meant that members of the public were not allowed to travel for non-essential purposes until March 2021. The number of cases and deaths also caused by the virus created increased fear and anxiety. Additionally, shortages in personal protective equipment meant that any available stock needed to be reallocated to health care and other

workers in essential capacities. All the above resulted in further delays in restarting research activities. When face to face research was allowed to resume, recruitment of participants for the second study that aimed to characterise patterns of cortical activity in children and adolescents with DLD started immediately. Given that the study was portfolio adopted, it was eligible for support by NUH research staff (e.g., Research Nurses/Research Practitioners) which would be crucial in identifying and recruiting patients in a timely manner. However, due to staff redeployments, the NUH could not offer any assistance to non-Covid-related recruiting studies. That further impacted our ability to recruit participants.

To deal with that, we decided to design and perform a new fNIRS hyperscanning experiment, that would not only strengthen the data presented in this thesis but also allow us to investigate a very novel avenue of neuroimaging that is of both academic as well as clinical interest. The above experiment was conducted in May and June of 2021. Recruitment for this study targeted mothers and children aged 3 to 5 years old. That population in contrast to the 6- to 16-year-olds had less school-related obligation and were thus easier to recruit outside of school-holidays.

3 Neural markers in typically developed children.

3.1 Introduction

The present study aimed to characterise the neural patterns of language processing in relation to age and task demands in a sample covering the developmental stages from late childhood to adolescence, using both receptive and expressive tasks that covered main linguistic domains (phonological awareness, semantics, syntax and verbal fluency). These domains were targeted because previous neuroimaging studies in typical language development have provided well-documented patterns of neural processing (Weiss-Croft and Baldeweg 2015, Skeide and Friederici 2016, Bartha-Doering et al. 2018). Overall language processing and working memory were assessed using a sentence repetition task. Even though, as described in section 2.2.1.5. neuroimaging findings of neural activations children in response to sentence repetition, it is also commonly used as a diagnostic, prognostic as well as a rehabilitation tool for language disorders and/or aphasia as a result of stroke or head injury (Hosomi et al. 2009, Schlaug et al. 2009, Kempler and Goral 2011, Ramanan et al. 2020).

fNIRS investigations of developmental maturation in the language network during overt language production, compared to receptive or covert paradigms, remain rare (Paquette et al. 2015, Walsh et al. 2017, Zhang et al. 2017). The tasks used have been well described in previous literature to reflect linguistic proficiency that starts to develop in preschool years and continues to grow through adulthood (Wiig et al. 2003, Dick et al. 2004, Wiig

et al. 2013, Paquette et al. 2015, Fu et al. 2016, Gallagher et al. 2016). Additionally, the decision was made to incorporate a diverse range of tasks, not only to target numerous linguistic domains but also due to the fact that the majority of documented neural activation patterns in response to these tasks originate from studies utilizing fMRI and other neuroimaging techniques. As a result, the inclusion of a wide array of tasks would facilitate an investigation into the neural markers associated with these tasks as measured by fNIRS. This approach aims to ascertain whether any specific tasks exhibit higher reliability in capturing selective language processing responses. To comprehensively characterise neural markers of language processing, we recorded fNIRS activations bilaterally over the left and right IFG and the left and right auditory cortices. We did not expect to detect significant activations in the right IFG since it is not heavily involved in speech and language processing. It was hypothesised that participants would exhibit left language lateralisation while completing the language tasks (Weiss-Croft and Baldeweg 2015). Additionally, if language specialization in temporal areas is established earlier in childhood, age would not be a predicting factor of brain activation patterns. In that case, participants who perceived the tasks as less demanding and/or performed better, would show left-lateralised activations mainly confined to more posterior brain regions reflecting an automation of language skills. In contrast, if language specialisation is not already established by late childhood, we expected that brain activations would be positively with age in the left IFG and perhaps the right auditory cortex irrespective of task performance.

3.2 Methods

3.2.1 Participants

Thirty children between the ages of 6 and 15 years 11 months old (11 males, mean age: 11.31 years, SD=2.42) participated in the study. The goal of having 25 individuals in each group was established using insights from earlier research on test-retest reliability carried out by our lab involving adults. This research indicated that a sample size of 24 was adequate for obtaining dependable fNIRS data (Wiggins et al. 2016). Subsequent to this, a sequence of investigations from our lab has unveiled strong results in paediatric studies with comparable sample sizes (Mushtaq et al. 2019, Lawrence et al. 2021). Our objective was to include an additional participant per group to accommodate potential data gaps. One participant was excluded from the analysis later due to missing data. Participants were recruited using posters in various setting such as staff rooms in the University of Nottingham, primary and secondary schools, and community centres. The study was also advertised online through social media in parent groups as well as through emails to existing participant databases of the NIHR Hearing theme of the BRC.

All participants were native English speakers with normal or corrected-to-normal vision, no known hearing problems, and no history of cognitive or motor impairment. They also passed a pure tone audiometry air-conduction hearing screen performed at 20 dB HL at 0.5, 1, 2, and 4 kHz in both ears (procedure adapted from BSA, 2018). All participants scored within or above the normal range in the behavioural and language assessment detailed in

section 3.2.2 and were considered to have typical language and cognitive abilities (table 3.1). Detailed results can be seen in the Appendix 9.1. Hand preference was assessed using the abbreviated Edinburgh Handedness Inventory (Oldfield 1971). All participants were right-handed except for three (handedness was entered as a between subjects' factor in the analysis but no effects were identified thus no further results are reported). Each participant gave verbal assent, and written informed consent was obtained from the accompanying parents or guardians. The study was approved by the University of Nottingham Faculty of Medicine and Health Sciences Research Ethics Committee (ref no: 192-1901).

3.2.2 Behavioural Assessments

All participants completed the standardised cognitive and language tests described in table 1. These were used to assess non-verbal skills and language proficiency. The assessments chosen are widely used in paediatric language research and clinical settings. Reported scores are scaled standard scores derived using the normative datasets provided in each assessment's handbook (mean 100 ± 15).

Non-verbal intelligence was assessed using the Block Design and Matrices subtests of the Wechsler Abbreviated Scale of Intelligence - Second Edition (WASI-II). The block design task requires participants to reconstruct a given design using red and white blocks within a specified time-limit. This task reflects the child's ability to visually perceive analyse and reconstruct abstract figures. It measures perceptual organization, spatial visualization and

reasoning and visual-motor coordination. The matrices task requires participants to select the option that completes an incomplete matrix or series. It reflects the child's ability to perform mental manipulations of abstract symbols and perceive the relationships between them. It measures non-verbal fluid reasoning.

Receptive and expressive vocabulary skills were assessed using the Vocabulary subtest of the WASI-II. Participants were asked to name pictures and give definitions to words presented by the examiner visually and orally. This assessment is a measure of expressive and receptive vocabulary, verbal knowledge and fund of information. It also provides information regarding other cognitive abilities of the examinee such as memory, learning ability and language development.

Receptive grammar skills were assessed using the Test for Reception of Grammar- Version 2 (TROG-2). TROG-2 assesses the examinee's understanding of grammatical contrasts marked by inflections, function words and word

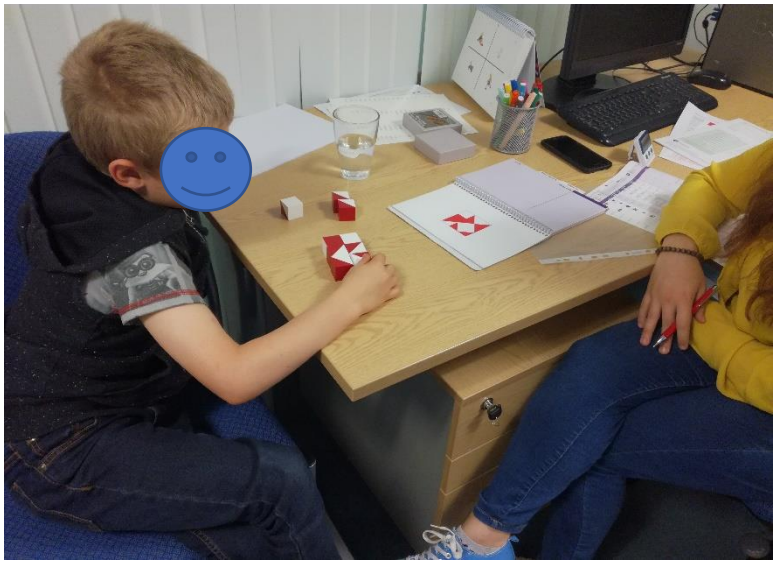


Figure 3.1 Participant completing the Block Design subtest of the WASI.

order. Participants are given a sentence comprised of a restricted simple vocabulary of nouns, verbs and adjectives and are asked to choose between four pictures the one that better depicts the sentence.

Reading ability was assessed using the Test of Word Reading Efficiency (TOWRE). More specifically, the TOWRE evaluates sight word recognition and phonemic decoding. Participants were asked to read out loud two lists of words of increasing difficulty: the Sight Word Efficiency (SWE) list and the Phonemic Decoding Efficiency (PDE) list. The SWE subtest assesses the number of real words printed in vertical lists that an individual can accurately identify within 45 seconds. The PDE subtest measures the number of pronounceable non-words presented in vertical lists that an individual can accurately decode within 45 seconds.

Finally, the parents/ guardians of the children completed the Children's Communication Checklist – Second Edition (CCC-2) assessment. The CCC-2 was used to evaluate aspects of language and communication that are not easy to measure with tasks during the fNIRS recordings, particularly the domain of pragmatics.

N (male)	29 (11)	
	Mean	*SD*
Age	11.31	2.42
Cognitive Measures		
Performance IQ[a]	111.59	13.25
Estimate of general cognitive ability[a]	111.58	10.17
Grammar Comprehension[b]	101.97	9.79
Sight Word efficiency[c]	104.76	11.20
Phonetic decoding efficiency[c]	113.17	10.54
General Communication Composite[d]	75.00	19.95

Table 3.1 Age characteristics of the sample and group means and standard deviations scores for the standardised language and behavioural measures. Scores are standard scores (mean 100 ± 15) except for the general Communication Composite where scores greater than 58 are considered normal.

[a]Wechsler Abbreviated Scale of Intelligence – 2nd Edition, [b]The Test for Reception of Grammar - Version 2, [c] The Test of Word Reading Efficiency – 2nd Edition, [d]The Children's Communication Checklist - 2nd Edition.

3.2.3 Procedure

After obtaining informed consent from the participants and their parents/guardians and completing the behavioural assessments, participants completed the language tasks while their brain activity was recorded using fNIRS. During the fNIRS measurements participants were seated comfortably in a sound-attenuated room with dimmed lighting, approximately 80cm from a visual display unit and a Genelec 8030A loudspeaker mounted above the display. Each task was comprised of an equal number of language and control condition blocks. Both the task and block order were pseudorandomised for each participant. Each block had a 17-23s duration (depending on the specific task) and was followed by a rest period of passive cross fixation with random duration in the range 17-23s. The fNIRS imaging lasted approximately 40 minutes and was split in two runs for participant comfort.

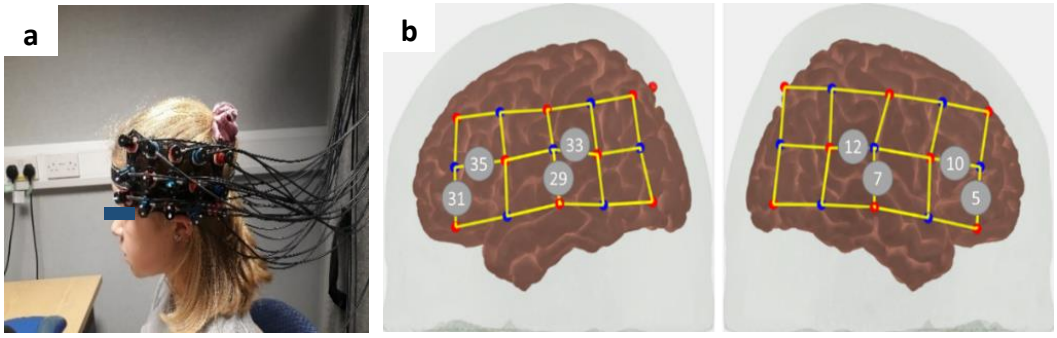


Figure 3.2: a) Photograph of the typical optode array placement on a participant, and b) Illustration of mean optode placement across the temporal and frontal regions obtained from the digital registration to the "Colin 27" atlas brain. Red/blue coding indicates optical sources/detectors, respectively. Channels 5, 10, 7, 12, 29, 31, 33 and 35 covered the predefined ROIs.

3.2.4 Equipment

Brain activity was measured with a continuous wave fNIRS system (Hitachi ETG-4000, Japan). Measurements were taken from a total of 44 channels using two 5x3 optode arrays placed bilaterally over the temporal and frontal lobes. Optode placement was standardized using the international 10–20 System, where the middle optode of the top row was aligned towards position Cz and the middle optode of the bottom row was placed vertical to the preauricular point (Lawrence et al. 2018) (figure 3.2a). To account for the average optode placement relative to underlying cortical anatomy a 3D digitizer was used to record anatomical surface landmarks (nasion, right and left tragus, inion and Cz) and optode placement. Additionally head circumference was obtained to account for potential anatomical differences due to head anatomy (details in the Appendix section 9.2) Digitisation measurements were obtained from a sample of 12 children between the ages of 6 and 16 years old. These recorded positions were registered to the "Colin 27" atlas brain (Collins et al. 1998) using the AtlasViewer tool (Aasted et al. 2015). Registration results are seen in figure 3.2b.

3.2.5 Stimuli/tasks

Participants completed five language tasks accompanied by control tasks. The control tasks attempted to replicate the non-linguistic cognitive demands of each language task such as motor movements, articulation and attention demands, as well as the response to auditory/visual sensory stimulation. Baseline measurements for each task were taken during rest while participants silently fixated on the computer screen.

Participants underwent a practice session prior to the fNIRS recording. Throughout the fNIRS procedure, all participants were instructed to focus on a centrally located black cross on the computer monitor. In tasks that required overt responses, the cross turned white whilst participants were expected to provide an answer and turned black again during rest periods or audio playback. The background colour of the screen was grey for all conditions and tasks. All overt responses were recorded.

All auditory stimuli were recorded prior to the experiment in a soundproof booth from a female native English speaker. Single word stimuli were spoken at a rate of approximately one word per 500ms and sentence stimuli were spoken at a rate of approximately one word per 300ms. All images were taken from the International Picture-Naming Project (https://crl.ucsd.edu/experiments/ipnp/) which is an open-access online resource (Szekely et al. 2004). Sentence and word stimuli in all tasks were adapted from the Clinical Evaluation of Language Fundamentals - Fifth Edition (Wiig et al. 2013). To minimize processing demands, especially in younger

participants who might not be proficient readers yet, all sentences and words were presented orally.

Language Condition

Participants completed 5 language tasks: semantic verbal fluency, phonological awareness, sentence repetition, syntactic comprehension, and semantic comprehension. Graphical examples are given in figures 3.3a and 3.3c. Participants also completed a short working memory task, but since the focus of the present study is specifically on language processing, we do not analyse the results of that task here.

Verbal Fluency

Verbal fluency tasks are commonly used to determine language laterality (Gallagher et al. 2012, Paquette et al. 2015). Five semantic categories meaningful to young children (animals, clothes, jobs, fruits, and sports) were visually presented and participants were given 20s to name as many words as possible belonging to the given category. Performance in this task was quantified by adding the number of unique words that belonged to each category. Number of words was converted to a percentage using the highest number of correct words recorded by a participant (60 words). Conversion to percentages was done to enable averaging of all task performance for later comparisons.

Phonological awareness

Phonological awareness was investigated using a phoneme substitution paradigm. The advantage of this approach over others is that it requires

participants to perform multiple levels of processing as they will be asked to identify, delete and replace phonemes as well as voice the new word that will occur (Wiig et al. 2013). More specifically, participants were orally presented with a word followed by a phoneme. They were instructed to substitute the first phoneme of the original word with the phoneme they heard and overtly name the new word (e.g., word: “dive”, phoneme: /v/, new word: “vive”). The task was comprised of 15 trials split into 5 blocks. Participants received 1 point when producing the correct word and 0 points for any mistakes.

Sentence repetition

Ability to decode sentences, store them in phonological working memory process word order and semantic relationships, interpret syntactic meanings and reproduce them was assessed using a sentence repetition task (Stokes et al. 2006). Participants were asked to repeat overtly an orally presented sentence. The sentence length was between 10 and 14 words. Shorter sentences were not used as they might not allow for investigations of the language system. If the sentence length is short enough to be within their memory capacity, participants are able to imitate a sentence perfectly without utilizing their linguistic knowledge (Wiig et al. 2013). This task was comprised of 10 trials. Participants received 2 points if they recalled the sentence perfectly and 1 point if they had a minor mistake. The highest possible score was 20 points.

Syntactic comprehension

Syntactic sentence comprehension was assessed using an agent assignment task. Tasks like that evaluate children’s ability to decode complex syntactic

structures (Dick et al. 2004, Montgomery and Evans 2009, Hsu and Bishop 2014). Participants listened to 10 sentences and were asked to click on the picture across a choice of three that depicted the agent of the sentence. The sentences were semantically implausible to ensure that agent assignment depended predominantly on syntactic knowledge rather than semantic plausibility.

Semantic comprehension

Semantic sentence comprehension was assessed using a semantic violation task, that examines participants' ability to decode semantic meaning (Wang et al. 2021). Participants listened to 10 sentences and were asked to judge by clicking on happy green or sad red face whether the sentence made sense semantically or not, respectively. During the syntactic and semantic comprehension tasks participants were awarded 1 point for each correct response and 0 points for any missed or incorrect response.

Control condition

The language tasks that involved auditory stimuli were accompanied by a control condition where that same stimulus was time reserved. Language tasks requiring an overt response following the auditory stimulus included an overt digit articulation control task. Participants were instructed to read aloud the digits "1" and "3". The period of presentation was equal to the response period of the corresponding language task (figure 3.3d). The digits "1" and "3" were chosen because saying "1" involves pushing the lips and saying "3" involves protruding the tongue (Richardson et al. 2010). Language tasks

requiring a mouse click response following the auditory stimulus included a control mouse click condition. In this control task participants were presented with the same visual stimuli as the corresponding language task. One of the images was starred and participants were instructed to click on the starred item (figure 3.3b).

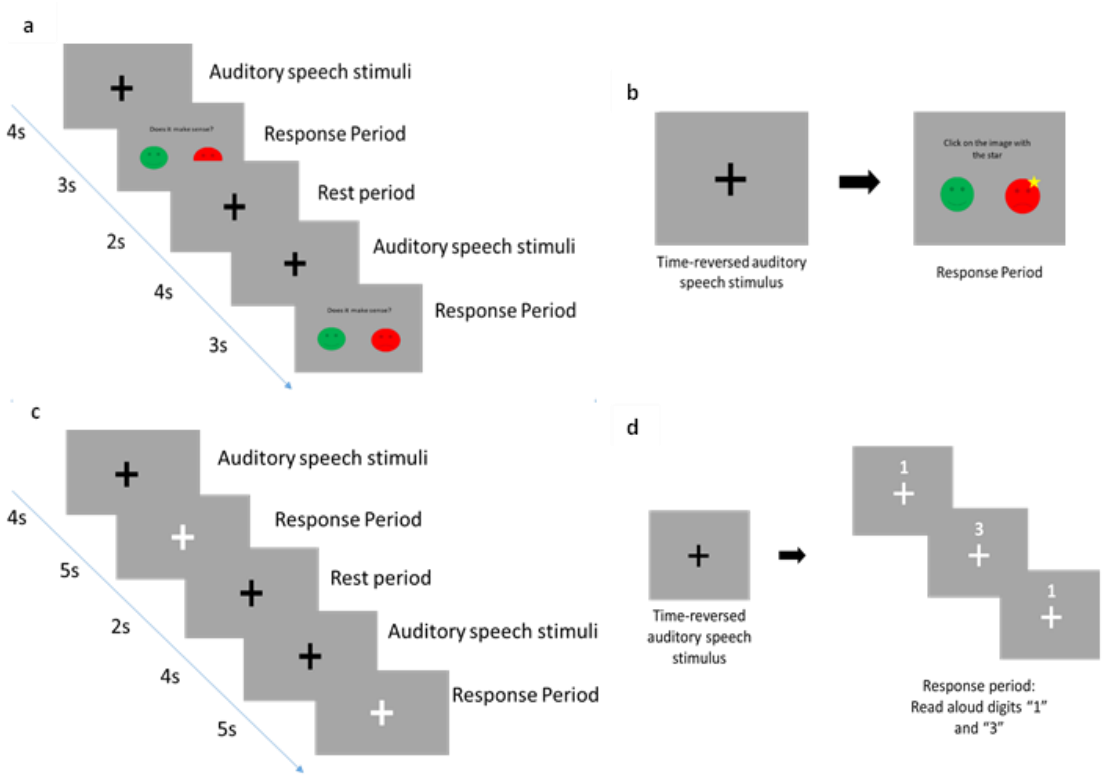


Figure 3.3 Graphical representations of the computer-based language tasks and the control conditions. a) One block of the semantic comprehension task. b) One trial of the control mouse clicking task for the semantic comprehension task. c) One block of any of the tasks comprised by an auditory stimulus and an overt response period. d) One trial of the control articulation task.

3.2.6 fNIRS data

fNIRS data were pre-processed via MATLAB 2019b (MathWorks, Natick, MA) using the HOMER2 package (Huppert et al. 2009) incorporating with customised scripts (Wiggins and Hartley 2015, Anderson et al. 2017, Mushtaq et al. 2019, Lawrence et al. 2021). The raw fNIRS intensity signals were first

converted into changes in optical density followed by correction of motion artifacts using wavelet filtering (via the HOMER2 *hmrMotionCorrectionWavelet* function that removed outlying wavelet coefficients outside the 0.725 inter-quantile range) (Molavi and Dumont 2012). The signals were then bandpass filtered between 0.01 and 0.5 Hz (via a zero-phase 3rd-order Butterworth filter) to attenuate low frequency drifts and cardiac oscillations. Using the modified Beer-Lambert Law, optical density was converted to estimated changes in the concentration of HbO and HbR (Huppert et al. 2009). The haemodynamic modality separation (HMS) algorithm was used to extract cortical activation (Yamada et al. 2012). This was done by trying to isolate the functional component of the haemodynamic signals from systemic physiological interference(Yamada et al. 2012) assuming that changes in HbO and HbR are negatively correlated in the functional responses but positively correlated in the motion and physiological noises (Yamada et al. 2012). Using this algorithm has demonstrated greater reliability of fNIRS signal quality (Wiggins et al. 2016). Moreover, to further improve the signal quality, channels with potential poor signals were detected using scalp coupling index (SCI) (Pollonini et al. 2014). Following protocols developed by our lab (Wijayasiri et al. 2017, Anderson et al. 2019, Mushtaq et al. 2019, Lawrence et al. 2021), signals were bandpass filtered at 0.5-2.5 Hz and channels with poor signal quality were excluded for subsequent analyses. Lastly, the General Linear Model (GLM) was used to quantify the response amplitude (Wiggins et al. 2016, Lawrence et al. 2018). The conditions included

in the design matrix were a set of thee regressors for each experimental condition (i.e., language processing, control and rest).

After applying the HMS algorithm, HbO and HbR become statistically redundant therefore only the beta estimates of the HMS signal (mean beta weights) were used in the subsequent analysis (Wiggins et al. 2016, Lawrence et al. 2018). These beta weights were used to quantify the amplitude of cortical activation for the language condition vs rest and the language vs the control condition. The false discovery rate (FDR) method was applied across channels in all fNIRS analyses to correct for multiple comparisons (Benjamini and Hochberg 1995).

Brain activations were derived from predefined regions of interest (ROIs) that were determined based on previous adult and paediatric cortical fNIRS responses to language tasks (Lawrence et al. 2018, Mushtaq et al. 2019). More specifically, channels covering Broca's area in the left frontal cortex and Wernicke's area in the left temporal cortex, as well as the corresponding regions in the right hemisphere, were selected. The channels covering the frontal regions were numbers 31, 35 in the left hemisphere and 5, 10 in the right hemisphere. The channels covering temporal regions were numbers 29 and 33 in the left hemisphere and 7 and 12 in the right hemisphere (figure 3.2b).

3.2.7 Statistical analysis

Beta weights were obtained for each language task separately. Preliminary analysis suggested that the variations in stimuli didn't alter cortical fNIRS responses. Therefore, to explore language processing overall and increase the

statistical power to detect activation, especially after controlling for multiple comparisons across channels, the beta weights were averaged across language tasks for subsequent analysis.

A mixed measures ANOVA was performed to explore the effects of region, hemisphere, condition, on mean beta weights. The within-subject factors were hemisphere (left, right), region (frontal, temporal) and condition (language vs control). Bonferroni correction for multiple comparisons and Greenhouse–Geiser adjustments for violation of sphericity were performed (corrected p values are reported).

In addition, to exploring the relationship between age, performance and hemodynamic responses, age and performance were added as covariates in the linear models. Additionally, correlation and regression analyses were conducted. Histograms and the Shapiro-Wilk test confirmed normality of the distribution of beta weights, age and standardised language assessments and post-hoc diagnostic measures verified that the assumptions of bivariate linear regression were met in each model: 1) a scatterplot indicated linearity between the predictor and dependent variable; 2) a Durbin-Watson test demonstrated independence of observations; 3) case wise diagnostics confirmed the absence of significant outliers; 4) visual examination of histograms and normal P-P plots indicated that the standardised residuals of the regression model were normally distributed, and; 5) the assumption of homoscedasticity was met. The Bonferroni correction was applied to all

comparisons and correlations to counteract the problem of multiple comparisons and statistical significance was set at $p < .05$.

3.3 Results

3.3.1 Behavioural results

All participants completed the computer-administered language tasks successfully. Details for each task separately are presented in table 2. Age was positively correlated with average performance across all participants ($R(27)=.83$, $p<.001$, Bonferroni corrected for 6 comparisons) and as well as performance in each task separately (Verbal Fluency: $R(27)=.762$, $p<.001$, , Bonferroni corrected for 6 comparisons Sentence Repetition: $R(27)=.546$, $p=.015$, , Bonferroni corrected for 6 comparisons, Syntactic Comprehension: $R(27)=.723$, $p<.001$, Bonferroni corrected for 6 comparisons, Semantic Comprehension: $R(27)=.545$, $p=.01$, Bonferroni corrected for 6 comparisons, Phonological Awareness: $R(27)=.611$, $p<.001$, Bonferroni corrected for 6 comparisons).

Task	*Mean*	*SD*
Verbal Fluency (%)	40.45	12.08
Sentence Repetition (%) [a]	86.07	14.93
Syntactic Comprehension (%)	79.66	16.58
Semantic Comprehension (%)	83.10	17.55
Phonological Awareness (%)	79.31	12.13

Table 3.2 Performance in each language task. Reported means are derived from the conversion of scores to percentages. [a]Performance from one participant was not recorded.

3.3.2 fNIRS results

Figure 3.4 shows the topographic representations of the contrast between activity recorded during the language condition vs rest, during the control condition vs rest and during the language vs the control, for all participants.

In the language condition vs rest contrast, channel 14 showed significant activation at a group level but no other individual channel showed significant activation compared to rest ($q < 0.05$, FDR corrected) (figure 3.4a). However, to confirm that successful fNIRS measurements were taken, haemodynamic activity over the preselected ROIs was contrasted against rest using one-sample t-tests. Activity was significantly higher than 0 over the left (t_{24} = 3.609, $p< 0.05$) and right (t_{28} = 3.178, $p<0.05$) auditory cortices but not over the left (t_{28} = 1.709, p= 0.099) and right (t_{24} = 0.242, p=0.810) IFG.

When activity during the control condition was contrasted against rest multiple channels showed statistically significant activation (Ch 7, 11, 14, 19, 20, 21, 24, 29, 33, 34) ($q < 0.05$, FDR corrected) (figure 3.4b), however the t values between the language vs rest contrast and the control vs rest contrast were in most cases very similar. Thus, to examine whether more channels were activated in the control vs the language condition, the two conditions were directly compared (figure 3.4c). Channel 31 covering inferior frontal areas showed significant activation ($q < 0.05$, FDR corrected) in the language vs the control condition (figure 3.4c). Activity in other channels did not reach significance because perhaps that contrast is more subtle requiring greater

power to detect a significant effect. Plots of the block-averaged time course of haemoglobin concentration change for the language and control condition for each of the four ROIs are presented in figure 3.5.

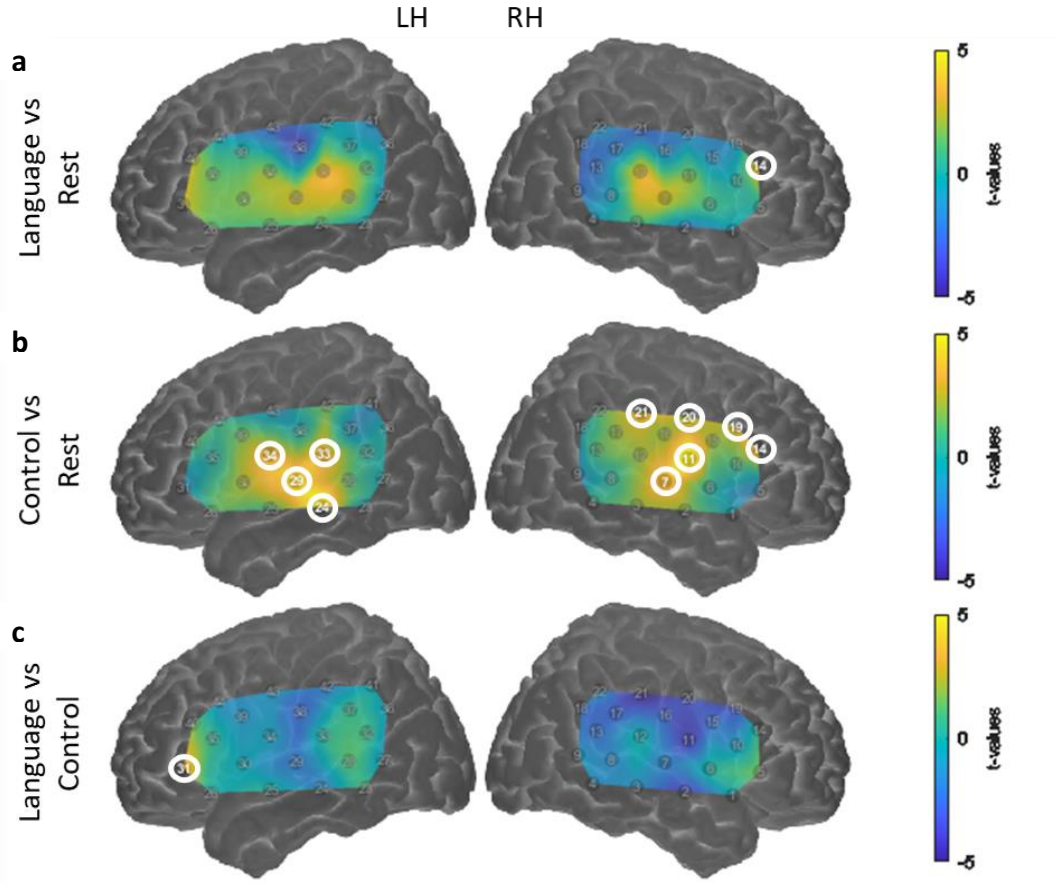


Figure 3.4 Topographic representation of the mean hemodynamic response recorded overall over bilateral temporal and frontal regions. Circled highlighted channels show significant activation (q < .05, FDR corrected). (a) Contrast between the language condition vs rest. (b) Contrast between the control condition vs rest. (c) Contrast between the language condition vs the control. Note that the maps are interpolated from single-channel results and the overlay on the cortical surface is for illustrative purposes only.

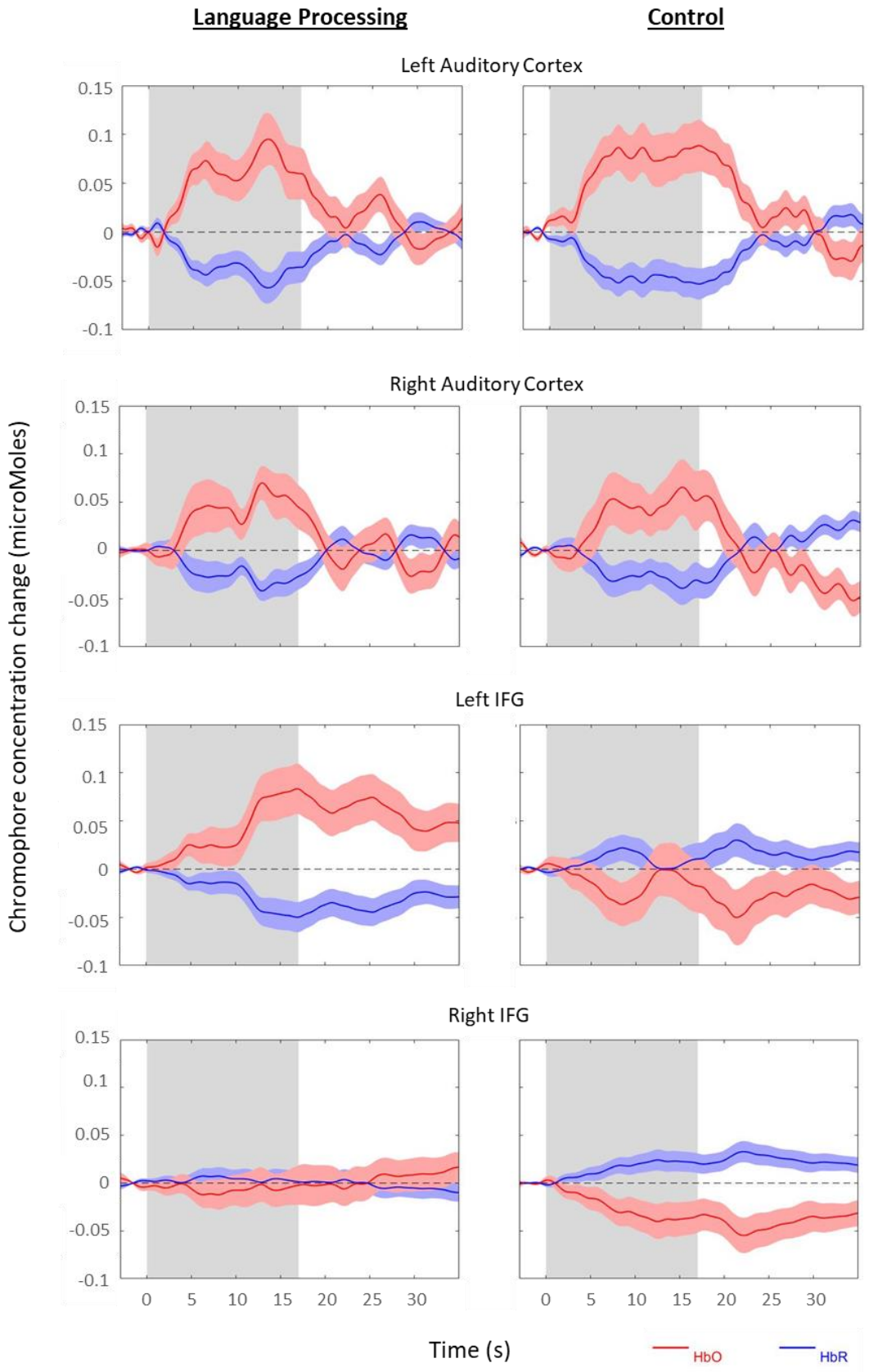


Figure 3.5 Block-averaged haemodynamic time courses. These are displayed for the language processing (left panel) and control conditions (right panel) for each of the 4 ROIs. The shaded grey areas indicate the stimulation period (0s to ≈17s).

3.3.3 Effects of region and hemisphere per condition

To begin with two separate RM-ANOVAs were performed using the mean beta weights to examine the effects of region (auditory vs frontal) and hemisphere (left vs right) in the language processing and control condition to explore ipsilateral and contralateral neural activity during language processing vs silence and during active control vs silence respectively. In the language condition there was a statistically significant effect of hemisphere ($F(1,28) = 11.477$, $p < .01$, Bonferroni corrected for 3 comparisons) with increased activation in the left hemisphere over the right hemisphere (mean dif. = .027, SE =.008, df=28, $p = .002$). In the control condition there was only a significant main effect of region ($F(1,28) = 34.894$, $p < .001$, Bonferroni corrected for 3 comparisons) with increased neural activity in the auditory regions compared to frontal regions (mean dif. = .068, SE =.011, df=28, $p < .001$). Detailed results in table 3.3.

Language Condition		
Main effects		
Region	$F(1,28) = 3.581$	$p > .05$
Hemisphere	**$F(1,28) = 11.477$**	$p = 0.006$
Two-way Interactions		
Region x Hemisphere	$F(1,28) = 0.353$	$p > .05$
Control Condition		
Main effects		
Region	**$F(1,28) = 34.89$**	$p < .001$
Hemisphere	$F(1,28) = 0.071$	$p > .05$
Two-way Interactions		
Region x Hemisphere	$F(1,28) = 1.118$	$p > .05$

Table 3.3 The results of the 2-way ANOVA between region and hemisphere. Highlighted in yellow is the main effect of hemisphere that reached statistical significance at p<.05.

3.3.4 Relationship between ROI and condition

An MR-ANOVA was performed to explore the effects of ROI (LA, LIFG, RA, RIFG) and condition (language processing, control). There was a main effect of ROI ($F(3,84)=11.549$, $p<0.01$, Bonferroni corrected for 3 comparisons) and a significant interaction between ROI and condition ($F(3,84)=6.301$, $p<0.001$, Bonferroni corrected for 3 comparisons). There was no effect of condition ($F(1,28)=.881$, $p>.05$, Bonferroni corrected for 3 comparisons).

Pairwise comparisons indicated that haemodynamic responses were significantly higher in language processing vs the control condition in the LIFG area (mean dif. = .051, SE=.014, df=28, p< .001). In the RA area responses were significantly higher in the control condition vs the language processing condition (mean dif.= .02, SE = .009, df=28, p =.044). The was no difference in activity between conditions in the LA (mean dif.= .011, SE = .02, df=28, p

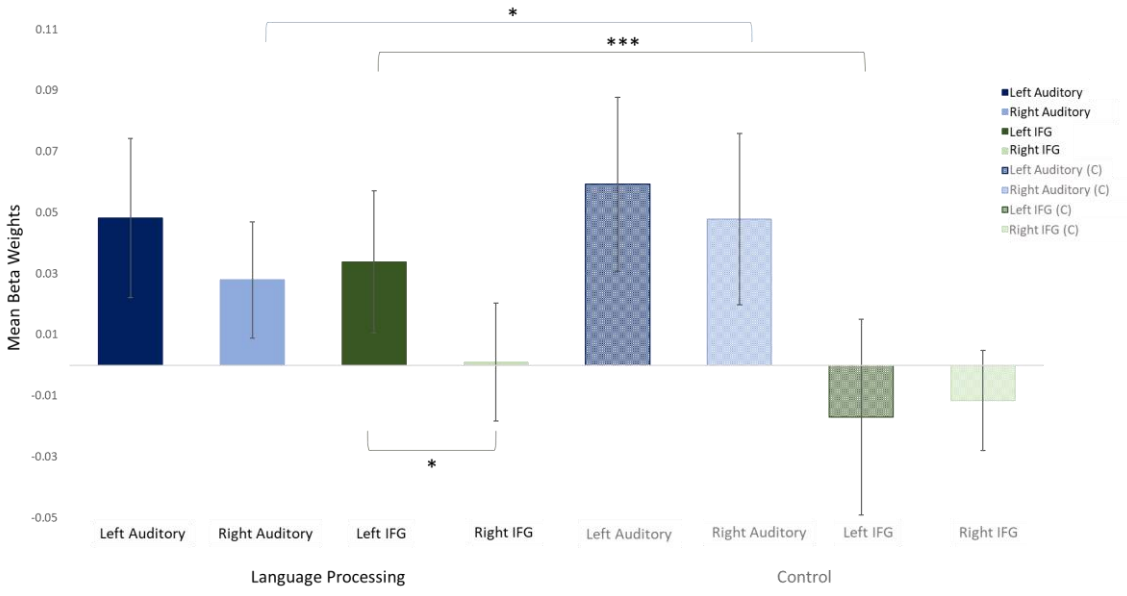


*Figure 3.6 Mean beta weights derived from each ROI for the language processing and control conditions. Dotted columns represent mean beta weights during the control condition. Error bars represent 95% confidence intervals. Not depicted the statistically significant difference between LA-RIFG in the language processing condition and the statistically significant difference between LA-LIFG, LA-RIFG, RA-LIFG, RA-RIFG in the control condition. * p<.05, ***p<.001.*

=.593) and RIFG regions (mean dif.= .013, SE = .009, df=28, p =.178) (figure 3.6).

Also worth mentioning is that in the control condition activity in the LA and RA regions was higher compared to both the LIFG and RIFG regions. (LA vs LIFG: mean dif. = .076, SE=.015, df=28, p<.001, LA vs RIFG: mean dif. =.071, SE=.013, df=28, p<.001, RA vs LIFG: mean dif. =.065, SE=.018, p=.009, RA vs RIFG: mean dif. =.059, SE=.013, df=28, p<.001). In the language condition activity over the LA and LIFG regions were higher compared to the RIFG region (LA: mean dif. =.047, SE=.015, df=28, p=.026, LIFG: mean dif. =.033, SE=.011, df=28, p=.029) (figure 3.6).

3.3.5 Task analysis

Sentence repetition

There was a statistically significant effect of ROI (F (3,84)=.10.147, p<.001, Bonferroni corrected for 3 comparisons) and condition (F(1,28)= 8.478, p= .021, Bonferroni corrected for 3 comparisons) but no interaction between the two (F(3,84)=1.945, p=.128). Activity in the RIGF was lower compared to activity in the LA (mean dif = -.071, SE = .012, df=28, p<.001), the RA (mean dif = -.066, SE = .015 df=28, p<.001) and the LIFG (mean dif = -.057, SE = .015, df=28, p=.003). Pairwise comparison showed that activity in the language processing condition was higher compared to the control condition (mean dif. =.045, SE=.016, df=28, p=.007).

Verbal Fluency

There was not a statistically significant effect of ROI (F (3,84)=.1.19, p=.319, Bonferroni corrected for 3 comparisons) and condition (F(1,28)= .297, p= .59, Bonferroni corrected for 3 comparisons). The interaction between the two was (F (3,84)=9.529, p<.001, Bonferroni corrected for 3 comparisons). Pairwise comparison showed that activity in the LIFG region was higher in the language processing condition vs the control condition (mean dif. =.064, SE=.029, df=28, p=.035). The reverse was observed in the LA and RA areas (LA: mean dif. = -.076, SE=.027, df=28, p=.008, RA: mean dif. = -.058, SE=.026, df=28, p=.032). No difference in activity between conditions was found in the RIFG region (mean dif. =.031, SE=.023, df=28, p=.197).

No differences were found between ROIs in the language processing condition. In the Control condition activity in the LA was higher compared to the LIFG and the RIFG (LA vs LIFG: mean dif. =.104, SE =.026, df=28, p=.003, LA vs RIFG: mean dif. =.082, SE =.023, df=28, p=.008).

Phonological Awareness

There was a statistically significant effect of ROI (F (3,84)=9.255, p<.001, Bonferroni corrected for 3 comparisons). Activity in the RIGF was lower compared to activity in the LA (mean dif = -.071, SE = .012, df=28, p<.001), the RA (mean dif = -.066, SE = .015 df=28, p<.001) and the LIFG (mean dif = -.057, SE = .015, df=28, p=.003). The effect of condition did not survive the correction for multiple comparisons (F (1,28)= 5.462, p= .081, Bonferroni corrected for 3 comparisons) and there was no interaction between the ROI and condition (F(3,84)=1.935, p=.13, Bonferroni corrected for 3 comparisons).

Receptive Syntax

There was not a statistically significant effect of condition (F (1,24)=1.186, p=.285, Bonferroni corrected for 3 comparisons) but the effect of ROI (F(3,84)= 3.975, p= .033, Bonferroni corrected for 3 comparisons) and the interaction between the two was statistically significant (F(3,84)=3.862, p=.036, Bonferroni corrected for 3 comparisons).

Pairwise comparison showed that activity in the RA region was higher in the control condition vs the language processing condition (mean dif. =.074, SE=.027, df=28, p=.009). No difference in activity between conditions was found in the RIFG region (mean dif. =-.020, SE=.019, df=28, p=.306), the LA region (mean dif. =-.031, SE=.025, df=28, p=.238), and the LIFG region (mean dif. =.047, SE=.039, df=28, p=.235).

No differences were found between ROIs in the language processing condition or the control condition.

Receptive Semantics

There was no statistically significant effect of ROI (F (3,84)=2.012, p=.118, Bonferroni corrected for 3 comparisons) and condition (F(1,28)= 1.154, p= .292, Bonferroni corrected for 3 comparisons) and there was no interaction between the ROI and condition (F(3,84)=1.15, p=.325, Bonferroni corrected for 3 comparisons).

3.3.6 Relationship between neural activity and age during language processing tasks

We hypothesised that age might be a predicting factor of neural activity during the language processing condition and vice versa. However, result showed that there was no interaction between ROI and age (F (3,81)=1.297, p=0.281, Bonferroni corrected for 3 comparisons). Separate regression analysis for each ROI showed no association with age (LA: R(27)=.07, p=.718, LIFG: R(27)=-.312, p=.10, RA: R(27)=-.304, p=0.109, RIFG: R(27)=-.044, p=.819).

3.3.7 Relationship between neural activity and performance during language processing tasks

We also hypothesised that performance might be a predicting factor of neural activity during the language processing condition and vice versa. However, result showed that there was no interaction between ROI and performance (F(3,81)= 2.397, p=0.074). Separate regression analysis for each ROI showed that performance and activity in the RA and the LIFG regions were associated with each other (RA: R(27)=-.534, p=.003, LIFG: R(27)=-.423, p=.022). After controlling for age, performance was still associated with activity in the RA but activity in the LIFG regions was not (RA: R(27)=-.530, p=.004, LIFG: R(27)=-.311, p=.108).

There was no association between performance and the LA and RIFG regions (LA: R(27)=.051, p=.791, RIFG: R(27)=-.137, p=.478). There was no interaction between age and performance for any ROI for any task and thus no further

analysis was conducted (figure 3.7). Detailed results for each task can be found *Appendix section 9.2.*

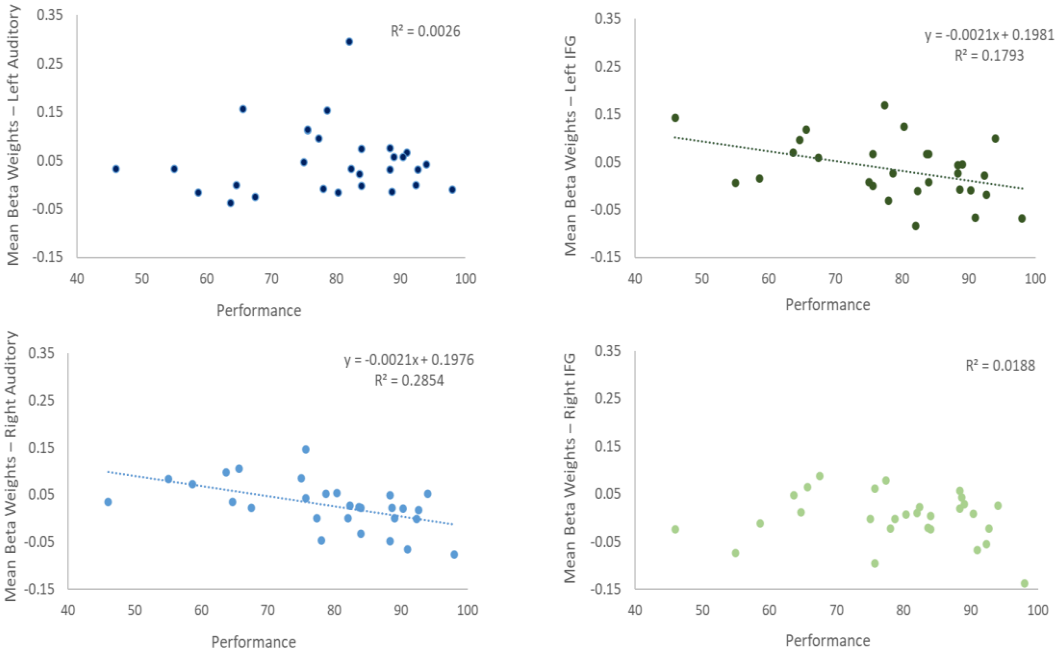


Figure 3.7 Correlation graphs between mean beta weights during the language condition and performance in each ROI. The top row of panels corresponds to activations in the left hemisphere (auditory cortex and IFG). The bottom row of panels corresponds to activations in the right hemisphere. Fit lines and equations included for the correlations that reached statistical significance.

3.3.8 Relationship between neural activity and behavioural language assessments during language processing tasks

Lastly, we explored whether neural activity, age and performance were associated with the behavioural language assessments that the participants completed. Scores were not associated with performance, age or neural activity for any ROI for the Sight Word efficiency ($F(6,28)=.472$, $p=.422$, Bonferroni corrected for 3 comparisons), Phonetic decoding efficiency ($F(6,28)=.557$, $p=.759$, Bonferroni corrected for 3 comparisons) or the General Communication Composited ($F(6,28)=.453$, $p=.438$, Bonferroni corrected for 3 comparisons). However, the model was statistically significant for the Test for Reception of Grammar - Version 2 that measures grammar comprehension

(F(6,28)=.2.85, p=.033, Bonferroni corrected for 3 comparisons). The only statistically significant coefficient was neural activity over the right auditory regions (p=.002) and that relationship remained significant after controlling for age and performance (R(27)=-.520, p=.005) (figure 3.8).

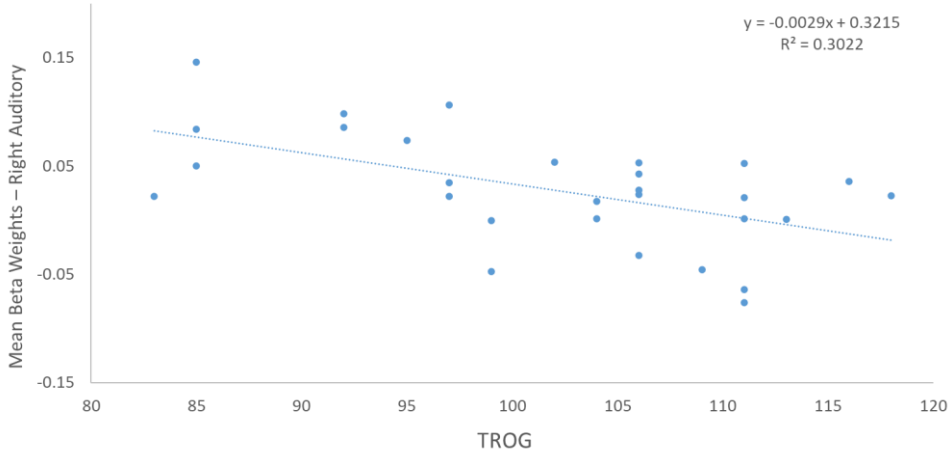


Figure 3.8 Correlation graph between mean beta weights during the language condition and scores in the Test for Reception of Grammar - Version 2 in the right auditory cortex.

3.4 Discussion

In the present study we aimed to investigate the maturation of language processing from late childhood to adolescence as a function of age and performance using fNIRS. Our results showed that haemodynamic activity in response to language processing in the right auditory depends on performance but not age. Better performers showed decreased activations in right auditory regions irrespective of age. This finding suggests that cerebral specialisation in the left auditory regions for language processing could potentially already be established by late childhood and suggests that increased activity in right auditory regions could be indicative of language processing difficulties. Our results suggest that during late childhood, language processing becomes predominantly localized in the left temporal regions, while the right temporal regions become active based on task demands. Additionally, the left IFG appears to continue to undergo developmental changes throughout late childhood and adolescence.

As discussed in the introduction, a shift in activation with increased age is observed from frontal regions, associated with higher level processing, to more posterior regions, associated with lower-level processing, and indicates an automation in skills (Weiss-Croft and Baldeweg 2015, Gaudet et al. 2020). Our results indicate that this shift is established prior to 6-7 years old as we found no association between age and neural responses in our sample. However, no differences were observed between activations within the left hemisphere. This perhaps means that intrahemispheric specialisation to more

posterior regions of the left hemisphere is still developing throughout late childhood and adolescence.

The left IGF is typically associated with higher level conceptual processing and executive functioning and is recruited as a result of increased cognitive demands (Binder et al. 2009, Taylor et al. 2013). Thus, that could potentially explain the negative relationship between left frontal neural activations and performance in our study; participants who performed worse, found the tasks more challenging and recruited their left IFG more to complete the tasks. However, controlling for age mitigated that relationship, potentially because of the strong positive correlation between age and task performance. This finding could also indicate that the left IFG is still undergoing age-related specialisation across late childhood and adolescence hence the impact of age and is in line with findings suggesting that frontal regions mature later compared to more temporal regions (Turkeltaub et al. 2003, Shalom and Poeppel 2008, Berl et al. 2014, Skeide and Friederici 2016, Weiss et al. 2018). We can speculate that in adults age would not impact the relationship between performance and left IFG activity.

On the other hand, activity in the right auditory cortex was associated with performance regardless of age. RA regions were engaged more in language processing when participants struggled more with the tasks and that relationship was not affected by the age of the participant. This finding suggests that interhemispheric lateralisation of temporal areas is established by late childhood and resembles adult-like patterns of activation for language

processing (Rysop et al. 2022). This conclusion is corroborated by the strong negative correlation between RA neural activity and grammar comprehension, as measured by the Test for Reception of Grammar - Version 2, after controlling for both age and performance. This is particularly important when considering that to date very few investigations have explored the relationship between brain activations and objective language skills measured by standardised language assessments (Bartha-Doering et al. 2018, Gaudet et al. 2020). This indicates that RA activity might be a suitable neural marker for linguistic proficiency in school aged-children and adolescents. That can be particularly relevant when exploring the neural underpinnings of language processing in clinical populations with language deficiencies.

It is worth mentioning that during the language processing condition, the overall left hemispheric lateralisation observed is in line with previous findings that have reported that language lateralisation in the left hemisphere is present very early in life. However, in our sample activity over the left auditory region was not significantly higher compared to the right auditory regions. That could be due to the stimuli used in the language processing condition. To begin with, all stimuli (except for the verbal fluency task) involved processing of auditory speech and imaging literature from both adults as well as school-aged children show that processing of speech acoustic engages mainly temporal areas in both hemispheres (Hickok and Poeppel 2007, Peelle 2012, Price 2012, Mushtaq et al. 2019). Additionally, most stimuli included phonological as well as semantic processing. Previous literature has shown bilateral temporal activations in typically developed school-aged

children in response to semantic processing (Chou et al. 2006, Yeatman et al. 2010, Bartha-Doering et al. 2018).

Methodological considerations

One major limitation of previous language investigations was the lack of an appropriate higher level control condition to isolate language specific activity (Weiss-Croft and Baldeweg 2015). In this study we tried to overcome this by using time-reversed speech to account for the non-linguistic properties of speech. Time-reversed speech has similar acoustic and phonetic complexity to the original speech; harmonic complexity, spectro-temporal variations and many phonetic features are retained. We also used a control mouse clicking task and a number articulation task, which included overt repetition of the numbers “1” and “3” (Richardson et al. 2010), where appropriate, to account for the response elements of each task. Comparisons between the brain responses during the language tasks differed significantly compared to brain responses during the control condition in the left IFG and right auditory cortex. That confirms the validity of using a more complex control condition rather than rest to distinguish between language processing and neural responses to the non-linguistic cognitive demands. The lack of difference in the left auditory region might be due to the nature of the time-reversed speech stimulus. Even though, it can be used as a control in terms of the spectro-temporal content of the stimulus, it is neither a speech nor a non-speech stimulus. As a result, listeners could have recognised the stimulus as speech played backwards and tried hard to understand it, explaining the brain activations in left and right auditory regions observed in the control condition.

Our results in the left auditory region are in agreement with a previous study from our laboratory by Mushtaq and colleagues who found that neither time-reserved speech nor signal correlated noise appear to be suitable auditory controls for isolating speech-specific processing using fNIRS (Mushtaq et al. 2019). Another methodological strength of our study was the use of overt expressive language tasks as we were not limited by concerns regarding in-scanner movement contaminating our data (Quaresima et al. 2012, Zhang et al. 2017). That allowed us not only to accurately measure task performance but to also include sentence-level expressive language.

Additionally, the left lateralisation of neural activity in the left IFG, indicates that the chosen language tasks were sufficiently demanding to elicit robust activations in that region. This is important given that all participants completed the same tasks and task difficulty was adjusted to be suitable for both the younger and older participants.

Unfortunately, we were not able to draw any conclusions regarding specific maturational changes and influence of task demands when examining each task separately for different language functions. However, averaging neural responses across all language tasks offers us the opportunity to look at language processing using a more holistic approach. This has high ecological validity and is crucial to understanding language difficulties in populations where deficiencies are not confined in one linguistic domain (e.g. phonological processing) but co-occur, such as developmental language disorder (DLD) (Bishop et al. 2017). DLD is characterised by a constellation of language

problems ranging from phonological to syntactic deficits. To date little is known about the brain basis of this atypical language development, however, given its complex phenotype the answer is not likely to lie only in one linguistic domain (Liégeois et al. 2014).

Limitations and Future directions

In this investigation a cross sectional study design was used to examine developmental patterns of language from late childhood to adolescence with a relatively small sample size. However, unlike the maturational changes in infancy and early childhood, developmental trajectories in childhood and adolescence occur over longer timescales and are characterised by high inter-individual variability (Parviainen et al. 2011, Hoff et al. 2013, Irimia et al. 2014, Brown 2017). Thus, collecting longitudinal data from a larger sample of participants would enable us to define more precisely the trajectory of language development and validate some of the results presented here. Furthermore, other than task type and task demands other factors could also be influencing maturational changes of the language network such as maternal education and maternal depression. In our sample socioeconomic status and maternal factors did not vary significantly, thus we do think that they affected our findings, but future investigations should aim to recruit participants from a wider range of socioeconomic backgrounds and take that into consideration when analysing their data (Conant et al. 2017, Younger et al. 2019, Farah et al. 2021). Additionally, our neuroimaging data were limited by the relatively modest spatial resolution (on the order of 1.0-1.5cm) of the fNIRS technology and the lack of measurements beyond the outer cortex

(Quaresima et al. 2012). Furthermore, even though the fNIRS data were pre-processed to account for systemic physiological interference, it is important to consider that the possibility that breathing in relation to speech could cause fNIRS artefacts (Tachtsidis and Scholkmann 2016). In the present study the risk of that was minimised by including a high-level baseline that mimicked the breathing demands of the language task. However, ongoing advancements in fNIRS technology such as the use of multi-distance channel set ups that can improve fNIRS' low signal to noise ratio regress out influences from the extracerebral layer (Phan et al. 2016) (Tachtsidis and Scholkmann 2016) as well as the use of high density diffuse optical topography (HD-DOT) (Wheelock et al. 2019, Borjkhani and Setarehdan 2020, Liu et al. 2020) that can provide greater spatial sensitivity are very promising avenues for future investigations. Lastly, it is important to acknowledge that even though differences in head size could influence optode placement and consequently the recorded fNIRS responses (Whiteman et al. 2018), previous investigation from our lab with similar samples have not found head circumference to be a confounding factor.

3.5 Summary

To conclude, we explored maturational changes and effects of task demands on neural patterns of language processing from late childhood to adolescence. Our findings indicate that language processing is left lateralised in temporal regions by late-childhood and the right temporal regions are recruited as a function of task performance. The left IFG is still undergoing maturational changes throughout late childhood and adolescence. Future studies with

larger sample sizes are required to further strengthen this conclusion. Our results provide some insights into the changes the language network undergoes from late childhood to adolescence in typically developed children and may lay the groundwork for future investigations of language disorders in this age range.

4 Sentence repetition in TD and DLD

4.1 Chapter Overview

In this study we aimed to use sentence repetition to study neural markers of language processing in children and adolescents with and without DLD. As described in section 2.2.1.5, the ability to repeat words or sentences has extensive clinical applications as a diagnostic, prognostic and rehabilitation tool (Hosomi et al. 2009, Schlaug et al. 2009, Kempler and Goral 2011, Ramanan et al. 2020). Investigations particularly in the field of aphasia have used sentence repetition to study neural markers of stroke and brain trauma in the language network (Macoir et al. 2021). Sentence repetition is also being used routinely as a behavioural diagnostic marker for DLD (Pham and Ebert 2020). Thus, we want to explore the neural signature of sentence repetition in typically developed children as well as children with DLD to potentially uncover neural markers of DLD that could be used for the diagnosis, prognosis and intervention pathways. The purpose of this study was two-fold; firstly, to describe the neural network supporting sentence repetition in typical development and DLD and secondly to determine if sentence repetition can be used to identify atypical neural activity in children with DLD compared to typically developed children.

We used fNIRS to record neural activations in areas conventionally assumed to be recruited during sentence repetition; namely bilateral regions covering the auditory cortices and the inferior frontal cortices. fNIRS is particularly suited for this study as it allows for overt sentence repetition. Covert language processing not only activates different neural pathways but also makes it

challenging to measure task compliance and performance (Shuster and Lemieux 2005, Pei et al. 2011).

Participants also completed a non-verbal n-back working memory (NVWM) task to help us isolate neural activations as a result of working memory demands. NVWM does plays a role in processing linguistic stimuli, but there is no indication that it is causal factor in DLD. Behavioural findings are mixed with some studies reporting NVWM deficits in children with DLD (Bavin et al. 2005, Im-Bolter et al. 2006, Marton 2008, Henry et al. 2012, Vugs et al. 2014) while others do not (Archibald and Gathercole 2006, Archibald and Gathercole 2007, {Ellis Weismer, 2017 #24, Ellis Weismer et al. 2017). Thus, we also investigated neural patterns of non-verbal working memory in children with DLD to shed light in the ongoing debate regarding the role of non-verbal working memory in DLD.

We hypothesised that children with DLD would show deficits in sentence repetition but not in NVWM compared to typically developed children. Based on the findings of our previous investigation on language processing in children and adolescents we predicted that both groups would show greater activation in right temporal regions as a function of performance, but that activations in that region would be greater in magnitude for the DLD group. Given the previously reported sentence repetition deficits in children with DLD, we hypothesized that we would observe reduced left-hemispheric lateralisation and more widespread activations, including in the right inferior frontal regions in children with DLD compared to children with TD. Lastly, we

anticipated that both groups would show greater activations in frontal regions compared to temporal regions in the NVWM task and that activity would not differ between the two groups after controlling for age and performance.

4.2 Methods

4.2.1 Participants

Five typically developed children (1 male, mean age=13.12 years, SD=.073) and one child with DLD (female, age = 6.9 years) between the ages of 6 and 15 years 11 months participated in the study. Typically developed participants were recruited though physical and online advertisement posters in schools, community spaces and social media. Children with DLD were recruited through the same channels as TD participants but also through targeted emails to all the private speech and language practitioners in the Nottinghamshire area, and to the Special Educational Needs Coordinators of primary and secondary schools. Additionally, parent support groups and charity organisations shared the study through their newsletters and social media accounts. Lastly, participants with DLD were identified through the Nottinghamshire Healthcare and the Derbyshire Community Health Services NHS Foundation Trusts.

The initial recruitment target of 25 participants per group was not reached due to a halt of research activity during the Covid-19 pandemic as described in section 2.5. Please see section 3.2.1 for a justification on the target sample size.

All participants were native English speakers with normal or corrected-to-normal vision, no known hearing problems, and no history of cognitive or motor impairment. They also passed a pure tone audiometry air-conduction hearing screen performed at 20 dB HL at 0.5, 1, 2, and 4 kHz in both ears (procedure adapted from (BSA 2018)). All participants completed the standardised cognitive and language tests described in section 3.2. Reported scores are scaled standard scores derived using the normative datasets provided in each assessment's handbook (mean 100 ± 15) (table 4.1). The typically developed children scored within the normal range and were considered to have typical language and cognitive abilities. The child with DLD scored below 58 at the CCC-2 assessment and at least 2 SD units below standard scores for the TROG assessment confirming their DLD diagnosis. Hand preference was assessed using the abbreviated Edinburgh Handedness Inventory (Oldfield 1971). All participants were right-handed except for one in the TD group (handedness was entered as a between subjects' factor in the analysis but no effects were identified thus no further results are reported). Each participant gave verbal assent, and written informed consent was obtained from the accompanying parents or guardians.

The study was approved by the Nottingham Research Ethics Committee and sponsored by the University of Nottingham Faculty of Medicine and Health Sciences Research Ethics Committee (ref no: 269962).

TD		
N (male)	5(1)	
	Mean	*SD*
Age	13.12	.073
Cognitive Measures		
Performance IQ[a]	96.00	5.19
Estimate of general cognitive ability[a]	103.20	6.04
Grammar Comprehension[b]	100.40	7.03
Reading Ability[c]	98.2	4.62
General Communication Composite[d]	74.00	5.41
DLD		
N (male)	1(0)	
	Value	
Age	6.92	
Cognitive Measures		
Performance IQ[a]	85	
Estimate of general cognitive ability[a]	70	
Grammar Comprehension[b]	76	
Reading Ability[c]	120	
General Communication Composite[d]	13.00	

Table 4.1 Age characteristics of the sample and group means and standard deviations scores for the standardised language and behavioural measures. Scores are standard scores (mean 100 ± 15) except for the general Communication Composite where scores greater than 58 are considered normal.

[a]Wechsler Abbreviated Scale of Intelligence – 2nd Edition, [b]The Test for Reception of Grammar - Version 2, [c] The Test of Word Reading Efficiency – 2nd Edition, [d]The Children's Communication Checklist - 2nd Edition.

4.2.2 Procedure

After obtaining informed consent from the participants and their parents/guardians and completing the behavioural assessments, participants completed the computer tasks while their brain activity was recorded using fNIRS. During the fNIRS measurements participants were seated comfortably in a sound-attenuated room with dimmed lighting, approximately 80cm from a visual display unit and a Genelec 8030A loudspeaker mounted above the display. Both the task and block order were pseudorandomised for each

participant. Each block had a 17-23s duration (depending on the specific task) and was followed by a rest period of passive cross fixation with random duration in the range 17-23s. The fNIRS imaging lasted approximately 40 minutes and was repeated twice (20 minutes per run).

4.2.3 Equipment

The laboratory set up and equipment were identical to the on described in section 3.2.4. Briefly, brain activity was measured using a continuous wave Hitachi ETG-4000 fNIRS system bilaterally over the IFG and the auditory cortices with two 3x5 arrays. ROIs were predefined based on previous research conducted by our laboratory and visual inspection of the digitisation measurements obtained from a sample of 12 children.

4.2.4 Stimuli

The sentence repetition condition was accompanied by a control condition as described in section 3.2.5. To summarise participants were asked to listen to a time-reversed sentence and read aloud the digits “1” and “3”. The period of presentation was equal to the response period of the corresponding sentence.

Sentence Repetition

In a block design, participants were presented with 40 sentence stimuli that were between 10 and 14 words long. Shorter sentences were not used as they might not allow for investigations of the language system. If the sentence length is short enough to be within their memory capacity, participants are able to imitate a sentence perfectly without utilizing their linguistic knowledge (Slobin and Welsh 1967, Wiig et al. 2013). Sentences were adapted from the

Sentence Repetition subtest of the Clinical Evaluation of Language Fundamentals- Fifth Edition (CELF-5) standardised language assessment. The CELF is standardised for ages 5 to 21 years old and is widely used in paediatric research and clinical settings for the diagnosis of language impairments. Therefore, the sentence stimuli used in this task contained appropriate vocabulary for our study population (Wiig et al. 2013).

Participants completed two runs of the task. Each run comprised of 20 sentences split into 10 blocks. During each block, participants listened to two sentences each lasting approximately 4 seconds and were then given an additional 5 seconds to repeat it aloud as accurately as they could. While listening to the stimulus, participants focused on a black cross in the middle of computer screen. When the cross turns white they were prompted to repeat the sentence. The background colour of the screen was grey for all conditions and tasks. Trials were separated by an interval rest period of approximately 2 seconds to ensure participants had stopped talking before the start of the next trial. Each block lasted approximately 20 seconds and blocks were separated from each other by a 20-second resting period.

Working memory

In a block design, participants were presented with 40 shapes during a visual N-back task. In line with Ellis Weismer et al. (2017) abstract shapes were used to limit the use of verbal mediation or rehearsal strategies (Ellis Weismer et al. 2017). The N-task was split into two difficulty levels to minimise the risk of ceiling or floor effects. On the easier version participants were asked to assess

whether the shape on the screen matched the shape that appeared on the screen immediately before (1-back). On the harder version they were asked to assess whether the shape on the screen matched the shape that appeared on the screen one trial before (2-back).

Participants completed two runs of the task comprised by 40 trials split into 4 blocks. During each block, participants were presented with an instruction indicating whether the block is 1-back or 2-back. Block presentation was randomised across participants. Each stimulus was presented for 1.5 seconds, with an inter-stimulus interval of 0.5 seconds. During stimulus presentation children had to press a green button if the shape matched the shape immediately presented before or one trial before (depending on the block) or a red button if it did not. Each block lasted approximately 20 seconds and blocks were separated from each other by a 20-second resting period. While at rest participants looked silently at a black centrally placed cross.

4.2.5 FNIRS Data

fNIRS analysis was conducted in an identical manner to the one described in section 3.2.6. To summarise, it was conducted with custom scripts developed in our laboratory (Wijayasiri et al. 2017, Anderson et al. 2019, Mushtaq et al. 2019, Lawrence et al. 2021), along with functions provided by the Homer2 package using MATLAB. The pre-processing process included the application of algorithms that accounted for movement artefacts, poor optode-scalp contact and interfering signals from cardiac and respiratory oscillations. The modified Beer-Lambert Law was then applied to convert the optical density to estimated changes in HbO and HbR concentrations with a differential path-

length factor of 6 (Huppert et al. 2009). The separation algorithm (HMS) was applied to isolate the functional component of the haemodynamic signal, suppress physiological interferences, and detect cortical activations (Yamada et al. 2012, Wiggins et al. 2016, Wijayasiri et al. 2017, Lawrence et al. 2018). Response amplitude was quantified using the GLM and the beta estimates of the HMS signal (mean beta weights) were used in the subsequent analysis (Wiggins et al. 2016, Lawrence et al. 2018).

These beta weights were used to quantify the amplitude of cortical activation for the sentence repetition condition vs rest, the sentence repetition vs the control condition and the NVWM condition vs rest. The false discovery rate (FDR) method was applied across channels in all fNIRS analyses to correct for multiple comparisons (Benjamini and Hochberg 1995).

4.2.6 Statistical analysis

A mixed measures ANOVA was performed to explore the effects of region, hemisphere, condition, on mean beta weights. The within-subject factors were hemisphere (left, right), region (frontal, temporal) and condition (language vs control, 1-back vs 2-back). Bonferroni correction for multiple comparisons and Greenhouse–Geiser adjustments for violation of sphericity were performed (corrected p values are reported).

In addition, to explore the relationship between age, performance and hemodynamic changes responses, age and performance were added as covariates in the linear models. Additionally, correlation and regression analyses were conducted. The Bonferroni correction was applied to all

comparisons and correlations to counteract the problem of multiple comparisons and statistical significance was set at $p < 0.05$.

4.3 Results

4.3.1 Behavioural results

All participants completed the computer-administered language tasks successfully. Details for each task separately are presented in table 4.2. Age was positively correlated with average performance in the sentence repetition task and the NVWM 1-Back and moderately correlated with performance in the NVWM 2-Back task, however, none of the relationships were statistically significant (Sentence Repetition: R(3)=.667, p=.219, NVWM 1-back: R(3)=.783, p=.118, NVWM 2-Back: R(3)=.300, p=.624). Additionally, there was not a statistically significant difference between performance in the 1-back and 2 -back tasks (mean dif: 14.17, SE: 5.53, df=4, p=.062). The DLD participant scored lower in all tasks compared to the TD group. In the sentence repetition task, the participant attempted to repeat the stimuli demonstrating comprehension of task demands but based on the grading methods the participant received a score of 0.

TD

Task	*Mean*	*SD*
Sentence Repetition (%)	75.00	6.47
NVWM 1-Back (%)	90.00	7.29
NVWM 2-Back (%)	75.83	8.98

DLD

Task	*Score*
Sentence Repetition (%)	0
NVWM 1-Back (%)	41.67
NVWM 2-Back (%)	8.33

Table 4.2 Performance in each task for each group. Reported means are derived from the conversion of scores to percentages.

4.3.2 fNIRS results

To confirm that successful fNIRS measurements were taken, haemodynamic activity over the preselected ROIs was contrasted against silence for each task and each condition using one-sample t-tests. These comparisons could not be performed in the DLD group due to the small sample size; therefore, the results below refer to the TD group alone.

During the sentence repetition task activity was significantly higher than 0 over the right IFG (t_4 = 6.674, p= .012) and left IFG (t_4 = 2.289, p=0.042) but the later did not survive correction for multiple comparisons (p=.168). Activity was not different than 0 over the left (t_4 = -.758, p= 0.245) and right (t_4 = -1.902, p=0.065) auditory cortices.

During the control condition of the sentence repetition task activity was significantly higher than 0 over the right IFG (t_4 = 2.984, p= .04) and significantly below 0 over the left auditory cortex (t_4 = -5.044, p=.016). There were no differences in activity over the left IFG (t_4 =.824, p=.228) and the right auditory cortex (t_4 =1.187, p=.150).

During the NVWM 1-back task, activity was not significantly different than 0 over any ROI (LA: t_4 = .815, p= .23, RA: t4 = -.906, p= .208, left IFG: t_4 =.828, p= .227, right IFG: t_4 = -1.458, p= .109). During the NVWM 2-Back task activity was significantly lower than 0 over the left (t_4 = -3.671, p= .044) and right (t_4 = -3.862, p= .036) IFG but not over the left (t_4 = -1.458, p= 0.109) and right (t_4 = 1.856, p=0.069) auditory cortices.

Plots of the block-averaged time course of haemoglobin concentration change for the sentence repetition and working memory conditions for the TD and DLD groups for each of the four ROIs are presented in figure 4.1, 4.2 and 4.3 respectively.

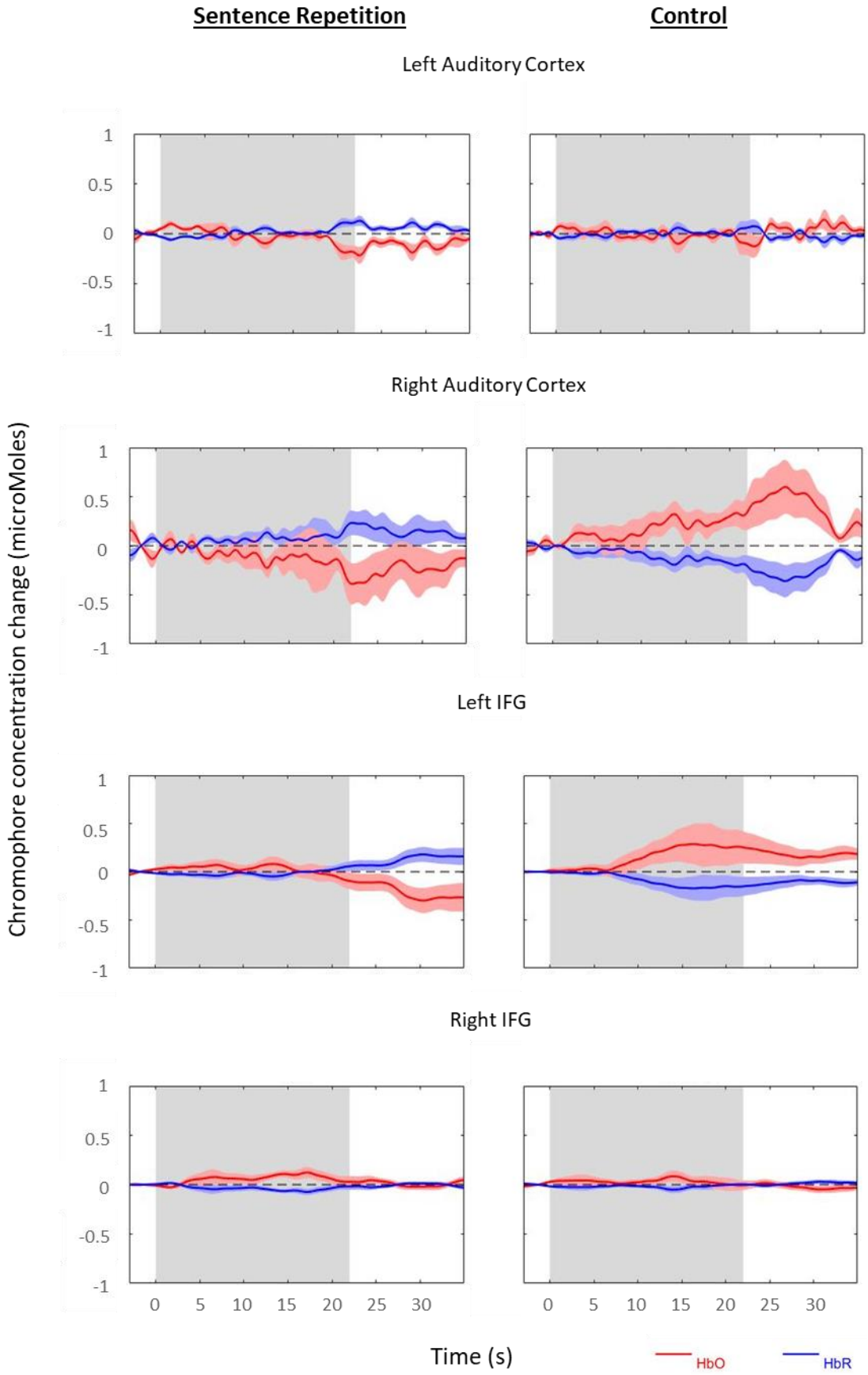


Figure 4.1 Block-averaged haemodynamic time courses. These are displayed for the sentence repetition (left panel) and control conditions (right panel) for each of the 4 ROIs. The shaded grey areas indicate the stimulation period (0s to ≈22s).

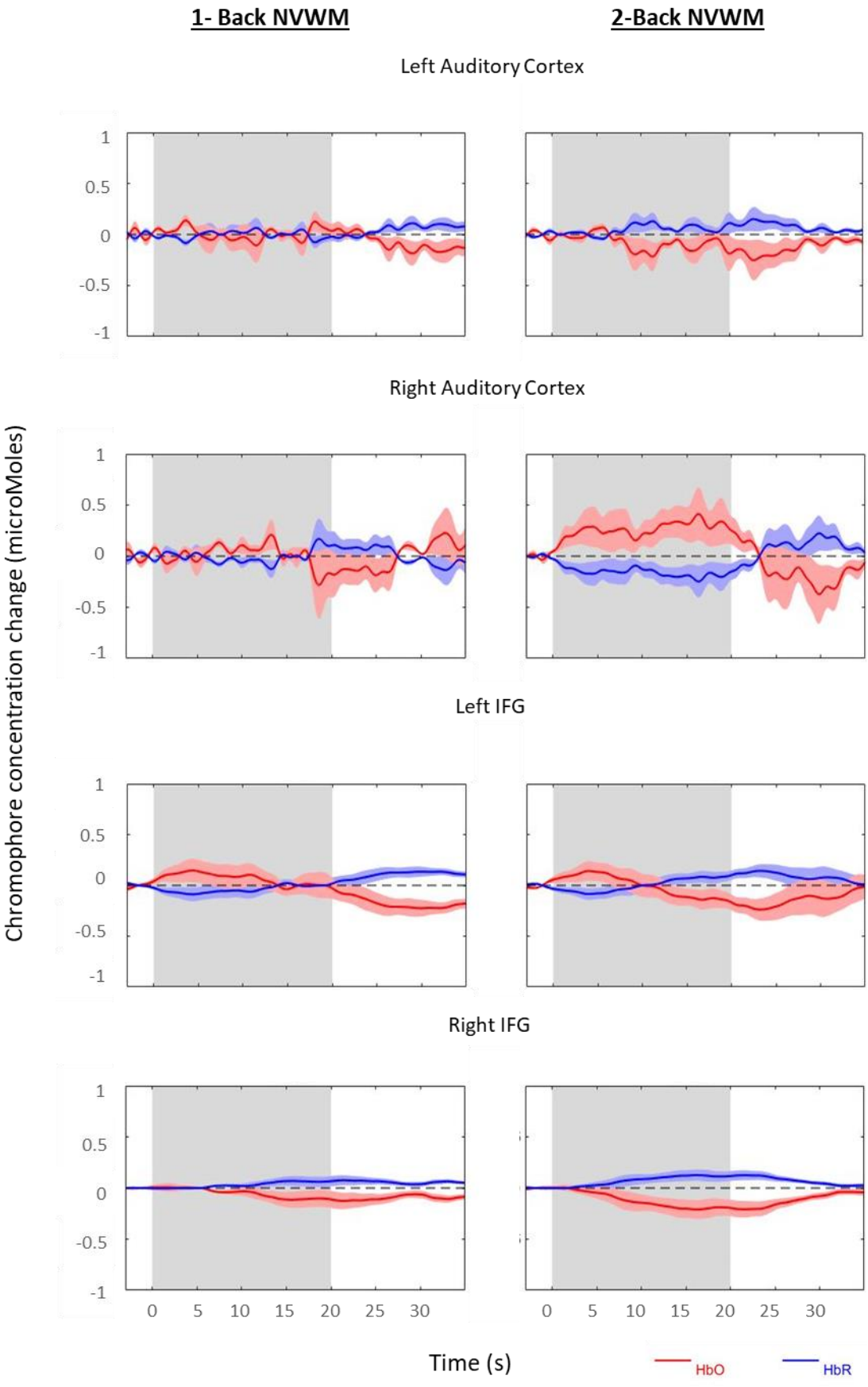


Figure 4.2 Block-averaged haemodynamic time courses. These are displayed for the 1-back NVWM (left panel) and 2-back NVWM (right panel) for each of the 4 ROIs. The shaded grey areas indicate the stimulation period (0s to ≈20s).

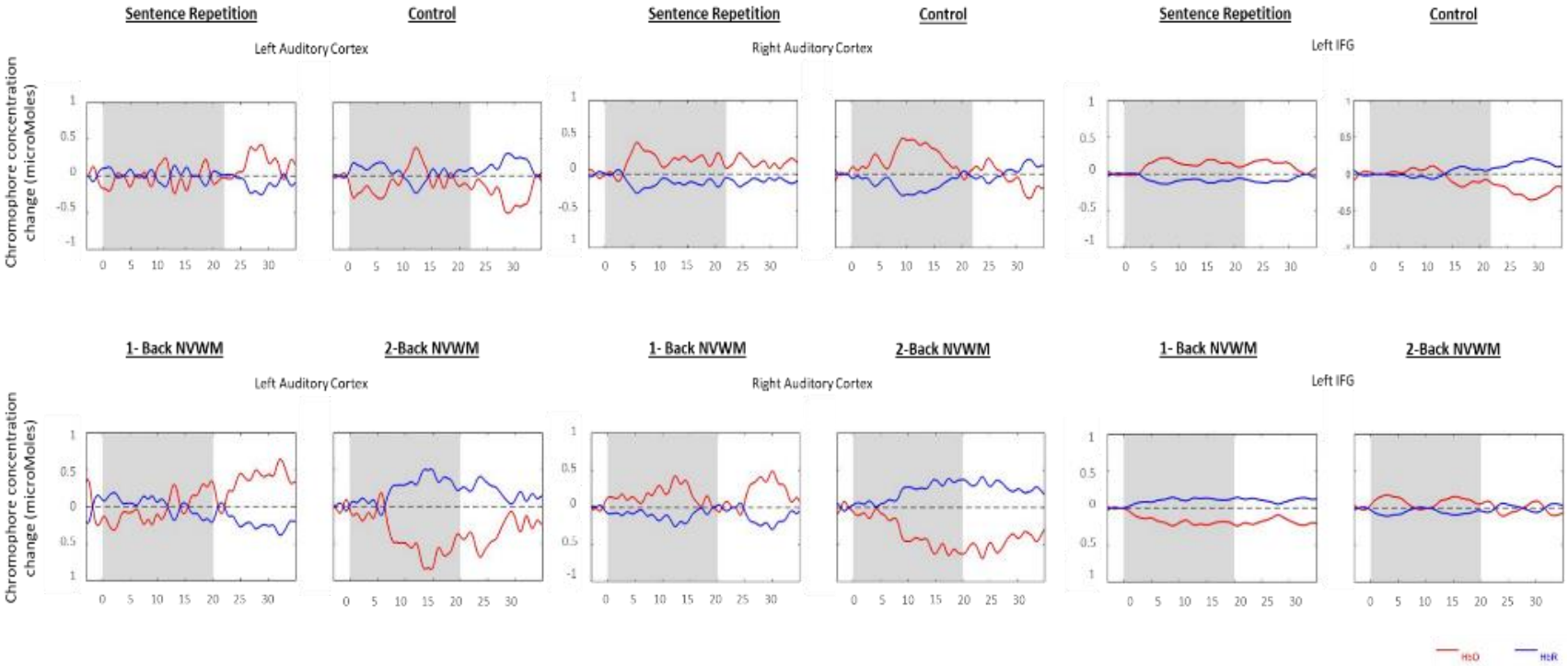


Figure 4.3 Block-averaged haemodynamic time courses. These are displayed for the sentence repetition task (top panels) and the NVWM task (bottom panels) for 3 of the ROIs. Due to missing data, no time-courses could be produced for the right IFG in either task. The shaded grey areas indicate the stimulation period (0s to ≈20s).

4.3.3 Effects of region, hemisphere and condition per task

Two separate RM-ANOVAs were performed using the mean beta weights to examine the effects of i) region (auditory vs frontal), ii) hemisphere (left vs right) and iii) condition in the sentence repetition (language processing vs silence) and the NVWM tasks (1-back vs 2-back). Some main effects and interactions were statistically significant prior to applying statistical corrections but none survived statistical corrections.

Namely, in the sentence repetition condition, there was a statistically significant effect of region ($F(1,4) = 18.421$, $p = .013$, effect size: .822, Bonferroni corrected for 7 comparisons) with increased activation in the frontal regions over the auditory cortices (mean dif. = .084, SE =.020, df=3, $p = .013$). Even though the interaction effect between condition and region did not meet the threshold for statistical significance ($F(1,4)= 7.270$, $p=.054$, effect size: 645, Bonferroni corrected for 7 comparisons), the post hoc comparison showed that that was mainly driven by increased activity in frontal regions in the active condition (SR: frontal vs auditory mean dif. = .16, SE =.045, df=3, $p = .025$, control frontal vs auditory mean dif. = .009, SE =.016, df=3, $p = .603$) (figure 4.4).

There was no effect of condition ($F(1,4)= .301$, $p=.612$, Bonferroni corrected for 7 comparisons) and hemisphere ($F(1,4)= .000$, $p=.997$, Bonferroni corrected for 7 comparisons) and there were no interactions between region and hemisphere ($F(1,4)= .648$, $p=.466$, Bonferroni corrected for 7 comparisons), hemisphere and condition ($F(1,4)= 3.432$, $p=.138$, Bonferroni

corrected for 7 comparisons) or region, hemisphere and condition (F(1,4)= 1.375, p=.306, Bonferroni corrected for 7 comparisons) (figure 4.4).

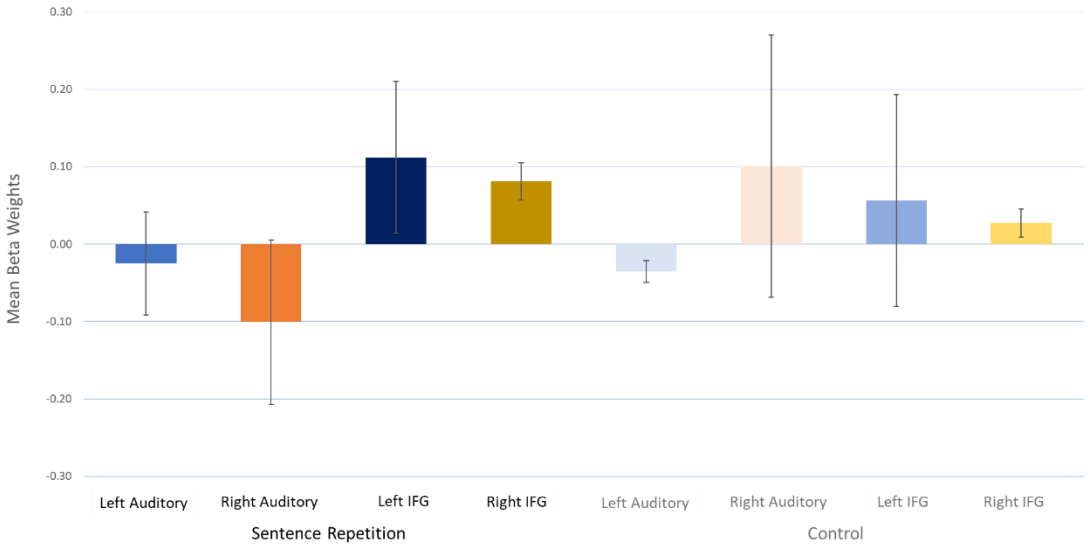


Figure 4.4 Mean beta weights derived from each ROI for the sentence repetition and control conditions. Faded columns represent mean beta weights during the control condition. Note that no statistically significant differences were found. Error bars represent 95% confidence intervals.

In the NVWM back task there were no significant main effects (condition: F(1,4)= .553, p=.498, , Bonferroni corrected for 7 comparisons, region: F(1,4)= 2.627, p=.180, Bonferroni corrected for 7 comparisons, hemisphere: F(1,4)= 005, p=.945, Bonferroni corrected for 7 comparisons). There was a statistically significant interaction between region and hemisphere (F(1,4)= 17.819, p=.013, effect size: .817, Bonferroni corrected for 7 comparisons), driven by greater activation in the RA compared to the right IFG (mean dif. = .127, SE =.017, df=3, p = .002). There were no differences in the left hemisphere (mean dif. = -.024, SE =.048, df=3, p = .650). There were no other interaction effects that reached statistical significance; condition & region: F(1,4)= 5.857, p=.073,

Bonferroni corrected for 7 comparisons, Condition & hemisphere: F(1,4)= 4.362, p=.105, Bonferroni corrected for 7 comparisons, condition, region and hemisphere: F(1,4)= 3.590, p=.131, Bonferroni corrected for 7 comparisons) (figure 4.5).

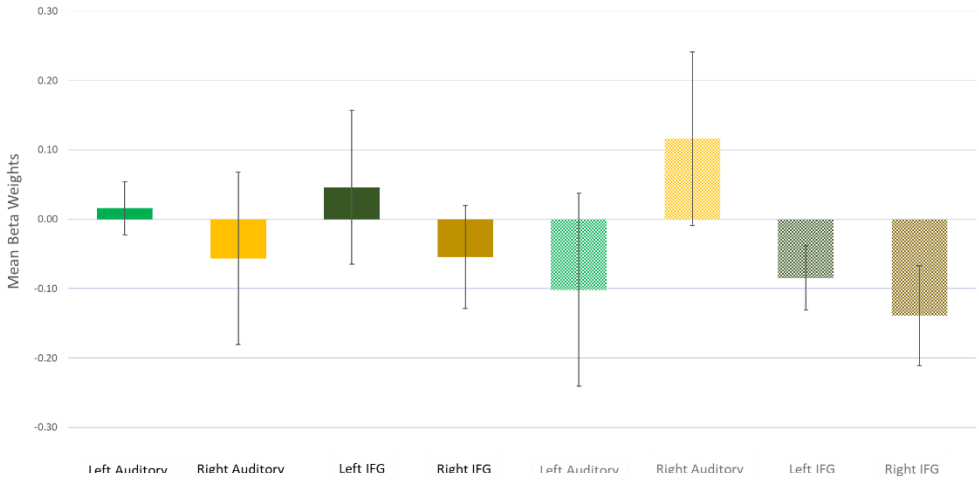


Figure 4.5 Mean beta weights derived from each ROI for the 1-back and 2-back NVWM tasks. Dotted faded columns represent mean beta weights during the 2-back NVWM. Note that no statistically significant differences were found. Error bars represent 95% confidence intervals.

Due the small sample size in the DLD group (N=1), it was not possible to conduct a formal statistical analysis. Figure 4.6 below depicts the cortical activations recorded in the DLD group (figure 4.6).

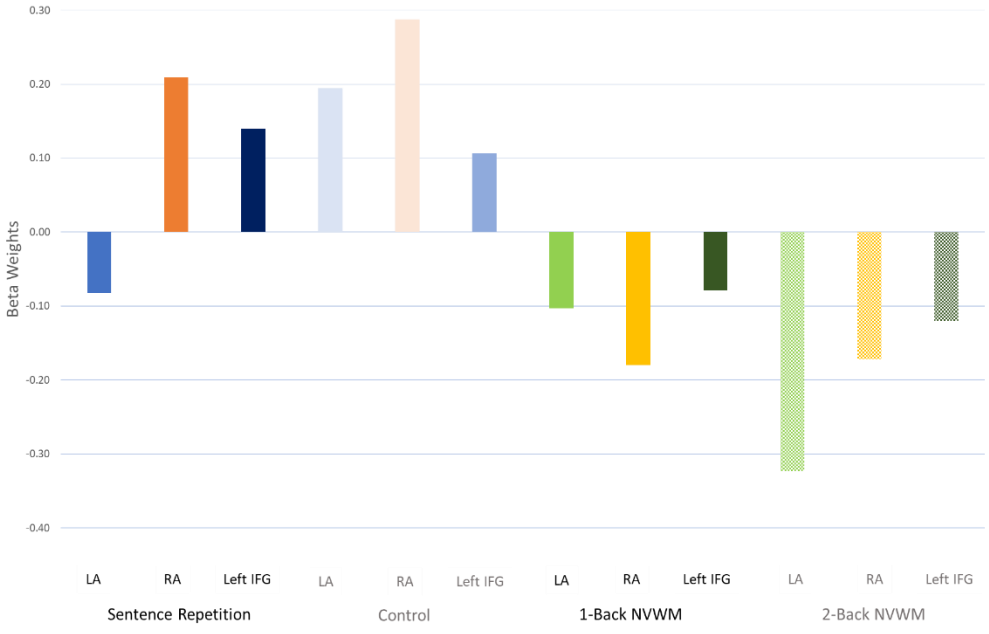


Figure 4.6 Beta weights derived from each ROI (except the right IFG) for the sentence repetition (blue and orange) and NVWM tasks (green and yellow). Faded columns represent the control condition of the sentence repetition task and the 2-back NVWM task. Beta weights during the control condition.

4.3.4 Relationship between neural activity, age and task performance

To explore the relationship between neural activity and age and task performance we included age and performance as covariates in three separate linear models. However, neither age nor performance seemed to covary with neural activity. (2-back: age: F(3,6)=.339, p=.707, Bonferroni corrected for 2 comparisons, performance: F(3,6)=.092, p=.961, Bonferroni corrected for 2 comparisons, back1: age: F(3,6)=2.085, p=.204, Bonferroni corrected for 2 comparisons, performance: F(3,6)=.926, p=.484, Bonferroni corrected for 2 comparisons, SR age: F(3,6)=.545, p=.670, Bonferroni corrected for 2 comparisons, performance: F(3,6)=1.785, p=.250, Bonferroni corrected for 2 comparisons).

4.3.5 Relationship between neural activity and performance during behavioural assessments

Because the sample size was too small it was not possible to explore whether neural activity was a predictor of task performance or performance in the behavioural assessments. Thus, instead, we ran a partial correlation analysis controlling for age.

During the sentence repetition task neural activity was only correlated between the sight word efficiency and activity in the left auditory cortex (R(2)=-.970, p=.024, Bonferroni corrected for 3 comparisons), however after controlling for age that relationship no longer held (R(2)=-.982, p=.072). Activity over the left IFG was correlated to TROG scores after controlling for age but that relationship did not survive statistical correction (R(2) = .957, $p_{uncorrected}$= .043). To further explore these two findings, we run two linear regression models, one for SWE with age and LA activity as predictors and one

with age and LF activity as predictors for TROG. It is worth mentioning, that due to the small sample size it was difficult to determine whether assumptions of linear regression analysis were met. Visual inspection of the histogram and p-p plot of residuals suggested no notable violation of the assumption of normal distribution of the residuals. A plot of standardised residuals versus standardised predicted values was generated but with only five data points the assumption of homoscedasticity could not be suitably assessed. LF activity during SR and age accounted for 94.2% of the observed variability in TROG (R^2= .942), with an adjusted R^2 of .884. The model however did not reach statistical significance (F (2,4)=16.264, p= .058). LA activity during SR and age accounted for 96.4% of the observed variability in SWE outcomes (R^2= .962), with an adjusted R^2 of .928. The model reached statistical significance (F (2,4)=26.696, p= .036). However only activity over the LA was a significant contributor. The model without age also reached statistically significant with an adjusted R^2 of .921 (F (2,4) =47.954, p= .006). No other relationships were present before or after controlling for age.

4.4 Discussion

The present work aimed to explore the neural markers of language processing in response to sentence repetition in typically developed children and children with DLD.

It is important to highlight that due to effects of the COVID-19 pandemic the sample sizes of both groups were very small (DLD: n=1 and TD: n=5). Unfortunately, that led to a low statistical power. As a result, it is highly likely that we detected effects that were not genuine (type I errors) or that we were

unable to detect genuinely true effects (type II errors or false negatives) (Sterne and Davey Smith 2001). We tried to control for type 1 errors as much as possible by applying the Bonferroni correction for multiple comparisons, which is considered a rather conservative method (Curtin and Schulz 1998). Additionally, when reporting results that reached statistical significance, we also reported the effect sizes, as those do not depend on the sample sizes. However, that might have further led to an increased probability of false negative findings (Button et al. 2013). Nonetheless in the typically developed group some trends were identified. These are discussed below.

To begin with, in our sample we did not observe strong left lateralised activations in response to sentence repetition. In temporal areas that was expected given the auditory nature of the stimulus. As discussed in chapter three, both the right and left auditory cortices are involved in decoding auditory linguistic information. Additionally, processing of relatively longer length of the sentences is thought to engage right temporal regions (Cooke et al. 2002).

In frontal regions even though it was hypothesised that activity over the left IFG would be higher compared to the right IFG, no difference between the two was found. One possible explanation for that could lie in the function of the right IFG in attentional control (Hartwigsen et al. 2019). That region is not only recruited in parallel to its left homologue during overt language production but is also heavily involved when sustained attention is required. Thus, in our study it is plausible that the lack of hemispheric lateralisation in

frontal regions during sentence repetition resulted from the nature of the stimuli that participants were expected to repeat. Additionally, a trend that did not reach statistical significance after applying statistical corrections indicated that frontal regions had increased activations compared to temporal regions. That potentially reflects a combination of processing demands including syntactic processing, working memory processing and articulation demands. Untangling these could be a very interesting avenue for future research as it would further our understanding of the neural network that supports sentence level processing and overt language production. A possible way of achieving this would be to add a varying waiting period between the sentence and the repetition time allowing to separate sentence processing demands, memory retrieval and articulation.

Based on the findings of our previous study, described in chapter 3, we expected that activity over the right auditory cortex during language processing would be predictive of task performance as well as performance in a standardised assessment of grammatical contrasts. However, in this study we did not find a relationship between language performance and RA activity. Instead, we identified activity over the LA was associated with reading ability as measured by a standardised assessment where greater negative activation related to poorer reading ability. This is in agreement to other neuroimaging studies of reading that have reported that children with reading difficulties showed greater suppressed activity in left temporoparietal brain regions (Simos et al. 2011). This finding can have important clinical applications for DLD given that it is well documented that children with DLD have a lower

performance in phonological awareness tasks as well as in reading abilities (Lara-Díaz et al. 2021).

Lastly, based on the findings of the study described in chapter three, we expected that the control condition would allow us to isolate unique frontal lobe activity in response to sentence repetition. However, we did not see an effect of condition on brain activity in any ROI. One possible explanation is that in the present study the control condition required an overt verbal response that posed significant demands on the frontal language network for articulation, thus preventing us from detecting difference between the sentence repetition and control conditions. In contrast, in our previous study the control condition required both overt as well as covert responses, perhaps resulting in overall lower recruitment of the IFG. This finding indicates that a high-level control condition with overt articulation might not be ideal for fNIRS investigations of sentence repetition. However, future investigation with larger sample sizes are required to draw further conclusion from this.

A secondary aim of this work was to explore the differences, if any, between NVWM neural responses between TD children and children with DLD. Unfortunately, due to the small sample size of both groups that was not feasible in the context of this study. Nonetheless, we were able to replicate some findings of previous neuroimaging work of NVWM in TD children.

To begin with, NVWM in both children and adults is supported by areas in the bilateral temporoparietal cortices. Particularly, the right inferior parietal gyrus is involved in pattern recognition, memory retrieval and attentional shifts to

salient features of a stimulus (Tops and Boksem 2011). In our sample we recorded high activation over the right auditory regions in response to the n-back memory task. Given the relatively poor spatial resolution of fNIRS combined with the proximity between the auditory cortex and the supramarginal gyrus, it is likely that the activations we recorded over the RA reflect activations in the inferior parietal gyrus.

Secondly, we did not find stronger frontal activations compared to temporal activations nor a left lateralised activation in frontal areas. This is in agreement with the findings of a large meta-analysis of neural responses to n-back memory tasks in late childhood that reported that hemispheric dominance was not established and brain activations in frontal regions were less homogenous compared to those of adults (Yaple and Arsalidou 2018). This is possibly due to the delayed maturation of frontal regions in children.

We hypothesised that we would detect a difference in neural activations between the 1-back and the 2-back tasks. However, we did not find a statistically significant difference between the two that was also reflected behaviourally by the participants' task performance. Future investigations could perhaps include a third condition of 3-back or a longer delay between stimulus presentation and response to further alter task demands.

Non-verbal working memory (or visual working memory) is supported by brain regions dedicated to sensory processing including frontal and temporoparietal areas (Ungerleider et al. 1998, Eriksson et al. 2015, Ren et al. 2019). Activations in frontal areas and specifically the IFG bilaterally are involved in

maintaining attention to the stimuli as well as the overall task goals assisting ultimately in successful task completion (Raye et al. 2002, Zhang et al. 2003). Activity in frontal areas in children is not yet strongly lateralised by late childhood perhaps due to delayed maturation of frontal areas. Thus, the lack of hemispheric lateralisation in our sample was expected.

NVWM is also supported by parietal networks including the inferior and superior parietal gyri, (Koenigs et al. 2009). A large meta-analysis of neural responses in late childhood to n-back memory tasks similar to the one performed by our participants highlighted the role of the right parietal gyrus (Yaple and Arsalidou 2018). Parietal regions are thought to be involved in pattern recognition (Finke et al. 2006), memory retrieval and attentional shifts to salient features of a stimulus (Arsalidou and Taylor 2011, Tops and Boksem 2011, Seghier 2013).

Similarly, there were no differences between 1-back and 2-back NVWM. Given the increased demands of the 2-back we hypothesized increased activity in the IFG in that task. Even though results did not reach significance there was reduced activity in the left IFG in the 2-back compared to the 1-back, if that observation reflects a true difference (not due to small sample size) that could be explained by the fact that when increased cognitive demands we disengage if a task becomes too difficult (Pergher et al. 2019) . Behaviourally that could be reflected by the marginally significantly higher performance in the 1-back task compared to the 2-back task.

We hypothesised that children with DLD would exhibit different patterns of activations in response to sentence repetition compared to TD children but similar patterns in NVWM. Based on the limited body of neuroimaging studies in DLD we also hypothesised that children with DLD would show reduced activations compared to TD children. Unfortunately, due to the small sample size it was not possible to examine these hypotheses in children with DLD. However, this very preliminary work demonstrated the feasibility of imaging a relatively young child with DLD using an overt task. The child comfortably competed both runs of the sentence repetition and NVWM tasks demonstrating the suitability of fNIRS as a suitable image modality for assessment of individuals with DLD.

4.5 Summary

This chapter sought to establish the feasibility of measuring cortical responses during sentence repetition in typically developed children and children with DLD. Unfortunately, we were not able to compare the two groups to uncover unique patterns of neural activation in DLD. However, we were able to show the feasibility of measuring cortical responses in TD children during an overt sentence repetition task using fNIRS. In our knowledge this is the first time an online overt sentence repetition paradigm has been deployed in this population. Even though most findings did not reach the threshold for statistical significance, some trends were observed. Namely, TD children showed strong frontal activations in response to language processing and activity over the left auditory cortex was associated with reading abilities. Further, the NVWM tasks led to increased activations over the right auditory

cortex and bilateral frontal activations in concordance to previous neuroimaging findings. Future work should seek to assess these trends with a larger number of both TD as well as children with DLD.

5 Resting state connectivity in the language network of typically developed children and adolescents

5.1 Chapter Overview

In this study, we explored the connectivity patterns of the resting state language network in typically developed children and adolescents. Investigation of RSC in language processing brain regions have identified an underlying network that spreads across both hemispheres and includes the inferior frontal gyrus, the middle frontal gyrus, and inferior temporal and temporo-parietal areas (such as the supramarginal gyrus, planum temporale, Sylvian parieto-temporal, superior temporal gyrus, and inferior parietal cortex) (Price 2010, Tomasi and Volkow 2012, Yin et al. 2019). The RSC language network appears to be left lateralised very early in life (Liu et al. 2022) and the degree of left lateralisation increases with age (Holland et al. 2007, Reynolds et al. 2019, Bruchhage et al. 2020). For instance, a study investigating RSC patterns in 3- and 5-year-old children reported higher degree of left lateralisation in RSC of the IFG and the STG in the older children (Xiao et al. 2016). The same group also showed that children appear to have stronger interhemispheric RSC between the right and left IFG whereas adults showed increased RSC between the IFG and STS in the left hemisphere (Xiao et al. 2016). Similarly, to findings from task-dependant studies of language processing it appears that connectivity also increases intra- hemispherically

within the left hemisphere whereas decrease or no change are observed in the connectivity within the right hemisphere (Gaudet et al. 2020). This increase in left connectivity asymmetry also reflects a shift from inter-hemispheric to intra-hemispheric connectivity with age (Yamada et al. 2010, Perani et al. 2011, Youssofzadeh et al. 2017) and potentially an automation of language skills.

However, even though the resting state language network is well investigated in younger children below the age of 6 years old and in adults, the age of maturation is yet unknown. Thus, it is important to continue building upon this literature by exploring the developmental trajectories of the language network in late childhood and adolescence.

The findings discussed above refer to investigations of cortical connectivity between brain regions have used functional connectivity (FC) analysis. FC describes the correlations across neurophysiological events that occur in spatial remote brain regions (Babaeeghazvini et al. 2021). FC analyses provide a wealth of information on statistical dependencies of neural activations patterns; however, it does not offer any insights into the causal relationships between neural systems (Babaeeghazvini et al. 2021). On the other hand, directed connectivity (DC) analysis overcomes this limitation by using the data to produce a model of the causal influences between different brain regions (Babaeeghazvini et al. 2021). DC is typically quantified using Granger Causality (Granger 1969) and dynamic causal modelling (Friston et al. 2013). However, in this project, DC will be assessed using Phase Transfer Entropy (PTE). PTE

addresses some of the limitations imposed by Granger Causality and dynamic causal modelling as it is not sensitive to signal noise and does not require a preconceived model of underlying neural patterns (Lobier et al. 2014). PTE has been traditionally used to characterise functional connectivity in electroencephalographic (EEG) and magnetoencephalographic (MEG) recordings (Lobier et al. 2014) and is now being increasingly incorporated to the analysis of fNIRS data, as it produces potential causal inferences about the observed relationships between neural entities without a requirement of any prior assumptions (Lobier et al. 2014, Martínez-Cancino et al. 2020, Wang and Chen 2020, Marriott Haresign et al. 2022).

5.2 Methods

5.2.1 Participants

Thirty-five children and adolescents between the ages of 6 and 15;11 years old (19 female, mean age= 11.43 years, SD= 2.51) took part in this study. Please see section 3.2.1 for a justification on the target sample size. Six participants were excluded from subsequent analysis due to excessive movement during the session that led to missing data from the right IFG. All participants were native English speakers with normal or corrected to normal vision and no known hearing, language, or cognitive problems; children with a history of cognitive or motor impairment, as reported by the parents, were excluded. All participants completed the behavioural assessments described in section 3.2.3. Mean scores can be found in table 5.1 and details can be found in section 9.3 of the appendix. Participants were identified from the

National Institute of Health Research (NIHR) Nottingham Biomedical Research Centre (BRC) Hearing Sciences participant database, and via online advertisements on parent Facebook groups in the Nottinghamshire area. This investigation was approved by the University of Nottingham Faculty of Medicine and Health Sciences Research Ethics Committee (ref: 192-1901) and the Nottingham Research Ethics Committee (ref: 269962).

N (male)	29 (15)	
	Mean	*SD*
Age	11.30	2.65
Cognitive Measures		
Performance IQ[a]	112.07	11.22
Estimate of general cognitive ability[a]	111.41	13.77
Grammar Comprehension[b]	102.83	9.98
Sight Word efficiency[c]	105.31	10.76
Phonetic decoding efficiency[c]	112.10	10.80
General Communication Composite[d]	74.93	17.94

Table 5.1 Age characteristics of the sample and group means and standard deviations scores for the standardised language and behavioural measures. Scores are standard scores (mean 100 ± 15) except for the general Communication Composite where scores greater than 58 are considered normal.

[a]Wechsler Abbreviated Scale of Intelligence – 2nd Edition, [b]The Test for Reception of Grammar - Version 2, [c] The Test of Word Reading Efficiency – 2nd Edition, [d]The Children's Communication Checklist - 2nd Edition.

5.2.2 Procedure

After obtaining informed consent from the participants and their parents/guardians and completing the behavioural assessments described in section 3.3.3, participants sat comfortably in a sound-attenuated room with dimmed lighting, approximately 80cm from a visual display unit. They were instructed to keep their eyes open focused on a centrally placed cross on the display and try to not think of anything specific. The background colour of the

screen was grey throughout the duration of the task. The duration of the resting state connectivity recordings lasted for 10 minutes. Following the resting state data collection participants completed the language tasks described in chapters three and chapter four.

5.2.3 Equipment

The equipment, study programming, laboratory set-up, optode array and positioning procedure used were identical to that described in chapter three and four (please refer to sections 3.2.4 and 4.2.3).

5.2.4 fNIRS Data

The first step in the analysis of the fNIRS data was the pre-processing of the fNIRS signal, which was conducted in a similar manner to the one described in section 3.2.

Following the application of the HMS algorithm and the GLM the isolated HMS signal was used with open-accessed MATLAB codes that calculate the PTE (Fraschini 2017). PTE calculates the degree of certainty in one signal given the past values of another signal using phase entropies. It thus quantifies the extent to which two different neural activities causally influence one another (Lobier et al. 2014).

The following formulas were used (Lobier et al. 2014):

$$PTE_{x\rightarrow y} = H(\theta_y(t),\theta_y(t')) + H(\theta_y(t'),\theta_x(t')) - H(\theta_y(t')) - H(\theta_y(t),\theta_y(t'),\theta_x(t')) \quad (1)$$

$$t' = t - \delta \quad (2)$$

$$H = -\Sigma p\log(p) \quad (3)$$

where PTEx→y (formula (1)) calculates the synchrony between two signals x(t) and y(t) with information flowing from x to y (i.e., y follows x). θx(t) and θy(t) refer to the instantaneous phase (via Hilbert transform) at time t of the two signals, respectively. δ (formula (2)) denotes the time lag between the two signals. The time lag δ can be predetermined or it can be modulated by the duration of the frequency cycle. In this instance we followed the open-accessed MATLAB codes by Fraschini (2017) and defined the time lag as the time duration of approximately one cycle of the selected frequency (0.01Hz-0.5 Hz) (Fraschini 2017). p refers to probability of instantaneous phases and H is the phase entropy where the summation was implemented over the number of phase bins, each of which corresponds to the probability (p in the formula) of the occurrence of that bin in the given time series (formula (3)) (Fraschini 2017). Greater PTEx→y reflects smaller entropy (i.e., greater certainty) of θy given in the past values of θx, hence informing greater information flows from x to y.

The pre-processed signals were averaged across channels within each ROI in the time domain before PTE was applied to measure the connectivity between each ROI. Even though, averaging across channels could potentially disrupt the temporal structure of the signal, here we opted for that approach following findings that suggested that averaging signals from a limited set of channels overlying a specific cortical region of interest enhanced the reliability of fNIRS measurements (Wiggins et al., 2016). Additionally, exploratory analysis of single channel recordings required increased comparisons for multiple comparisons that led to non-significant findings and thus these

results are not reported here. As there were four ROIs (bilateral IFG and bilateral auditory cortices), this resulted in 12 PTE values (information flow from left to right and right to left hemisphere and from auditory cortices to the IFG and from the IFG to the auditory cortices).

5.2.5 Statistical analysis

Mixed measures ANOVAs were performed to explore the effects of direction (frontal to sensory areas vs sensory to frontal and left to right hemisphere vs right to left hemisphere), region (IFG and auditory cortex) and hemisphere (left and right) on cortical connectivity. Gender was entered as a between subjects' factor. Linear regression analyses were performed to determine the relationship between standardised language assessments (TROG, CCC-2, TOWRE SE and TOWRE PE) and cortical connectivity and cortical connectivity and age. Histograms and the Shapiro-Wilk test confirmed normality of the distribution of PTE, age and standardised language assessments, and post-hoc diagnostic measures verified that the assumptions of bivariate linear regression were met in each model: 1) a scatterplot indicated linearity between the predictor and dependent variable; 2) a Durbin-Watson test demonstrated independence of observations; 3) case wise diagnostics confirmed the absence of significant outliers; 4) visual examination of histograms and normal P-P plots indicated that the standardised residuals of the regression model were normally distributed, and; 5) the assumption of homoscedasticity was met. The threshold for statistical significance was set at $p < .05$. To counteract the problem of multiple comparisons the Bonferroni

corrections were applied to the correlation analyses and the post hoc multiple comparisons.

5.3 Results

5.3.1 Effect of hemisphere, region and direction on information flow during resting state

5.3.1.1 Interhemispheric resting state connectivity

A repeated measures ANOVA with within subject variables the ROI (IFG vs auditory cortex) and the hemispheric direction of the information flow (left to right hemisphere vs right to left) was run to explore whether i) there was a difference in the connectivity from the left to right and from the right to the left hemispheres and ii) there was a difference in the connectivity within temporal regions compared to frontal regions. There was a statistically significant main effect of direction ($F(1,28)=6.674$, $p=.045$) with higher resting connectivity from right to left vs left to right hemisphere (mean dif.=.121, se=.047, $p=.015$) (figure 5.1a). Additionally, there was a significant main effect of ROI ($F(1,28)=25.127$ $p<.001$) with stronger connectivity between temporal regions compared to frontal regions (mean dif.=.304, se=.061, $p<.001$) (figure 5.1b). There was no interaction effect between ROI and hemispheric direction ($F(1,28)=2.065$, $p=.162$) (Table 5.2).

5.3.1.2 Intrahemispheric resting state connectivity

A repeated measures ANOVA with within subject variables the hemisphere (left vs right) and the regional direction of the information flow (frontal to sensory vs sensory to frontal) was run to explore whether i) there was a

difference in the connectivity from the IFG to the auditory cortex (frontal to sensory) vs from the auditory cortex to the IFG (sensory to frontal) and ii) there was a difference in the connectivity within the left compared to right hemisphere. There was a statistically significant main effect of direction ($F(1,28)=36.055$, $p<.001$, Bonferroni corrected for 3 comparisons) with higher resting connectivity from frontal to sensory areas vs connectivity from sensory to frontal (mean dif. =.263, se=.044, df=28, $p<.001$) (figure 5.1c). There was no effect of hemisphere ($F(1,28)=2.754$ $p=.108$, Bonferroni corrected for 3 comparisons) indicating that there is lack of evidence for significant difference in the connectivity between the left IFG and the LA vs the right IFG and the RA. There was no interaction effect between hemisphere and regional direction ($F(1,28)=.803$, $p=.378$, Bonferroni corrected for 3 comparisons) (Table 5.2).

5.3.1.3 Inter and Intra hemispheric resting state connectivity

A repeated measures ANOVA with within subject variables the regional direction of information (IFG to auditory cortex vs auditory cortex to IFG) and the hemispheric direction of the information flow (left to right hemisphere vs right to left) was run to explore whether i) there was a difference in the connectivity from the left auditory to right frontal regions and right auditory to left frontal regions and vice versa. There was a statistically significant main effect of hemispheric direction ($F(1,28)=6.408$, $p=.017$, Bonferroni corrected for 3 comparisons) with higher resting connectivity from right to left vs left to right hemisphere (mean dif. =.119, se=.047, df=28, $p=.017$) (figure 5.1a). Additionally, there was a significant main effect of regional direction

(F(1,28)=36.803 p<.001, Bonferroni corrected for 3 comparisons) with stronger connectivity from frontal to temporal regions compared to temporal to frontal regions (mean dif.=.274, se=.045, df=28, p<.001) (figure 5.1c). There was no interaction effect between regional and hemispheric direction (F(1,28)=.361, p=.553, Bonferroni corrected for 3 comparisons) (Table 5.2).

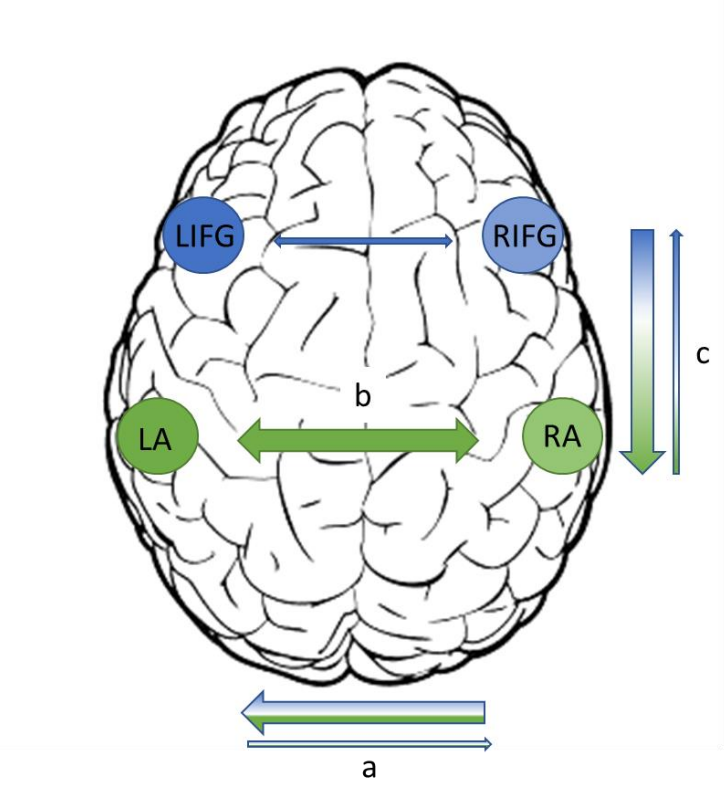


Figure 5.1 Graphical Representation of the resting state connectivity in children and adolescents. a) Stronger overall connectivity from the right towards the left hemisphere, b) stronger bilateral connectivity between temporal regions compared to the bilateral connectivity between frontal regions and c) stronger overall connectivity from frontal towards temporal regions.

Interhemispheric resting state connectivity		
Main effects		
Direction	F (1,28) = 6.674	p > .05
ROI	**F (1,28) = 25.127**	p < 0.001
Two-way Interactions		
Direction x ROI	F (1,28) = 2.065	p > .05
Intrahemispheric resting state connectivity		
Main effects		
Direction	**F (1,28) = 36.055**	p < .001
Hemisphere	F (1,28) = 2.754	p > .05
Two-way Interactions		
Direction x Hemisphere	F (1,28) = 0.803	p > .05
Inter and Intra hemispheric resting state connectivity ***Main effects***		
Hemisphere direction	**F (1,28) = 6.408**	p = .017
ROI direction	**F (1,28) = 36.803**	p < .001
Two-way interactions		
Hemisphere direction x ROI direction	F (1,28) = 0.803	p > .05

Table 5.2 The results of the 2-way ANOVA between region and hemispheric direction, hemisphere and ROI direction and ROI direction and hemisphere direction. Highlighted in yellow is the main effect of hemisphere that reached statistical significance at p<.05

5.3.2 Relationship between age and resting state connectivity

Regression analyses were performed with the age as the predictor and RSC as the dependant variable to explore whether the degree of connectivity changed with age. Age accounted for 14.4% of the variability observed in the connectivity from the RA to the RIFG and 18.2% of the variability observed in the connectivity from the RA to the LIFG with both models reaching the threshold for statistical significance (p=.042 and p=.021 respectively). Similarly age also accounted for 16.2% of the variability in the decrease of connectivity between left and right IFG (model statistically significant with p=.031). Lastly, age accounted for 14.6% of the variability observed in the connectivity from

the LA to the RIFG (model statistically significant with p=.041). All other models were not statistically significant. Detailed results in table 5.2.

Model	*Regression analyses of age as predictor of PTE*							
	R^2	**Adj. R^2**	**F**	**b**	**SE b**	**β**	**t**	**p**
Left Auditory to Left IFG	.052	.017	1.484	-.024	.019	-.228	-1.22	.234
Left Auditory to Right Auditory	.032	-.004	.881	-.018	.019	-.178	-.939	.356
Right Auditory to Right IFG	.144	.112	4.542	-.032	.015	-.379	-2.13	.042
Right Auditory to Left Auditory	.014	-.023	.371	-.009	.015	-.116	-.609	.548
Left IFG to Left Auditory	.000	-.037	.002	.001	.013	.009	.962	.962
Left IFG to Right IFG	.162	.131	5.211	-.040	.017	-.402	-2.28	.031
Right IFG to Right Auditory	.024	-.013	.651	-.019	.023	-.153	-.807	.427
Right IFG to Left IFG	.083	.049	2.436	-.037	.024	-.288	-1.56	.130
Left Auditory to Right IFG	.146	.115	4.630	-.033	.016	-.383	-2.15	.041
Left IFG to Right Auditory	.042	.006	1.171	-.024	.022	-.204	-1.08	.289
Right Auditory to Left IFG	.182	.152	6.024	-.043	.018	-.427	-2.45	.021
Right IFG to Left Auditory	.037	.001	1.036	-.012	.012	-.192	-1.02	.381

Table 5.3 Summary of bivariate linear regression statistics for age in the prediction of resting-state connectivity. Statistically significant models with p <.05 are highlighted in red. b refers to the unstandardised regression coefficient, while β symbolises the standardised regression coefficient.

5.3.3 Relationship between resting state connectivity and standardised language assessments

Regression analyses were performed with the RSC as the predictor and the standardised language assessments as the dependant variable to explore whether RSC could predict language skills in children and adolescents. No model of RSC statistically predicted performance in the CCC-2, the TROG (table 5.3) or the TOWRE Phonemic Word Efficiency. However, connectivity between the RA and the RIFG accounted for 13.4% of the variability observed in the TOWRE Sight Word Efficiency assessment. All other models were not statistically significant. Detailed results in table 5.4. Given that age accounted for the connectivity between RA and RIFG, they were fitted in the same model with TOWRE SE as the dependant variable. The model was statistically significant (R^2= .272, Adj. R^2= .216, F= 4.855, p=.016) (figure 5.2).

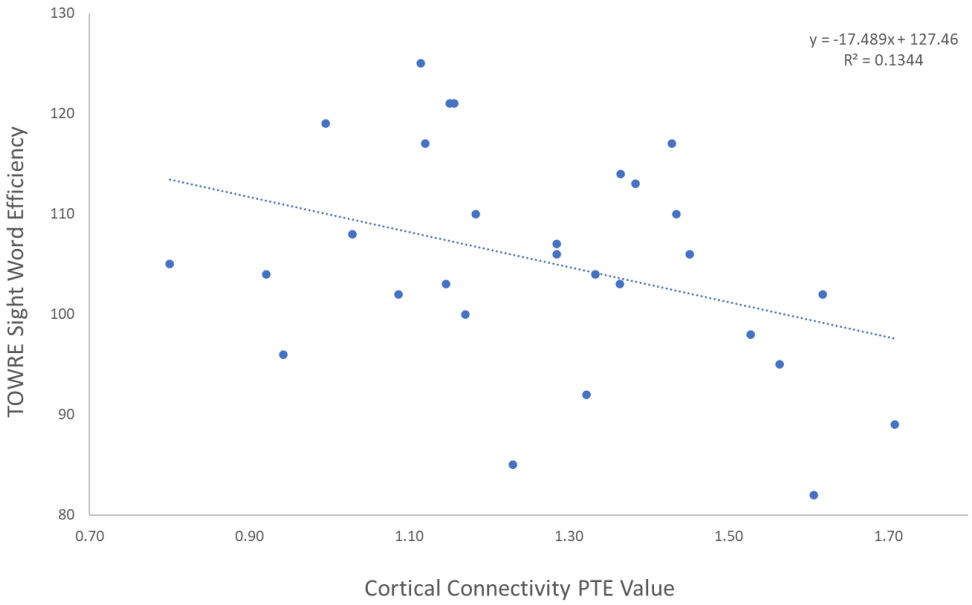


Figure 5.2 Correlation graph between the PTE value of cortical connectivity RA-RIFG (x-axis) and scores in the TOWRE Sight Word Efficiency assessment (y-axis).

Model	*Regression analyses of PTE as predictor of CCC-2*							*Regression analyses of PTE as predictor of TROG*						
	R^2	**Adj. R^2**	**F**	**b**	**SE b**	**β**	**t**	**R^2**	**Adj. R^2**	**F**	**b**	**SE b**	**β**	**t**
Left Auditory to Left IFG	.004	-.033	.116	-4.262	12.509	-.065	-.341	000	-.037	.000	.070	6.974	.002	.010
Left Auditory to Right Auditory	.008	-.029	.217	-5.980	12.829	-.089	-.466	.001	-.036	.035	-1.335	7.162	-.036	-.186
Right Auditory to Right IFG	.024	-.012	.678	12.450	15.121	.156	.823	.007	-.03	.185	3.656	8.489	.083	.431
Right Auditory to Left Auditory	.022	-.014	.616	13.060	16.640	.149	.785	.008	-.029	.206	-4.232	9.327	-.087	-.454
Left IFG to Left Auditory	.023	-.014	.623	-15.48	19.619	-.150	-.789	.002	-.035	.060	-2.698	11.028	-.047	-.245
Left IFG to Right IFG	.002	-.035	.052	2.991	13.179	.044	.227	.002	-.035	.061	1.817	7.331	.048	.248
Right IFG to Right Auditory	.006	-.030	.175	-4.448	10.632	-.080	-.418	.001	-.036	.019	-.821	5.932	-.027	-.138
Right IFG to Left IFG	.000	-.037	.013	1.1.59	10.158	.022	.114	.009	-.028	.241	-2.761	5.628	-.094	-.491

Table 5.4: Summary of bivariate linear regression statistics for resting-state connectivity in the prediction of CCC-2 scores (left) and TROG scores (right). No model was statistically significant with p >.05. Please note that regression models for the resting state connectivity between the following areas were not included as resting state connectivity between those areas was not expected to provide meaningful information with regards to changes in CCC-2 or TROG scores: Left Auditory to Right IFG, Right IFG to Left Auditory, Right Auditory to Left IFG and Left IFG to Right Auditory.

Model	*Regression analyses of PTE as predictor of TOWRE_SE*							*Regression analyses of PTE as predictor of TOWRE_PE*						
	R^2	**Adj. R^2**	**F**	**b**	**SE b**	**β**	**t**	**R^2**	**Adj. R^2**	**F**	**b**	**SE b**	**β**	**t**
Left Auditory to Left IFG	.023	-.013	.645	5.964	7.428	.153	.803	.032	-.003	.906	7.069	7.425	.180	.952
Left Auditory to Right Auditory	.059	.025	1.706	-9.784	7.490	-.244	-1.306	.002	-.035	.043	-1.605	7.750	-.040	-.207
Right Auditory to Right IFG	.134	.102	4.194	-17.49	8.540	-.367	-2.048	.016	-.021	.427	-5.980	9.147	-.125	-.654
Right Auditory to Left Auditory	.003	-.034	.087	2.973	10.074	.057	.295	.033	-.003	.915	9.531	9.967	.181	.956
Left IFG to Left Auditory	.015	-.022	.405	7.519	11.809	.122	.637	.022	-.014	.618	9.290	11.815	.150	.786
Left IFG to Right IFG	.040	.004	1.121	-8.205	7.750	-.200	-1.059	.008	-.029	.205	3.584	7.914	.087	.453
Right IFG to Right Auditory	.130	.098	4.042	-11.99	5.964	-.361	-2.010	.028	-.008	.777	-5.582	6.333	-.167	-.881
Right IFG to Left IFG	.010	-.027	.267	3.130	6.062	.099	.516	.055	.020	1.558	7.426	5.949	.234	1.248

Table 5.5 Summary of bivariate linear regression statistics for resting-state connectivity in the prediction of TOWRE SE scores (left) and TOWRE PE scores (right). Statistically significant models with p <.05 are highlighted in red. Please note that regression models for the resting state connectivity between the following areas were not included as resting state connectivity between those areas was not expected to provide meaningful information with regards to changes in TOWRE_SE or TOWRE_PE scores: Left Auditory to Right IFG, Right IFG to Left Auditory, Right Auditory to Left IFG and Left IFG to Right Auditory.

5.4 Discussion

This study aimed to explore the direction of interhemispheric and interhemispheric connectivity in the language network in children and adolescents during a resting state paradigm. Additionally, the relationship between age and RSC as well as between RSC and language performance were investigated. The use of PTE as a novel approach to analyse neural connectivity patterns also provided valuable insights into the direction of the flow of information between the examined regions.

To begin with, we hypothesised that the left lateralisation of the language network would be evidenced by an increased intrahemispheric connectivity between frontal and auditory regions in the left vs the right hemisphere. Similarly interhemispheric connectivity between homologue areas would be less compared to intra hemispheric connectivity. However, electrophysiological studies of auditory and phonological processing have demonstrated a faster transmission of information from the non-specialised to the specialised hemisphere that is reflected by a unidirectional flow of information (Vallar et al. 1988). In our study we found that information overall flowed from the right to the left hemisphere supporting that notion.

Age related changes in the RS language network remain elusive. In the present study a decrease in the flow of information from the left auditory region and the left IFG towards the right IFG as a function of age was found. Previous work has also demonstrated that as age increases the language network is comprised by local connections rather than long-range and

bilateral ones (Doesburg et al. 2016, Kadis et al. 2016, Poblano et al. 2016, Youssofzadeh et al. 2017). Furthermore, as described in chapter 3, the maturation of the language network and consequently of language skills is reflected by a shift in activation to more posterior brain regions. The findings of this study provide further evidence for that theory by demonstrating reduced connections of all areas with the right IFG as age increases. Additionally, the increased bilateral connectivity between the right and left auditory regions compared to connectivity between frontal regions provides further evidence that that shift is perhaps established early in childhood. Similarly others have reported that the language network is already tightly synchronised by the age of 6 (Weiss-Croft and Baldeweg 2015), (Wilke et al. 2009).

Results also showed an increased connectivity from frontal to sensory areas vs connectivity from sensory to frontal areas. This finding is in agreement with others that have shown that development is characterised by an increase in the modulatory influence of the IFG in temporal and parietal regions. This recruitment of frontal to sensory control might facilitate the specialisation of the language network that supports the separation of language processing with development. For instance, the specialisation of temporal regions for phonological processing and parietal regions for orthographical control. The increase of frontal to sensory control might also reflect an automation in language skills as frontal to sensory processing involves using previous learnt skills and information.

In our sample we found no gender differences in RSC patterns. Previous findings remain inconclusive as to whether there are gender differences in brain connectivity within the language network. Some have found that females display increased structural and functional interhemispheric connectivity compared to males (Satterthwaite et al. 2015, Zhang et al. 2016), however other studies have not detected any differences in RSC patterns (Solé-Padullés et al. 2016). One possible explanation is that these differences are task dependant; many of the studies that have shown gender differences in connectivity have utilised active paradigms where participants completed language tasks (Rubia 2013). Thus, it is possible that we did not detect any differences due to our paradigm, however future work is needed to further investigate this and continue accounting for gender in statistical analyses.

In the current study, RSC between bilateral temporal and frontal regions did not predict grammatical acknowledge, parental communication evaluation and phonemic discrimination, however it was associated with sight word efficiency. Specifically, reduced connectivity between the right auditory cortex and the right IFG was associated with higher TOWRE SWE scores. When accounting for age the predictiveness of the model increased indicating that younger children with lower connectivity from the right auditory cortex to the right IFG had better scores. This finding might indicate that increased language proficiency correlates with a decreased reliance on the right IFG and points towards a refinement of phonological processing towards more temporal regions. It is noteworthy however that very few investigations have

considered the RIFG when exploring effective connectivity of the intrinsic language networks.

However, these findings did not replicate others that have reported positive correlations between increased RSC within the left hemisphere and measures of language skills. Many studies that have reported on that have measured language proficiency in younger children when skills develop at a much faster pace. Thus, we might not have found an effect between connectivity with the left hemisphere and language skills because connectivity plays a salient role in early development and reaches maturation in late childhood (Su et al. 2021). Another possible explanation is that the standardised assessments that were used to assess language skills might not have been sufficiently challenging to generate a large variability in testing scores. Even though celling effects were not observed, most participants performed above the average score for their age. More comprehensive assessments such as the CELF-5 (Wiig et al. 2013) could be used in the future to explore whether RSC predicts language proficiency in older children.

The present study explored RSC patterns in a cross-sectional sample of children and adolescents, however a longitudinal study capturing a wider age range would offer invaluable insight into the development of the language RSC network. It is also important to mention that a small portion of recruited participants was excluded from the final analysis due to missing data. Participants were instructed to stay still and avoid head movements but were not interrupted during the session unless the cap had visibly moved. The

excluded participants moved significantly during the 10 minutes of the imaging sessions and that resulted in poor optode-scalp contact especially over the right IFG region. Examining the study notes revealed that those participants were quite unrestful towards the end of the 10 minutes. Thus, perhaps future investigations could deploy shorter paradigms or split their resting state data collection session in two offering participants a break in between. A shorter session could still reliably record resting state connectivity patterns. Wu and colleagues demonstrated that a paradigm as short as 2 minutes was sufficient to differentiate between typically developed children and children with autism (Wu et al. 2022). In the present study after piloting the experiment with three children aged 6, 10 and 12 years old we considered the 10-minute duration appropriate but that might not be feasible for all children, particularly those with additional needs. Another alternative would be presenting a silent visual stimulus (such as an animated movie clip) on the screen during the RSC sessions it has been shown that does not affect recordings from the fronto-tempoparietal networks. This type of paradigm is typically deployed when imaging infants and toddlers (Bell and Cuevas 2012, Whedon et al. 2020) but could also be applied with older children to ensure that they stay engaged. Nevertheless, it's crucial to emphasize that the patterns observed during the resting state signify inherent manifestations of spontaneous cognitive processes. Consequently, these patterns could vary among individuals based on the approaches they employ during the resting state task. For instance, participants who concentrate on visual stimuli in their vicinity while attempting to achieve a state of mental quietude may exhibit

distinct resting state connectivity patterns compared to those who contemplate future plans. Conducting additional research would provide the means to ascertain potential dissimilarities in resting state connectivity patterns among individuals, as well as methods to systematically account for these variances.

5.5 Summary

This chapter explored the resting state connectivity patterns of the language network of typically developed children and adolescents. The use of PTE offered novel insights into the direction of the flow of information. Overall, the findings of this study reveal that the network continues to mature throughout this period with widespread connections towards right frontal regions points towards decreased reliance on that region as age increases. A strong interhemispheric connectivity between auditory cortices resembles adult like patterns of activation indicating that these regions have already reached maturation by late childhood. This work demonstrates the feasibility of measuring RSC patterns in the language network using fNIRS in this population. Given this, the simplicity of taking these recordings as well as the applications of RSC measurements in other developmental disorders, it would be very valuable to examine the resting state language network in children with DLD.

6 Hyperscanning

This chapter has been adapted from:

Papoutselou, E., Harrison, S., Mai, G., Patil, N., Buck, B., Wiggins, I. and Hartley, D., Investigating mother-child inter-brain synchrony in a naturalistic paradigm: A functional near infrared spectroscopy hyperscanning study Manuscript submitted for publication December 2022, European Journal of Neuroscience.

Author contributions: EP and DH conceived and designed the study, EP and SH collected the data, GM, BB, and IW contributed the analysis tools, EP, NP and GM performed the analysis, EP wrote the paper, SH, GM, BB, NP, IW and DH revised the paper.

6.1 Chapter Overview

This chapter explores the patterns of neural synchrony between mothers and their children while they play together and separately. As described in chapter 2.2.7 interbrain synchrony patterns could potentially be a neural marker of the underlying mechanisms that support language development in children with DLD. Thus, as a first step we explored these patterns in a sample of typically developed children to test the feasibility of a paradigm that could be deployed with young children with DLD.

To date, the majority of this research has been conducted using tasks that do not accurately reflect naturalistic social interactions between parents and children and many that are too complicated for prelingual children and/or children with communication needs. Typically employed paradigms are either passive (book reading to a child; for instance, see (Bembich et al. 2022)) or are goal-directed (solve a puzzle, play a computer game etc; e.g.(Liao et al. 2015)). Very few studies have examined neural synchrony between parents and

children during ecologically valid interactions that represent real-life scenarios. Piazza and colleagues (2020) showed that there was an alignment in neural synchrony between infants and unrelated adults which appeared to be supported by mutual eye gaze and changes in the adult's infant directed speech patterns (Piazza et al. 2020). Whilst their paradigm included free play, book reading and rhythm signing, the authors did not discuss the specific structure of their task. Consequently, it was unclear how long each element lasted for and what the duration of the free play was (Piazza et al. 2020). In another study with a naturalistic paradigm, Nguyen et al., (2021) demonstrated that neural synchrony increased as a function of the number of conversational turns taken during conversations between toddlers and their mothers (Nguyen et al. 2021). Investigations of neural synchrony during adversity and child irritability have utilised free play as a recovery condition. (Quiñones-Camacho et al. 2020, Hoyniak et al. 2021). Recently, Norton et al., developed a "social EEG" paradigm where they were able to successfully measure neural synchrony between parent-child pairs using a naturalistic set up where participants solved age-appropriate puzzles, read books and watched movies (Norton et al. 2022).

The current study aims to examine the feasibility of measuring neural synchrony patterns between mothers and their young children using a naturalistic free play paradigm. In this paradigm, the pairs were instructed to play as they would at home with toys that did not have any performance demands and allowed the pairs to interact as much or as little as they wanted. We also introduced an independent condition where the pairs played with the

same toy but separately. This allowed us to mimic a situation where the parent and the child attend to the same stimuli without interaction. In turn, this allowed for confirmation that any observed neural synchrony was not the result of similar motor and attentional requirements of the stimuli. We hypothesised that, with the naturalistic paradigm, neural synchrony between the pairs will be higher in the interactive compared to the independent condition.

Neural synchrony was measured bilaterally over frontal and temporoparietal brain regions in line with previous fNIRS hyperscanning studies involving verbal communication and problem solving (Nguyen et al. 2020, Nguyen et al. 2021). Regions of interest (ROIs) included 4 channels covering the temporoparietal junction (TPJ) and 4 channels in the prefrontal cortex (PFC) in each hemisphere (Nguyen et al. 2021, Zhou et al. 2022). The TPJ is involved in attention, language, and memory processing as well as self-awareness (Lee and McCarthy 2016). The PFC is also recruited during attention and inhibition control and decision making (Fuster 2001).

Neural synchrony was analysed using phase transfer entropy PTE. PTE has significant benefits particularly in the field of hyperscanning as it accounts for the potential time lags between the brain activities of the two participants and quantifies the degree of interbrain synchrony in different directionalities (i.e., how the brain of one participant follows the other and vice versa) (Marriott Haresign et al. 2022). This method is advantageous over other hyperscanning analysis techniques that do not specifically identify or compare synchronies in different directionalities (Lobier et al. 2014).

To investigate what might be driving the hypothesised increased neural synchrony (or lack thereof) in the interactive condition we examined conversational patterns between the pairs and personality traits of both the mother and the child. Since previous hyperscanning studies have shown that neural synchrony is positively correlated with patterns of verbal communication (Dollar and Stifter 2012, Ahn et al. 2018, Pérez et al. 2019, Nguyen et al. 2021), we were interested in examining this behaviour, given that participants were free to talk with each other but, unlike previous studies, they were not required to do so. Considering that participants were not obligated to engage in interactions, we opted for a straightforward approach by using turn-taking as a metric to measure verbal communication patterns. This allowed us to investigate whether a connection existed between verbal communication and neural synchrony. We refrained from employing a more intricate analysis, similar to the one detailed by Nguyen and colleagues (Nguyen, Schleihauf et al. 2021), as there was no assurance that participants would engage in substantial conversations.

Additionally, both behavioural and neuroimaging studies have reported that personality traits influence the quality of behavioural and neural synchrony in mother-child dyads (Reindl et al. 2018, Azhari et al. 2019). Thus, we also studied the association between child temperament and neural synchrony, as well as maternal emotion regulation.

6.2 Methods

6.2.1 Participants

Twelve pairs of mothers (mean age= 35.42 years, SD= 5.21) and children between the ages of 3 and 4 years 11 months old (7 female, mean age= 3.97 years, SD= 0.62) took part in this study. All participants were native English speakers with normal or corrected to normal vision and no known hearing, language, or cognitive problems; children with a history of cognitive or motor impairment, as reported by the parents, were excluded. Participants were identified from the National Institute of Health Research (NIHR) Nottingham Biomedical Research Centre (BRC) Hearing Sciences participant database, and via online advertisements on parent Facebook groups in the Nottinghamshire area. This investigation was approved by the University of Nottingham Faculty of Medicine and Health Sciences Research Ethics Committee (ref: 18-0520).

6.2.2 Behavioural Assessments

To assess the mothers' and children's personality traits, mothers were asked to fill in two questionnaires prior to the hyperscanning session. Child temperament was quantified using the Very Short form of the Early Childhood Behaviour Questionnaire (VS-ECBQ) (Putnam et al. 2001, Putnam and Rothbart 2006). The VS-ECBQ is comprised of 36 questions that relate to 3 child temperament dimensions: Surgency, Effortful Control and Negative Effect. Surgency refers to levels of activity, impulsivity, shyness, and positive anticipation. Effortful Control encompasses levels of attention and inhibition control. Negative affectivity describes levels of discomfort, anger/frustration,

sadness, and fear. The VS-ECBQ is rated on a Likert scale with a score of 1 indicating “never” and a score of 7 indicating “always”. A “Not Applicable” (NA) option was available if the parent had not encountered a particular situation. Items included statements such as: “When playing indoors, how often did your child like rough and rowdy games?”.

Maternal emotion regulation was assessed using the Emotion Regulation Questionnaire (ERQ) (Gross and John 2003). The ERQ is a 10-question survey with 6 questions comprising the Cognitive Reappraisal subscale and 4 the Expressive Suppression subscale. Questions were rated on a 7-point Likert scale where a score of “1” indicated “strongly disagree” and a score of “7” “strongly agree”. Items included statements like: “When I am feeling negative emotions, I make sure not to express them.”

6.2.3 Procedure

The mother-child dyads attended one research appointment where the mothers provided written informed consent and the children expressed verbal assent. Pairs were comfortably seated at a 90° angle at a table suitable for toddlers whilst wearing the fNIRS caps. They were given age-appropriate toys that included a potato head with a variety of accessories or building blocks to play with. These toys were chosen as they did not pose any performance demands and would allow the pairs to play freely.
Each session was recorded by two cameras placed to capture both participants. The experiment lasted for approximately 20 minutes and was

comprised of two conditions (interactive and independent) that were repeated twice in a pseudorandomised order.

During the interactive condition, the dyads were instructed to play together for 5 minutes “as they would at home”. The researchers observed the interactions from outside the room and mothers were allowed to remove their face coverings to allow for a more organic environment. During the independent condition, the mother and child were separated by an opaque screen and were instructed to play with their respective toys silently for 5 minutes. One researcher remained in the room to ensure the child’s safety.

6.2.4 Turn taking analysis

Turn-taking was quantified based on the recordings of the interactive condition manually One conversational turn was defined as a continuous pair of utterances between mother and child spoken in any order within 5s between speakers, i.e., the gap between speakers would not exceed 5s (e.g., M*other: “Do you like the blue arms?” Child: “Yes, blue arms!”*) (Bishop et al. 1998, Gilkerson et al. 2018, Romeo et al. 2018, Quiñones-Camacho et al. 2021). Laughs and acknowledgement sounds were counted as part of a turn if they were produced in response to something the other participant said. Ten percent of the video recordings were also coded independently by a second researcher with inter-rater reliability at 83%.

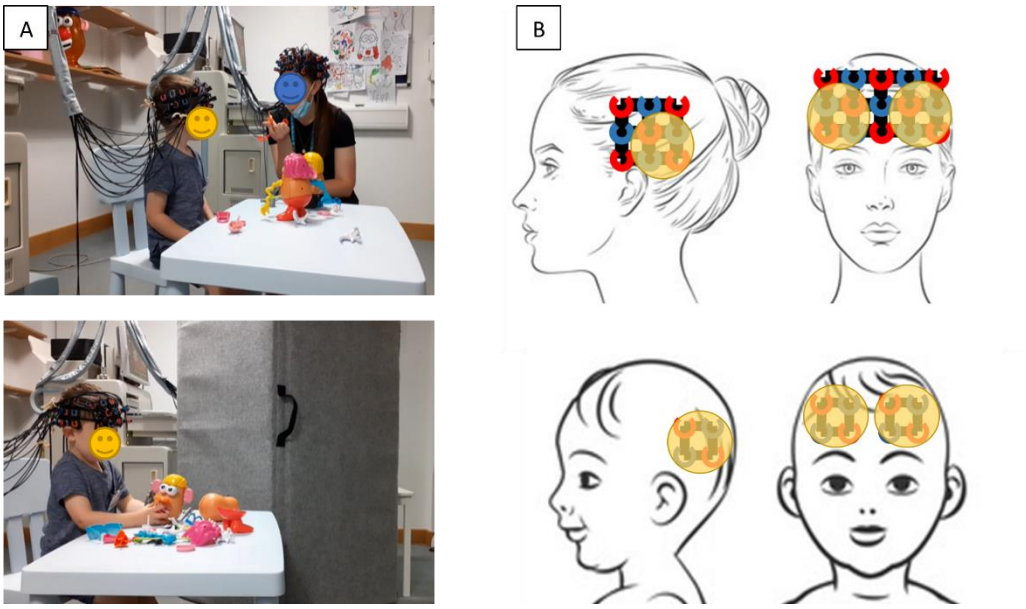


Figure 6.1 A) Experimental set up during the interactive (top panel) and independent conditions (bottom panel). B) Illustration of the probes overlaying the ROIs (yellow circles) for the mother (top panel) and the child (bottom panel) bilaterally over the prefrontal cortex and the temporoparietal junction (only the left hemisphere depicted here). The red circles represent the emitter optodes, the blue represent the detector optodes and the black lines represent the channels. The figures are for illustrative purposes only, not to scale.

6.2.5 Equipment

Two continuous wave fNIRS systems (Hitachi ETG-4000, Japan; sampling rate at 10 Hz) were used to measure brain activities in each dyad (one for each participant). The mother's cap was comprised of 48 optodes arranged in three arrays: one 3x5 array over the PFC and two 3x3 arrays bilaterally over the TPJ (see Fig 1). The child's cap was comprised of 16 optodes arranged in four 2x2 arrays over the same areas. Fewer optodes were used for the children to make the cap lighter and more tolerable for the children, whilst retaining coverage over the ROIs. Before placing the probes, child head circumference was measured using a tape measure to account for variability in head shape and size. Placement of the optodes was standardized using the international 10–20 System (Jasper 1958).

6.2.6 fNIRS Data

Pre-processing of the fNIRS data from both participants were analysed according to the process described in section 3.2. Some additional steps were added to account for the naturalistic free-play paradigm in the current study. To begin with, we considered that systemic physiological confounds may not be eliminated completely after the preprocessing. We thus further divided the pre-processed signals into frequency sub-bands that correspond to specific types of possible physiological confounds and then focused on the band which led to significant neural synchrony (i.e., synchrony that was significantly greater for the interactive than the independent play). This was conducted so that we could detect which frequency range may be least contaminated by these confounds that led to optimal measures for neural synchrony. To avoid arbitrary choices of frequency bands, we chose three sub-bands based on the previous literature: 0.01-0.05 Hz, 0.05-0.2 Hz, and 0.2-0.5 Hz which reflect ranges for the autonomic, myogenic, and respiratory activities, respectively (Rossi et al. 2007). It is important to note that these frequency bands rely on findings of adult participants. Literature on the frequency bands in paediatric populations remains scarce, however one investigation in infants reported comparable ranges for respiratory (approx. 0.25 Hz) and myogenic (approx. 0.1 Hz) activity (Boas et al. 2004). Zero-phase 3rd-order Butterworth filters were additionally applied to obtain fNIRS signals at each band (N.B., to avoid duplicate cut-off slopes applied on the lower/upper bound of the already-pre-processed signal, lowpass and high pass filters at 0.05 and 0.2 Hz was used to obtain the sub-bands at 0.01-0.05 and 0.2-0.5 Hz, respectively). We also

included the 0.01-0.5 Hz range (i.e., without further filtering the pre-processed signals). Here, we focused on the range at 0.05-0.2 Hz which was the only frequency band that showed significant neural synchrony. This reflected that myogenic confounds could be most effectively attenuated at this frequency range.

Neural synchrony between the mother-child dyads was measured using PTE (Lobier et al. 2014, Ursino et al. 2020). Compared to other methods typically used in fNIRS hyperscanning studies such as wavelet coherence transformation (WCT), PTE allows for measuring the directionality of neural synchrony that considers potential time lags between brain activities in each participant (Cao et al. 2018, Wang and Chen 2020). Also, as the haemodynamic response functions (HRF) could be different between children and adults (Minagawa-Kawai et al. 2011), PTE has a specific advantage for which it does not require the assumption of the same HRF for both participants as required by other methods like WCT and Granger Causality. We applied the open-accessed MATLAB codes that calculate the PTE (Fraschini 2017) using the formulas detailed in section 5.2.5.

Here, the time lag δ was set at 4 seconds according to previous reports that showed that neural synchrony between adults and children peaked when the time lag between the two signals (i.e. signal from adult and signal from child) was approx. 4s (Piazza et al. 2019, Zhao et al. 2021). The pre-processed signals were averaged across channels within each ROI in the time domain before PTE was applied to measure the neural synchrony between the dyads. As there

were four ROIs (bilateral TPJ and bilateral prefrontal cortices) for each participant and each ROI could potentially become synchronised with any ROI of the other participant, this resulted in 32 PTE values for each dyad i.e., 16 for each directionality (information flow from child to mother i.e., C2M or from mother to child i.e. M2C).

6.2.7 Statistical analysis

Statistical analysis was performed on IBM SPSS Statistics (version 27.0) (Corp 2020). Pearson's correlations were used to explore the relationships between the behavioural measures and turn taking (i.e., number of turns completed by each pair averaged across the two interactive sessions) and linear regressions were used to explore how behavioural measures and turn taking influenced the neural synchrony between the pairs. Histograms and the Shapiro-Wilk test confirmed normality of the distribution of PTE, age and standardised behavioural assessments. Repeated measures ANOVAs were performed to explore the effects of condition, direction, and ROI on neural synchrony. PTE was the dependent variable, and condition (interactive vs. independent play), directionality (child to parent vs. parent to child) and ROI (left TPJ, right TPJ, left PFC and right PFC) were the independent variables. The threshold for statistical significance was set at $p < 0.05$. To counteract the problem of multiple comparisons the Bonferroni corrections were applied to the correlation analyses and the post hoc multiple comparisons.

6.3 Results

6.3.1 Behavioural Results

Correlation analysis was performed to investigate the relationship between manually annotated turn taking, maternal emotional regulation, maternal age, and child temperament. There was no statistically significant association between turn taking and any other behavioural measure (surgency: r(10) = -.194, p = .547 , Bonferroni corrected for 5 comparisons, effortful control: r(10) = -.136, p = .674, Bonferroni corrected for 5 comparisons, cognitive reappraisal: r(10) = -.069, p = .830, Bonferroni corrected for 5 comparisons), but a weak negative correlation was found with the child's negative affect (r(10) = -.35, p= .27, Bonferroni corrected for 5 comparisons) and the mother's expressive suppression (r(10) = -.38, p = .23, Bonferroni corrected for 5 comparisons). Maternal age was also weakly correlated with expressive suppression (r(10) = -.527, p = .078, Bonferroni corrected for 5 comparisons) but no other behavioural measure (surgency: r(10) = -.011, p = .972, Bonferroni corrected for 5 comparisons, effortful control: r(10) = -.369, p = .237, negative affect: r(10) = .317, p = .315, Bonferroni corrected for 5 comparisons, cognitive reappraisal: r(10) = -.205, p = .524, Bonferroni corrected for 5 comparisons).

6.3.2 Neural synchrony during free play

We used fNIRS to measure neural synchrony in the mother-child pairs simultaneously while they played together (interactive condition) and separately (independent condition). fNIRS data were analysed across four regions (left and right temporo-parietal areas and left and right prefrontal

areas) using PTE which also provides information on the direction of the connectivity i.e., mother to child or child to mother).

Firstly, we investigated the effect of condition and direction on neural synchrony averaged across all ROIs. There was a statistically significant main effect of condition ($F(1,11) = 14.93$, $p = .009$, Bonferroni corrected for 3 comparisons). However, there was no effect of direction ($p = .07$, Bonferroni corrected for 3 comparisons) or an interaction between condition and direction ($p = .055$, Bonferroni corrected for 3 comparisons). Post hoc paired t-tests showed that neural synchrony in the interactive condition was statistically significantly higher compared to the independent condition (mean dif = .053, df=11, p =.003). The effects of condition were also significant after controlling for child's gender ($F(1,10) = 14.12$, $p = .024$, Bonferroni corrected for 4 comparisons).

We also performed an exploratory post hoc analysis for the interaction between condition and direction (even though it was not statistically significant). Descriptive statistics showed that in both the interactive and independent conditions C2M neural synchrony (Interactive mean = 1.16, SD = .020, independent mean = 1.08, SD = .023) was lower compared to the M2C neural synchrony (Interactive mean = 1.17, SD = .016, independent mean = 1.147, SD = .022). Paired t-tests showed that C2M and M2C neural synchrony were not statistically significantly different in either condition (independent: mean dif = -.07, p = .052; Interactive: mean dif = -.012, p = .557). However, when comparing neural synchrony in each condition for each direction, child directed neural synchrony was statistically significantly higher in the

interactive compared to the independent condition (mean dif = .08, df=11, p < .001). There was no statistically significant difference between conditions for the mother directed neural synchrony (mean dif = .025, df=11 p = .337) (figure 6.2).

However as stated above, since there wasn't a statistically significant main effect of direction or a statistically significant interaction between direction and condition, further analysis was conducted using the average neural synchrony between the two directions.

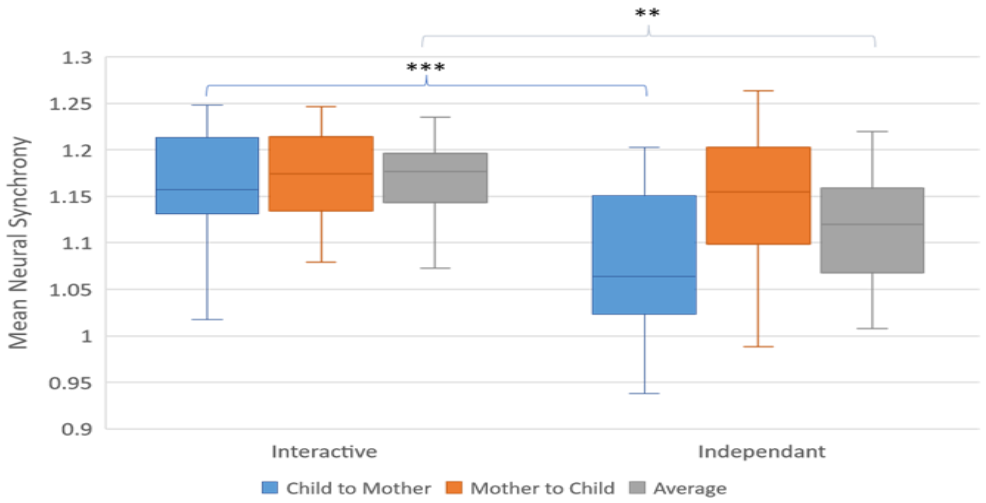


*Figure 6.2 Boxplots of mean neural synchrony across all ROIs in the interactive and independent condition. Bars represent neural synchrony for the two directions (child to mother in blue & mother to child in orange) and the average of the two in grey. Neural synchrony in the interactive condition was statistically significantly higher compared to the independent condition (mean=.053, p=.003). Child to mother neural synchrony was significantly higher in the interactive compared to the independent condition (mean=.08, p<.001). **p<.01, ***p<.001 (Bonferroni corrected).*

Subsequent analysis to determine whether there was an effect of region in the neural synchrony between the mother's and the child's brain areas found no evidence in either condition (child hemisphere: (F(1,11) = 2.44, p = .147, Bonferroni corrected for 3 comparisons), child region (F(1,11) = 4.37, p = .61,

Bonferroni corrected for 3 comparisons), mother hemisphere (F(1,11) = 3.24, p = .099, Bonferroni corrected for 3 comparisons), mother region (F(1,11) = 2.29, p = .159, Bonferroni corrected for 3 comparisons).

6.3.3 Neural synchrony in relation to turn taking

We assessed whether the observed increased neural synchrony in the interactive condition could be attributed to the conversational patterns of the pairs. A linear regression showed that turn taking was not a predictor of neural synchrony (F(1,10) < .001, p = .986) (Table 6.1).

Model	*Regression analyses of turn taking as predictor of neural synchrony*				
Variable	B	95% CI	β	t	p
(constant)	1.17	[1.05 1.28]		22.254	.000
Turn taking	-.001	[-.004 .004]	-.006	-.018	.986

Table 6.1 Regression analysis summary for turn taking as a predictor of neural synchrony. Note: R^2 adjusted <.001, CI = confidence interval for B

6.3.4 Neural synchrony in relation to personal characteristics

Maternal factors

We hypothesised that maternal emotion regulation might be a predicting factor of neural synchrony during the interactive condition. However, results showed that neural synchrony between the pairs was not affected by either cognitive reappraisal (F(1,10) = .144, p = .712, Bonferroni corrected for 3 comparisons) or expressive suppression (F(1,10) = .13, p = .726, Bonferroni corrected for 3 comparisons), nor a combination of the two (F (2,9) = .087, p = .917, Bonferroni corrected for 3 comparisons). Maternal emotion regulation was also not a predicting factor of the mother to child direction of the

synchrony (cognitive reappraisal: F(1,10) = .223, p = .647, Bonferroni corrected for 3 comparisons, expressive suppression: F(1,10) = .001, p = .978,Bonferroni corrected for 3 comparisons, combination: F(1,10) = .13, p = .88, Bonferroni corrected for 3 comparisons.

Child Factors

Child temperament was also considered as a potential candidate for predicting neural synchrony. We found that the combination of child temperament variables (negative affect, effortful control and surgency) did not significantly predict neural synchrony in the interactive condition (F(3,8) = 1.89, p = .21, R^2 = .415, Bonferroni corrected for 4 comparisons). However, when examined separately, child surgency was found to be associated with neural synchrony (F(1,10) = 6.4, p = .03). This factor explained 39.0% of the variance in neural synchrony (R^2 = .390). Further correlations showed that neural synchrony was negatively moderately correlated with child surgency (R(10) = -.625, p = .03) (figure 6.3). Similar results were found between C2M neural synchrony and child surgency (linear regression: F(1,10) = 13.56, p = .004, R^2 = .576; bivariate correlation: R = -.759, p = .004).

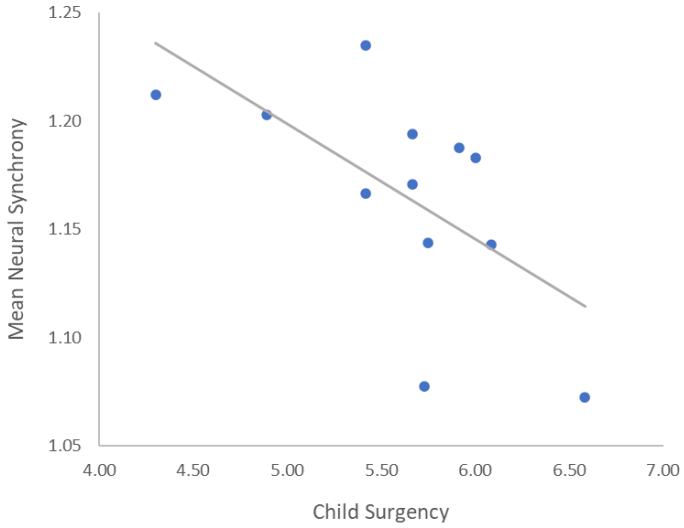


*Figure 6.3 Correlation between child surgency (x-axis) and mean neural synchrony in the interactive condition (y-axis). (R=-.625, p=0.03). Line of best fit equation: y=1.46-0.05*x*

6.4 Discussion

This study examined the neural synchrony between pairs of mothers and their young children under naturalistic conditions. In contrast to previous work that has established the presence of neural synchrony between parent-child pairs during problem solving-oriented tasks, we employed a free play paradigm where participants did not have a specific goal and could interact freely. As hypothesised, we showed higher levels of neural synchrony between the dyads in the interactive condition compared to the independent condition. This finding validates the use of free play paradigms in investigations of neural synchrony between parents and their children. We also explored the influence of turn taking and maternal and child personality traits on neural synchrony, but no strong association between any of the relationships examined was found.

Neural synchrony was significantly higher in the interactive compared to the independent condition over bilateral prefrontal areas and the bilateral temporoparietal junction. This is in line with previous research that has reported synchrony in prefrontal areas during parent-child cooperative performance (Reindl et al. 2018, Miller et al. 2019, Nguyen et al. 2020). These regions are also involved in attention and executive functioning, indicating that these processes support neural synchrony especially during cooperative interactions (Azhari et al. 2019). The TPJ is also recruited during interpersonal interactions as it is associated with language processing, self-reference and processing of one's own and others' mental states (Monticelli et al. 2021).

Further analysis into connections between specific ROIs between mother and child did not reveal an effect of hemisphere or region.

Consistent with previous work, we also found no effect of child gender on neural synchrony (Reindl et al. 2018, Azhari et al. 2019, Nguyen et al. 2020). However, previous studies of neural synchrony between adults suggest that there are differences in synchrony between same-sex pairs, compared with mixed-gender pairs (Cheng et al. 2015). Additionally, Miller and colleagues reported that in their sample mother-son dyads showed less synchrony than mother-daughter pairs in the control task but no differences in the cooperation task, perhaps reflecting differences in how their mother-son pairs approached the tasks (Miller et al. 2019). Nonetheless, it would be interesting to further explore whether child gender affects parent child interactions and the neural synchrony between them with larger sample sizes and across different developmental stages. It is also worth noting that in this study we only recruited pairs of children and their biological mothers. Initial findings have demonstrated that similar neural synchrony is present during biological father-child interaction (Azhari et al. 2021, Nguyen et al. 2021). It would be of great scientific, as well as ecological, interest to continue this work and further investigate neural synchrony in father-child pairs as well as carer-child pairs (where the adult is someone other than the child's biological parent, such as an adoptive parent, grandparent, or other primary caregiver).

Neuroimaging data from the pairs were analysed using PTE, which allowed us to also investigate the directionality of the neural synchrony. Even though the

effect of direction did not reach the assigned levels for statistical significance, it is worth mentioning that C2M neural synchrony in the interactive condition was statistically significant compared with the independent condition. A similar difference was not found for M2C neural synchrony. This might be an indication that the neural synchrony between the dyads could be primarily driven by the child. Similarly, Quiñones-Camacho et al. suggested that the neural synchrony in their set up might be driven by child-related, and not maternal characteristics (Quiñones-Camacho et al. 2020). However larger sample sizes and further work would be required to properly explore this.

In this study, participants were instructed to play as they would at home, be that interactively or separately; they were not explicitly told to collaborate, communicate, or aim for a specific goal. Nonetheless, despite the pairs being permitted to approach the task as they pleased, and despite varying degrees of communication between each dyad, higher neural synchrony was measured in the interactive condition compared to the independent one. Even though it is reported that levels of neural synchrony are affected by the intensity and type of the interaction (Gvirts and Perlmutter 2020), our findings are also corroborated by investigations in both adult dyads and parent-child dyads with similar paradigms, demonstrating significant levels of neural synchrony when dyads interact in low demand contexts (Piazza et al. 2020, Nguyen et al. 2021). Quiñones-Camacho at el. showed similar levels of neural synchrony when parents and toddlers completed a goal-oriented task and an unstructured free play task (Quiñones-Camacho et al. 2020). Above chance-level neural synchrony was also observed during face-to-face mother-child

and adult pair conversations (Jiang et al. 2012, Nguyen et al. 2021). A possible explanation of the presence of high neural synchrony in the absence of a complex, goal-oriented task is the setting of, and the interacting partners in, these low-demand interactions (Gvirts and Perlmutter 2020). Neural synchrony appears to be enhanced when partners are facing one another (Jiang et al. 2012, Jiang et al. 2017) and are sharing gazes and smiles (Nguyen et al. 2020, Piazza et al. 2020). Additionally, neural synchrony is fostered when interacting with "familiar" and "significant" partners and when exhibiting joint attention to mutually important stimuli (Kinreich et al. 2017, Pan et al. 2017, Djalovski et al. 2021). However, not all of these behaviours are required for neural synchronisation of individuals. For instance, it has been shown that neural synchrony can arise during verbal communication and joint computer games even if participants are unable to see each other (Ahn et al. 2018, Pérez et al. 2019). Conversely, it has been suggested that mutual eye gaze is a fundamental interactive stimulus that is associated with increased neural synchrony (Noah et al. 2020). Therefore, mechanisms that support neural synchrony appear complex and multifaceted. In this study, neural synchronisation was perhaps due to the fact that interacting partners were biological mothers and children who were able to exchange both verbal and non-verbal communication cues. It is possible that these factors "compensated" for the lack of a goal-oriented task and sustained face to face interaction. This finding is exceptionally important when considering its implications for examining neural synchrony in clinical populations with speech, communication, and behavioural disorders. Children with

communication problems are often unable to complete complex tasks that require verbal communication and/or sustained attention due to their poor language outcomes and behavioural difficulties that might stop them from completing (Wintgens 2013, Hollo and Chow 2015, Hage et al. 2021). Additionally, behavioural studies have highlighted time and time again that low quality parent-child interactions can have a negative impact on childhood development (Bornstein and Tamis-LeMonda 1989, Baumwell et al. 1997, Simpkins et al. 2006, Takeuchi et al. 2015, Justice et al. 2019, Scheiber et al. 2022). As a result, parent-implemented therapies, that target parent-child interactions and train parents how to optimally interact with their children, have been shown to be highly effective (McConachie and Diggle 2007, Thomas et al. 2017, Rieth et al. 2018, Curtin et al. 2021, Koly et al. 2021, Lyons et al. 2022, van Noorden et al. 2022). Deploying paradigms that would allow investigations into neural synchrony in these populations can offer valuable insights into the neural underpinnings of communication disorders as well as the mechanisms that drive the efficacy of parent implemented therapies. This could, in turn, help clinicians better evaluate the effects of their parent-implemented therapies and use it to personalise goals to ensure better outcomes for the child.

A secondary aim of this study was to explore the relationship between turn-taking and neural synchrony. Previous studies have found a positive correlation between turns and neural synchrony in adult dyads (Wilson and Wilson 2005, Stephens et al. 2010, Hasson et al. 2012, Ahn et al. 2018, Pérez et al. 2019). Nyugen et al. also presented similar findings during conversations

between mothers and children (Nguyen et al. 2021). However, such a relationship was not identified in the current study. One possible explanation might be the way turn taking was coded. In the present study, given the relatively young age of the participants, only relevant and alternating turns were included in the analysis as those would indicate more definitively that the participants - especially the children - were paying attention to one another. Another possible explanation for the lack of association between neural synchrony and turn taking may be the requirements of the task. The dyads were asked to 'just play', and direct communication between the pair was not required for successful completion of the task, therefore allowing less turns to be taken. Ergo, the activities the dyads have been asked to carry out could heavily affect the degree of correlation between neural synchrony and turn-taking.

A further aim of this work was to examine whether personality traits of both the mother and the child influenced neural synchrony. Previous studies have reported that emotional regulation as well as child temperament can affect neural and behavioural synchrony between parent child dyads (Azhari et al. 2019, Santamaria et al. 2020, Hoyniak et al. 2021, Quiñones-Camacho et al. 2021). In this study we observed that child surgency was negatively correlated to neural synchrony. Surgency characterises individuals that are cheerful, responsive, and impulsive (Putnam et al. 2001, Oldehinkel et al. 2004). Surgency in children can support relationships with their peers and help children to be socially competent (Putnam and Stifter 2005, Rimm-Kaufman and Kagan 2005). However, behavioural studies also suggest that surgency

can be maladaptive, leading to higher levels of externalising behavioural problems such as aggression (Gunnar et al. 2003, Berdan et al. 2008, Stifter et al. 2008). Additionally, children with high levels of surgency might employ distraction/self-soothing behaviours, which in some contexts might be advantageous (for example when an outcome is delayed) but problematic when faced with goal-oriented situations (Dollar and Stifter 2012). Since interpersonal synchrony requires mutual attentiveness, it is possible that high levels of activity and spontaneity can make a child more distracted by their environment and hinder their ability for neural synchrony with their parent.

We did not find any evidence that suggested that maternal emotional regulation and the other child temperament dimensions (i.e., effortful control and negative affect) were related to neural synchrony. In contrast, Reindl et al. reported a positive relationship between parent and child emotional regulation to their neural synchrony during collaboration, and Azhari et al found that maternal stress levels were negatively correlated with mother-child neural synchrony when the pairs watched a movie (Reindl et al. 2018, Azhari et al. 2019).In our study we did not measure maternal stress so we cannot speculate on how it might associate with our neural synchrony measurements. We might not have been able to detect an association between maternal emotional regulation and neural synchrony due to our small sample size. Additionally, Reindl and colleagues deployed a paradigm with higher-demands i.e., cooperative computer game which might have resulted in a higher degree of neural synchrony compared to our lower-demands interactive free play paradigm. That might have also accounted for

the lack of association between maternal factors and neural synchrony in our study.

Limitations

Our study had a few limitations. To begin with, participant recruitment was performed during the summer of 2021 amidst the ongoing Covid-19 pandemic, which led to our relatively small sample size. Even so, despite the relatively small sample size of 12 dyads, the study accomplished its aim of exploring the feasibility of measuring the relationship between neural synchrony and turn taking using a free play paradigm. Furthermore, the data from the dyads were analysed at group level and some research suggests that small sample size matters more for the analyses of individual differences than for the group analyses (Lakens and Evers 2014). It's important to note that when analysing the fNIRS data, given the emerging nature of the field, we drew from both prior research and exploratory pilot studies conducted by our team. As a result, we chose to extrapolate the PTE signal within the frequency range of 0.05-0.2Hz and set the time delay between brain signals at 4 seconds. It's highly probable that if a different frequency range had been chosen, it would have impacted the duration of the time delay, as this delay is dependent on the length of the frequency cycle (Fraschini 2017). Therefore, in future investigations, researchers should carefully examine their data to determine the most suitable frequency range and subsequently establish the most appropriate time delay. Additionally, it is well documented in behavioural investigations of synchrony and parent-child interactions that the

nature of the parent-child relationship evolves as the child grows up (Farran and Kasari 1990, Davis et al. 2018), thus longitudinal studies would be valuable in understanding how neural synchrony changes over a child's development. Thirdly, it is well documented that mutual eye gaze promotes interpersonal and inter-brain synchronisation (Hirsch et al. 2017, Dravida et al. 2020), Kelley et al. 2020, Noah et al. 2020). However, our video recording setup did not allow us to perform analysis on non-verbal behavioural cues such mutual eye gaze that could have offered additional information on the factors influencing neural synchrony. For that reason, in subsequent studies, we will employ eye tracking glasses that continue to allow for naturalistic experimental set ups but also capture eye gaze data (Nivetha Saravanan In Preperation). Furthermore, it's important to note that in our current study, we used the basic turn-taking metric to assess conversational patterns. However, future research endeavours could consider incorporating more comprehensive analyses to gain a deeper insight into the relationship between verbal communication patterns and patterns of neural synchrony. These additional analyses might encompass factors such as the total time each participant spends speaking, the number of utterances made by each speaker, and the relevance of responses (e.g., whether the speaker addresses the same thematic content as the previous speaker). Lastly, fNIRS has poor depth penetration that does not allow imaging of subcortical regions(Fukui et al. 2003)., Our fNIRS machines are wired and so they require participants to stay in one place. Truer naturalistic play may be recorded via the use of

wireless fNIRS set ups that do not have such strict restriction on movement around a room.

6.5 Summary

This study investigated examined neural synchrony between mother-child dyads in a low-demand free play paradigm. We found neural synchrony significantly increased while the pairs played together compared to when playing separately. These findings provide valuable evidence of neural synchrony in naturalistic interactions. The observed link between neural synchrony and child surgency suggests that the child's ability to engage with their parent is fundamental to the quality of parent child-interactions. Given the importance of mother-child interactions in childhood development, the findings of this study can form the foundations for future investigations of the neural underpinnings of parent-implemented therapies as well as neural synchrony in pre-lingual children and/or children with communication needs.

7 Opinions of clinicians and parents

This chapter has been adapted from:

Papoutselou, E., Harrison, S., Wiggins, I. and Hartley, D., under review. Clinicians' and parents' opinions of an objective measure of speech understanding for use in paediatric cochlear implant settings. Manuscript submitted for publication April 2023, International Journal of Language & Communication Disorders

Author contributions: EP and DH conceived and designed the study, EP collected the data, EP and SH performed the analysis, EP wrote the paper, SH, IW and DH revised the paper.

7.1 Chapter Overview

This chapter details the results of a qualitative survey of parents of children with DLD and clinicians working with children with DLD. The survey was conducted in the summer of 2020. Parents and clinicians were asked to provide their opinions on a neuroimaging-based tool for the diagnosis and monitoring of interventions for DLD. More specifically, given the variability in managing DLD, clinicians discussed the clinical pathways they currently use for the diagnosis and intervention of DLD. Parents and clinicians commented on the ideal age for the identification of DLD and the factors that would influence them when considering whether to support a neuroimaging tool for DLD. Lastly, given that parents would be the ones consenting on behalf of their child for any assessment to be done, they were asked how they would want a neuroimaging tool to be used for the diagnosis of DLD and the monitoring of interventions.

7.2 Methods

7.2.1 Participants

Forty-four parents of children with DLD (5 male) and forty-three clinicians working with children with DLD (1 male) completed a parental and clinician's survey, respectively. All participants were older than 18 years old. Detailed characteristics of both groups are presented in the Results section.

Both surveys were available online and the survey links were advertised through social media. The parental survey was also promoted by charity organisations working with children with DLD and their families such as "Afasic -Voice for Life", "I CAN" and "The Children's Communication Charity". The clinicians' survey was also shared with DLD professionals by the Association of Speech and Language Therapists in Independent Practice and the Royal College of Speech and Language Therapists.

Each participant gave informed consent prior to completing the survey. The study was approved by the University of Nottingham Faculty of Medicine and Health Sciences Research Ethics Committee (ref no: 37-0620).

7.2.2 Measures and Procedure

The surveys were hosted using the JISC platform and consisted of multiple-choice questions and free text questions. Questions for the clinicians' survey were developed in collaboration with professionals with paediatric and communication disorder experience. The advice of parents with children with speech and language difficulties was also sought when developing the parents' questionnaire. The surveys were also reviewed by the Biomedical

Research Centre Hearing Sciences Patient and Public Involvement Steering Group.

Both surveys included four basic demographic questions (age, gender, education level, employment). Parents were asked questions with regards to their child with DLD (age of child, age of DLD diagnosis etc) whereas clinicians were asked about their professional experience with DLD (years of experience, diagnostic and intervention pathways). In the core part of the surveys both groups were given a detailed explanation of how a neuroimaging tool like fNIRS might be used for diagnosis and monitoring of DLD. Subsequently, they were asked to comment on the suitability, acceptability, and potential benefits and/or disadvantages of such a tool. All questions were required to ensure participant compliance except for an optional question at the end where participants could express any other thoughts/comments or feedback. The option "Prefer not to say" was offered in the multiple-choice demographic questions. The full surveys can be found in the *Appendix* section 9.4.

7.2.3 Data analysis

7.2.3.1 Quantitative

Descriptive statistics were used to present the key sample characteristics. Frequencies and percentages were calculated for categorical variables and means, and their standard deviations were used for continuous variables. Results were presented in bar charts using the statistical software SPSS v.27 (Corp 2020).

7.2.3.2 Qualitative Data

Answers to open ended questions were analysed on NVivo 11/12 (QSR International Pty Ltd., 2015) using an inductive thematic analysis approach and the formal steps of thematic analysis (Braun and Clarke 2006) were followed as described below. Two independent researchers (EP and SH) examined the raw data extensively to familiarise themselves with its contents and categorise it into thematic codes. Coding was compared and any discrepancies were discussed until an agreement was reached between the two raters.

7.3 Results

7.3.1 Demographics & DLD experience

Forty-three clinicians (mean age: 42.35, SD= 10.45) completed the survey out of which only one was male (2.3%). All responders were Speech and Language Therapists (SLTs) who had either a Bachelor's (48.8%) or a master's degree (51.2%) and had on average 15.45 years (SD=8.88) of experience working with children with DLD.

Forty-four parents (mean age=39.98, SD=7.42) filled in the survey. Five had completed up to secondary education (11.4%), ten had completed further education (22.7%), fourteen had received a bachelor's degree (31.8%), thirteen a master's degree (29.6%), and two had received a Doctorate (4.5%). The average age of their children, at the time the survey was taken, was 8.95 (SD = 4.41) and the mean age of their child's DLD diagnosis was 6.14 years (SD = 3.65). The children received a diagnosis on average 3.30 years (SD = 3.71)

after the parents had initially sought help for their child's speech and language concerns. It is noteworthy that the time from referral to diagnosis was highly variable and ranged between 0 months to 14.33 years.

7.3.2 Current Clinical Pathways

Clinicians were asked to describe the clinical pathway that a child might follow once they are identified as potentially having DLD. Clinicians discussed the diagnostic process, the available interventions, and the monitoring of the child's progress. The themes that emerged from their responses were diagnosis, rehabilitation and change of strategy. These are elaborated upon in the following paragraphs.

7.3.2.1 Diagnosis

Clinicians described the process they would follow to diagnose a child as having DLD. Within this theme, they highlighted that the diagnosis for DLD is given over time and relies on monitoring the progress of the child. The following subthemes emerged: Case history and Assessments.

7.3.2.2 Case history

First, SLTs said that they would collect a child's case history, including information from the child's schools, their parents and other professionals involved in the child's care:

> *"Discussion with teaching and support staff as well as SENDCo, examination of school work, discussion with any other professionals involved" PT1: Female SLT, 41 yo*

7.3.2.3 Assessment

Responders described the types of assessments they would use to provide a diagnosis of DLD. These included standardised formal assessments (e.g., CELF-5) and clinical observations either at a home or during school visits. Some SLTs evaluated the impact of the deficiency on a child's everyday life when considering whether the child had DLD. They also relied on their previous clinical experience and informal assessments:

> *"The main thing I would be looking at are functional impact of language disorder." PT28: Female SLT, 36 yo*

> *"We might go and observe the child in school." PT20: Female SLT, 30 yo*

Clinicians highlighted that sometimes when using the currently available assessments they might not be able to give a definitive diagnosis of DLD, in which case they would consider a differential diagnosis while monitoring the child's progress. However, others stressed that a lack of a DLD diagnosis can limit the support children can access at school:

> *"The lack of reliable standardised assessment could jeopardise a child's access to a language class as there are some strict cut off points for standardised scores as part of the application criteria". PT36: Female SLT, 52 yo*

7.3.2.4 Rehabilitation

Clinicians said that children with DLD could receive, as part of their rehabilitation, SLT therapy, home plans and/or support at school. They mentioned that children would be offered blocks of individual therapy with an

SLT, but they stressed that this type of support is usually time restricted due to limited funding and capacity within the healthcare services.

Children might also receive therapy at school. The SLT services would design a programme based on the child's individual needs and train the school staff to deliver it. In some cases, if the school could "buy" SLT time, the therapists might deliver the intervention directly. However, that type of support is only available during term time and cannot be offered to students unless they have an education, health and care plan (EHCP) in place which usually requires an official diagnosis. For children younger than school age, the SLTs would provide treatment plans to be delivered by the parents at home:

> *"Very little direct language therapy done by SLTs. Delivered by school staff." PT18: Female SLT, 44 yo*
>
> *"If under the age of 4 this may be parent training". PT37: Female SLT, 47 yo*
>
> *"1:1 blocks of intervention that are time limited from SALT or SALT assistant". PT19: Female SLT, 33 yo*
>
> *"From KS2 onward students do not receive speech and language therapy unless they have an EHCP". PT30: Female SLT, 32 yo*

7.3.2.5 Change strategies

Clinicians discussed the different strategies they would use if there was uncertainty regarding the diagnosis or a treatment plan or if they needed to make changes to the diagnosis or the intervention a child was receiving.

Within this theme, clinicians highlighted that they would put in place a period of monitoring so that they could continue reassessing the progress and needs of the child.

> *"Continue assessment and observation with a view to establish nature of language disorder." PT09: Female SLT, 53 yo*

Three subthemes emerge:

7.3.2.5.1 Referrals/Second opinion

In this subtheme, participants explained that they would potentially seek out a second opinion from other colleagues and/or refer the children to other services. As a result, they hoped that they would be able to better understand the child's deficiencies in order to offer more appropriate support and to investigate whether a differential diagnosis might be needed:

> *"A second opinion may also be sought from a specialist speech and language therapist". PT30: Female SLT, 32 yo*

7.3.2.5.2 More support

If a child was not making the expected progress under their care plan, many clinicians would take steps to increase the level of support the child was receiving either by offering extra therapy sessions or by liaising with the child's school:

> *"Increased therapy sessions, further investigation into possible underlying barriers (e.g., a processing disorder). Advise parents on statutory assessment with a view to potential EHCP with increased*

support in mainstream school or possible specialist school setting then being considered." PT41: Female SLT, 47 yo

7.3.2.5.3 Less support

However, others explained that, in their setting, if a child was not progressing as expected that might lead to them receiving a lower level of support and potentially being discharged:

"They would move to a lower level of intervention". PT06: Female SLT, 47 yo

"Child likely to have episode closed until school or parent re contact". PT19: Female SLT, 33 yo

7.3.3 When would it be beneficial for parents and clinicians to know whether a child has DLD?

One benefit of a neuroimaging tool would be its ability to help provide a DLD diagnosis earlier that it is currently possible, thus, to begin with parents and clinicians were asked to comment on the ideal age for the diagnosis of DLD.

Both groups agreed that it would be beneficial to be able to identify DLD in prelingual children; 81.8% of parents (36 responders) and 86% of clinicians (37 responders) (figure 7.1).

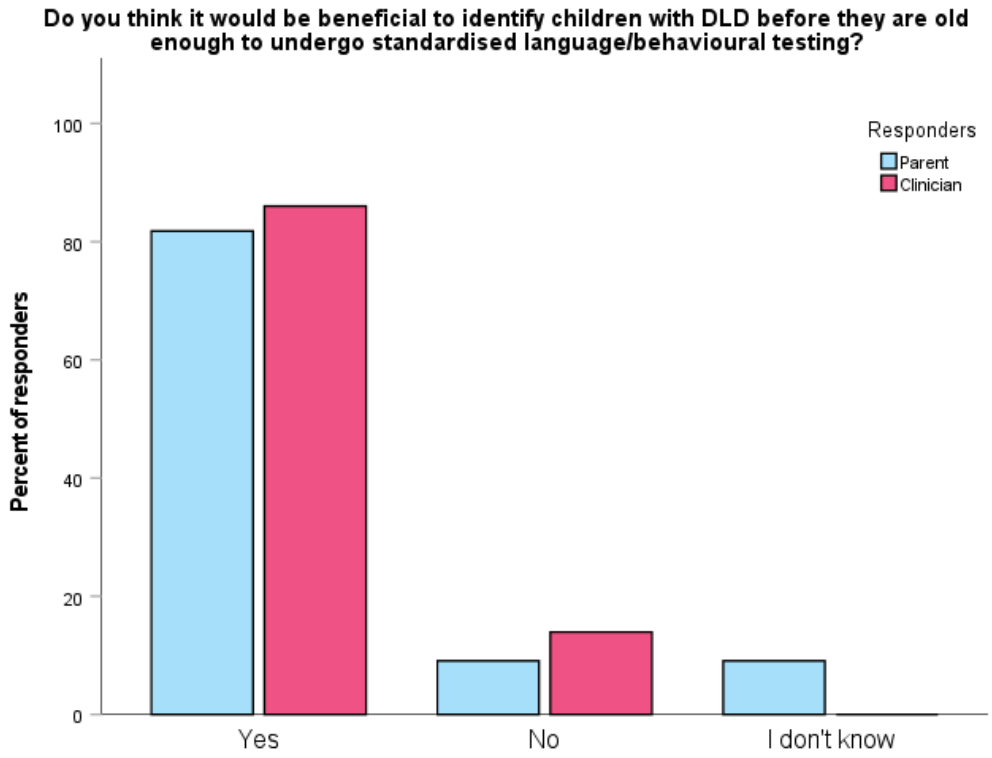


Figure 7.1 Bar chart representing parents' (blue) and clinicians' (pink) responses to whether it would be beneficial to know whether a child was likely to have DLD before they were old enough to demonstrate their language abilities behaviourally. Y-axis represents percent of responses.

Most parents would like a diagnosis as early as possible with 79.6% (35 responders) wanting to know by the time their child was 3 years old (43.2% between 0 and 18 months and 36.4% between 18 and 36 months old). However, 20.5% of parents thought a diagnosis of DLD would be beneficial when their child was 3 to 5 years old (figure 7.2).

Clinicians in general were more conservative with 44.2% considering the ideal age for diagnosis between 3-5 years old. 16.3% of clinicians thought children should be diagnosed with DLD between 0 to 18 months old, 30.2% between the ages between 18 and 36 months old and 2.3% between 5 and 6 years old (figure 7.2).

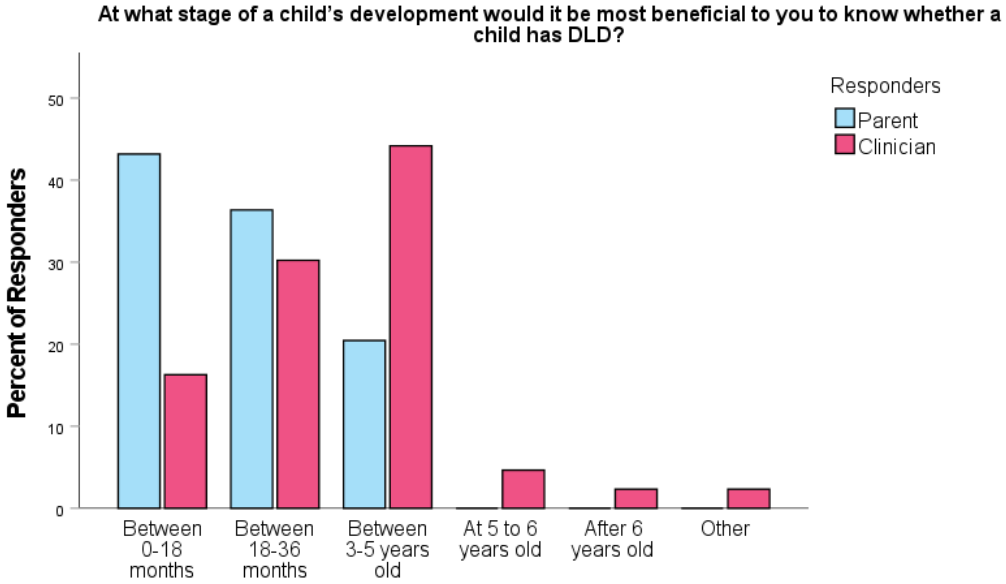


Figure 7.2 Bar chart representing parents' (blue) and clinicians' (pink) responses to the question "At what stage of a child's development would it be most beneficial to you, as a parent, to know whether your child has DLD?". Y-axis represents percent of responses.

When analysing participants' explanations regarding their ideal age of diagnosis, the following themes emerged: Future outcomes, Feeling prepared, Parental engagement, Effectiveness of intervention, and Accuracy.

7.3.3.1 Future Outcomes

Many responders, particularly parents, cited that the clinical diagnosis of DLD opens access to therapeutic interventions and, consequently, better outcomes for their children. Thus, many believed that an earlier diagnosis

than is currently possible may reduce the negative impact of DLD on a child's language and socio-behavioural development:

> *"This would allow us to implement the necessary advice /support at an earlier stage before their DLD becomes more severe and (hopefully) reduce the impact on child's academic attainment, mental health and social communication/interaction." PT02: Female SLT, 32 yo*

> *"Early identification and treatment is key and the window for early intervention is small. Support for language development is not harmful so risk is minimal." PT01: Female SLT, 41 yo*

However, some participants in the clinicians group felt that depending on how the tool was used to provide a diagnosis for prelingual children, it might have the opposite effect with some children receiving less support:

> *"The cut-off points are likely to be controversial and may lead to inequalities of access to services." PT33: Female SLT, 52 yo*

7.3.3.2 Feeling prepared

Both clinicians and parents felt that a diagnosis would help them prepare themselves on how to help the child. They argued that an earlier diagnosis may provide them with more time to find appropriate resources and support:

> *"Had I had known that he was 'high risk' of having it I could have put things into place and educated myself". PT20: Female Parent, 40 yo*

> *"If there was a non-invasive test that could be run even earlier, e.g., 1-*

2 years it would give huge insight for us professionally but also allow us to give more tailored support to both children and families." PT28: Female SLT, 36 yo

7.3.3.3 Parental engagement

Clinicians believed that an earlier diagnosis would allow them to engage with the parents and, vice versa, parents felt that an early diagnosis would facilitate their interactions with clinicians to benefit their child's care:

"We will be able to provide needed medical attention". PT15: Female Parent, 41 yo

"It would be helpful to convince parents of the importance of learning to sign to support comprehension, for example. They might engage more if we could say that we know their child will have persisting difficulties with language." PT25: Female SLT, 53 yo

However, others thought that a diagnosis before the language deficiencies had a functional impact on the child's day-to-day life might have a negative impact on parents and clinicians:

"I think as parents we can worry too much, and children develop in different ways and times. It would have been helpful to have it identified before his current age though." PT44: Female Parent, 41 yo

"I think that, before the age of 18 months (or possibly even later), it would be difficult for a parent to really understand DLD and it's (sic) implications." PT30: Female SLT, 32 yo

7.3.3.4 Effectiveness of Intervention

Participants commented that the ideal age for DLD diagnosis would depend on the existing treatment options. Many believed that the available treatment plans are targeted towards older children. Thus, an earlier diagnosis would not have a significant impact, since the current interventions might not be effective before a certain age:

> "S*trategies would be pretty much the same I think and there's no extra support for a child with DLD that I know of." PT07: Female Parent, 37 yo*

7.3.3.5 Accuracy

Participants argued that in some cases a language delay might be resolved as a child grows older. Thus, they were concerned that if diagnostic tools were used too early, they might not be able to provide an accurate diagnosis and differentiate between "late talkers" and those with DLD.

> *"May be easier at this age (5 years old) to differentiate between those will delay who will improve and those who will go on to meet the criteria for DLD." PT19: Female SLT, 33 yo*

However, some parents would welcome a tool that could provide an early and accurate diagnosis to avoid the "wait and see" advice from professionals:

> *"I had never heard of this I knew obviously of speech issues, but I feel we failed him and could have done something sooner, it was always a case of. Oh I didn't talk till I was twenty and I'm now a neuro surgeon."*

PT22: Female Parent, 38 yo

7.3.4 What factors would influence parents and clinicians to support a neuroimaging tool for DLD?

Clinicians and parents were further asked with free text questions to describe the factors that would influence them to adopt and accept a neuroimaging tool as part of the diagnostic and monitoring pathway for DLD. The following themes emerged: Consequences of result, Practical Considerations, Tool metrics.

7.3.5 Consequences of result

When discussing the adoption of a new tool, clinicians and parents considered the consequences of the test results for access to treatment and further support.

Some participants highlighted that a neuroimaging tool might be helpful but were concerned with the access to support after the test results:

"Availability of remedial and preventative treatment soon after identification." PT01: Female SLT, 41 yo

"Transparency of the support that might be offered based on such monitoring tests". PT26: Female Parent, 42 yo

Parents, also, noted that the test results needed to be recognised by schools and funding bodies as that would affect the support that their child can access:

"Whether the diagnosis was recognised by schools, helped schools get

funding to support my child etc." PT07: Female Parent, 37 yo

7.3.6 Practical considerations

Participants in both groups identified a wide range of practical considerations that were subdivided in the following subthemes: Accessibility, Child comfort, Cost, Ease of use, Location, Support from parents and clinicians, Compatibility with other assessment, Service administering the test, Clarity/ Interpretation of result, Time and Safety.

7.3.6.1 Accessibility

Clinicians were concerned with how accessible a neuroimaging tool would be to the families. A main point being whether the tool would be appropriate for bilingual and families who have English as an additional language:

"Language barriers – i.e., if parents are unable to access services in their own language – it's hard for the NHS to adapt this to make it accessible." PT13: Female SLT, 27 yo

7.3.6.2 Child Comfort

Participants also highlighted the importance of child comfort and non-invasiveness of the equipment during testing:

"From a service-user point of view it needs to be comfortable and not onerous". PT33: Female SLT, 52 yo

"If it would cause my child distress". PT11: Female Parent, 46 yo

7.3.6.3 Cost

Parents as well as independent and SLTs working within the NHS discussed cost as a factor that would influence their decision to adopt a new diagnostic tool:

> *"I'd be open to all however cost could be an issue within NHS". PT20: Female SLT, 30 yo*
>
> *"Expense I am an independent practitioner so I would not be able to afford a very expensive product". PT37: Female SLT, 47 yo*

Clinicians also commented on the additional resources and training that might be required. They were concerned with the additional cost that would be accrued when required to re-train staff and purchase resources:

> *"The time/expense of training could discourage managers". PT34: Female SLT, 29 yo*

7.3.6.4 Ease of use

Another practical concern that emerged particularly in the clinicians' group was the need for a tool that would be easy to use and administer:

> *"Ease of administration especially with younger children – (short attention span)". PT36: Female SLT, 52 yo*

7.3.6.5 Location

Participants in the parent group discussed the importance of the location of the testing. The distance they would have to travel to access the tool as well

as potentially being in an unfamiliar environment would influence their decision on whether to support its adoption:

> *"Overly long distance to reach a clinic that utilizes the device". PT36: Female Parent, 31 yo*

> *"It should be done in school/nursery where the child feels comfortable, and the parent is able to attend". PT14: Female Parent, 31 yo*

7.3.6.6 Support from parents and clinicians

Parents thought it was also important that any new tool should be recommended by clinicians and, respectively, clinicians believed that it was vital for parents to be supportive of any new test:

> *"Discuss with parents". PT21: Female SLT, 35 yo*

> *"Concerns raised from professionals". PT06: Female Parent, 50 yo*

7.3.6.7 Compatibility with other assessments

Both groups of participants agreed that an objective new tool should be used as an adjunctive tool rather than replacing existing measures. They thought subjective measures of the child's behaviour and progress such as clinical observations and functional impact of DLD should remain in the roster of tools for the diagnosis and monitoring of DLD:

> *"I am concerned that a monitoring tool might produce different results from what professionals and parents are seeing in their environment". PT06: Female SLT, 47 yo*

"As long as the tool is not used in isolation. I'd want it to be part of a wider assessment of progress". PT07: Female Parent, 37 yo

7.3.6.8 Service using the tool

In this subtheme, clinicians and parents discussed the role and characteristics that the service using the tool should have. Both groups noted that the staff in the service should be qualified and experienced. There should also be a strong line of communication between the service, the parents and other health professionals involved in the child's care:

"Strong liaison between the testing team and SALT team". PT28: Female SLT, 36 yo

"A test done by someone with no experience". PT32: Female Parent, 28 yo

7.3.6.9 Clarity/Interpretation of result

Another important factor when considering the adoption of a new tool was how clear the results would be and how easy it would be to disseminate them to others:

"If the results were difficult for parents and non-specialist colleagues to understand". PT32: Female SLT, 54 yo

"I would need to be absolutely clear what the results would show". PT25: Female SLT, 53 yo

7.3.6.10 Time

Within the time theme, responders discussed the importance of length of testing and length of waiting period for results.

They highlighted the need for a tool that would not require a lengthy testing paradigm and/or additional appointments as that would not only be uncomfortable for the child but it would also take up a considerable amount of clinician's time:

> *"Additional examinations can be very tiring for our kids as they work hard to try and get through everyday tasks that are simple and come natural to us but not to them". PT24: Female Parent, 37 yo*

> *"If it was quicker than doing other review assessments". PT34: Female SLT, 29 yo*

Additionally, parents and clinicians wanted the results of the new testing tool to be readily available so that they could offer the best possible support as soon as they could:

> *"Shorter time to diagnosis than is currently available". PT03: Male Parent, 38 yo*

7.3.6.11 Safety

Parents were concerned about the safety of any new tool and would want to know any side effects associated with it:

> *"Knowing the test was safe". PT42: Female Parent, 31 yo*

7.3.7 Tool Metrics

Participants in both groups highlighted the importance of certain metric characteristics the tool should have before they could support its implementation. Within this theme three subthemes emerged: Accuracy, Evidence-based and Effectiveness.

7.3.7.1 Accuracy

To begin with, participants wanted a diagnosis and monitoring tool for DLD to be accurate and reliable. Additionally, they would prefer a tool that can provide them with information on the severity and type of a child's DLD, as well as their future outcomes, since that would influence the necessary intervention. Lastly it would be important for any tool to be accurate for children with a more complex clinical picture such as children with genetic conditions and/or children with complex needs.

> *"Accuracy of findings, leading to targeted support leading to improved outcomes". PT02: Female Parent, 38 yo*

> *"Accuracy in terms of measuring outcome based on baseline and retest linked to interventions". PT08: Female SLT, 52 yo*

7.3.7.2 Evidence based

Similarly, responders in both groups described the need for sufficient scientific evidence for the tool:

> *"If there was a strong evidence base… the tool would be more likely to be funded". PT34: Female SLT, 29 yo*

7.3.7.3 Effectiveness

Parents and clinicians reported that any new tool would have to be effective. It would need to provide meaningful information, an accurate diagnosis and the ability to monitor progress:

> *"It actually does what it says it does". PT01: Female SLT, 41 yo*

> *"Proven effectiveness". PT28: Female SLT, 36 yo*

7.3.8 How would parents want a neuroimaging tool to be used for the diagnosis of DLD and the monitoring of interventions?

Children with DLD would be the end users of a potential neuroimaging tool and their parents would be the ones who would provide consent for the procedure. Thus, it was important to explore whether it was acceptable to parents for the tool to be used to alter the care their child received, even if it was part of the clinical pathway. Thus, parents were presented with four different circumstances where the neuroimaging tool could be used and were asked to discuss their opinions.

Quantitative data showed that the 100% parents would support a change in their child's care plan if a neuroimaging tool identified them as having DLD, but that percentage dropped to 81.8% if the tool identified their child as not having DLD (figure 7.3).

Similarly, most parents would be happy for their child's care plan to be changed if a neuroimaging tool indicated that their current treatment was wasn't effective (97.7%). However, that percent also dropped (79.5%) when parents were asked if they would consent to changes in a care plan that was shown to be effective by the neuroimaging tool, but not behaviourally (i.e., in the child's day to day life) (figure 7.3).

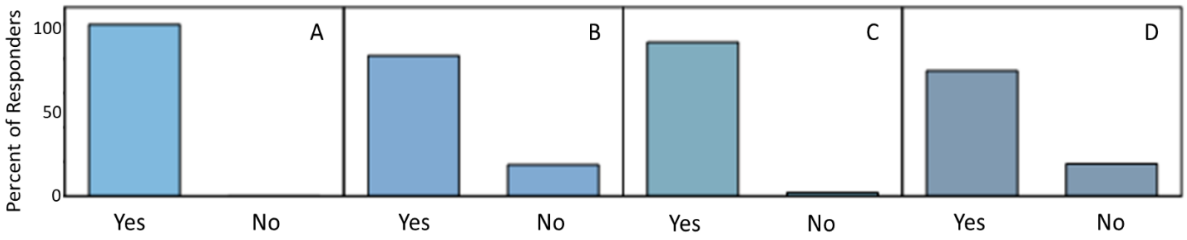


Figure 7.3 Bar charts representing parents' responses to four different scenarios where the neuroimaging-based tool could be used to guide clinical decisions. A) If a diagnostic test, such as the one described above, identified your child as likely to have DLD, would you be happy for their care plan in clinic to be altered accordingly? B) If a diagnostic test, such as the one described above, identified your child as likely to NOT have DLD, would you be happy for their care plan in clinic to be altered accordingly? C) If a monitoring test, such as the one described above, identified that your child's treatment plan is not effective, would you be happy for their care plan in clinic to be altered accordingly? D) If a monitoring test, such as the one described above, identified that your child's treatment plan is effective even though you might not be seeing results in the short-term, would you be happy for their care plan in clinic to remain the same? Y-axis represents percent of responses.

Analysis of the qualitative data where parents explained their reasoning led to the following themes.

7.3.8.1 Doing what's best for the child

To begin with responders highlighted that they would support any diagnosis, treatment plan or change to those because they want to help their child in any way possible. Quotes in this theme can be summarised by the following comment:

"Why wouldn't I? I would want the best possible care for him". PT16: Female Parent, 40 yo

7.3.8.2 Access to support

Parents discussed how a new tool would affect their ability to access support if the tool was used to provide or alter the child's care plan.

Some would welcome test results from a new tool as it could lead to early access to a more tailored and personalised care plan:

"Providing the correct support early is vital to good outcomes". PT23: Female Parent, 43 yo

"I would be happy for her therapy/plan to contain whatever she needed in order to receive appropriate support". PT33: Female Parent, 42 yo

Others, however, were concerned that they might be discharged from SLT services or be unable to access school-based interventions if they did not fit the specific criteria qualifying a child for an EHCP:

"I would want my child to be considered on their needs irrespective of whether or not they fit criteria for a condition". PT07: Female Parent, 37 yo

"I would be worried about them being discharged though". PT09: Female Parent, 51 yo

7.3.8.3 Tool metrics

Similarly, to when considering factors for the adoption of new tool in general, in this case participants also highlighted that in order for them to trust a new tool, it would need to satisfy certain tool metric standards. They strongly felt that the tool should be accurate and effective:

> *"Yes, but for us parents it's important that the test is accurate". PT15: Female Parent, 41 yo*

> *"But with a review within a few months and proof it is working". PT11: Female Parent, 46 yo*

7.3.8.4 Parental involvement

Parents also highlighted that it was vital that any decisions regarding their child's care plan were clearly communicated to them, and their consent was obtained:

> *"With discussion including the parents". PT41: Female Parent, 41 yo*

> *"It would be reassuring if that evidence was shared". PT17: Female Parent, 42 yo*

7.3.8.5 Trust in clinicians

In this theme, parents commented that they would trust a decision if it was recommended by their healthcare team:

> *"You have to trust experts on this". PT37: Female Parent, 40 yo*

> *"I cannot replace a professional". PT23: Female Parent, 43 yo*

7.3.8.6 Timelines for progress

When considering monitoring interventions for DLD with a neuroimaging tool, parents discussed their opinions on the timeline on which progress should be monitored.

Some parents explained that since DLD is a life-long condition, it is expected that sometimes a child's progress will be slow. As a result, they would be willing to adhere to a treatment plan shown by the neuroimaging tool to be working even if the child was not showing progress in the short-term:

> *"Given how long it takes for many therapies to actually work, I would be fine waiting longer if the data showed that it might be valuable." PT03: Male Parent, 38 yo*

Other parents, however, believed that stricter timelines needed to be put in place when judging whether a treatment plan is working. As a result, they would be able to change strategies quickly if their current one was not effective.

> *"I would support altering the plan with a measured time frame to assess the effectiveness of the changes made." PT34: Female Parent, 32 yo*

7.3.8.7 Raising awareness

Lastly, some parents considered that if a new tool could offer additional information regarding the diagnosis of DLD and/or the monitoring of interventions that would be beneficial as it would help raise awareness for the disorder:

"Also, helping improve understanding of the condition in general is an added bonus." PT29: Female Parent, 39 yo

7.4 Discussion

The present study explored the views of parents and clinicians regarding the incorporation of a neuroimaging tool in the diagnostic and treatment pathways of children with DLD. There is a well-documented gap between scientific best practice approaches and actual clinical care (Grol and Wensing 2004, Ploeg et al. 2007, McArthur et al. 2021). One of the reasons is that research endeavours often attempt to change clinical practice or introduce new tools without taking into consideration the opinions and characteristics of the patients, their families and the professionals that care for them (Grol and Wensing 2004). Thus, in parallel to developing a new neuroimaging-based tool for DLD we explored clinicians' and parents' views in order to incorporate their feedback early on the research pathway. Our aim was to better understand the current clinical pathways, the ideal age for diagnosis of DLD, the factors that would influence parents and clinicians whether to support a new tool and lastly parental views on using new tools to alter their child's care plan.

Clinical Pathways

Currently in the UK there is not a standardised pathway for the diagnosis and treatment of DLD. There are no published guidelines by the National Institute for Health and Care Excellence (NICE) for DLD (or language disorders in general). In comparison there are ten published guidelines on autism and

specifically there is guidance on recognition, referral diagnosis, support and management (NICE 2011). The 2017 DELPHI Consensus was instrumental on better defining DLD and thus helping develop some common criteria for the diagnosis of DLD (Bishop et al. 2016, Bishop et al. 2017) but the fact remains that there is a lot of heterogeneity in clinical settings that treat children with DLD. Thus, one of the first things we attempted to explore were the clinical pathways that were followed by the clinicians that took part in this study.

Overall, the diagnostic approach of the clinicians in our sample was consistent and was comprised of considering the child's case history from parents/ carers teachers and other professionals, observing the child either at school or at home and relying on standardised assessments of language. However, clinicians also highlighted the diagnostic process can be particularly lengthy. A child would be identified as being at risk of DLD but would continue to be monitored for a while before receiving a clinical diagnosis. The gap between referral and diagnosis was also reflected by the parents in our sample, who reported that it took, on average, 3 years to receive a diagnosis after they had identified a problem with their child's language development and sought professional help. One possible explanation is the lack of tools that can discriminate between language difficulties that will resolve and those that will persist as a child grows up (Roos and Weismer 2008). Thus, clinicians can sometimes be reluctant to offer a diagnosis before the child has entered formal education, since by that age it is highly unlikely that the child will be able to overcome their language impairment without professional intervention. Additionally, DLD is often manifested through complex

phenotypes. Many children present speech patterns that might resemble that of a younger child and/or might exhibit deficiencies in some but not all linguistic domains (Ellis Weismer 2013). As a result, clinicians would have to spend extensive periods of time with each child to untangle the child's disorder and ensure that a diagnosis of DLD is appropriate. However, given the cost of speech and language therapy, the long waiting lists and the ongoing impact of the Covid-19 pandemic (Confederation 2022), services often cannot offer the support required to diagnose DLD in a timely manner. Introducing a neuroimaging-based tool in the diagnostic pathway for DLD could be instrumental in reducing the time between referral and diagnosis in a cost-effective manner, and perhaps help clinicians to assess children more reliably and earlier, compared with current practice.

Clinicians also described the treatment pathways that they deploy in clinical settings. Depending on the child's age and severity of the condition, three main routes are available: parent-implemented therapies, teacher-implemented therapies or SLT-implemented therapies. In parent-implemented therapies, the primary carer of a child is trained to support the child's development and incorporate speech and language therapy techniques in the home environment under the guidance of an SLT (Tosh et al. 2017). Research has shown that these can be highly effective in promoting the child's language, social and behavioural development (Tosh et al. 2017). Additionally, they can be help empower families and provide them with life-long tools and techniques (Tosh et al. 2017). However, from the responses in our sample, they didn't appear to be routinely offered to children above the age of 5 years

old. That might be partially because, children spend a large part of their days at school after the age of 5.

Teacher and SLT implemented therapies seemed to be the most offered types of interventions. However, many clinicians highlighted that there was great heterogeneity in the duration, frequency and setting that these were provided. Other than factors such as disorder severity, funding and SLT availability were described as major considerations when considering treatment plans. School-based SLT support requires the student to have an EHCP plan as well as sufficient school funding to contract an SLT. Direct SLT therapy can be provided via the NHS or via independent practitioners. NHS SLT services, due to large waiting lists, often prioritise cases based on need and even then, are unable to offer long term support. Independent services, even though they might have more availability, can be quite expensive. As a result, access to suitable treatment plans resembles a “postcode lottery” as often deprived areas have less well-funded schools and more overburdened NHS service leading to children being unable to receive support (Longfield 2019).

Lastly, in this theme clinicians discussed the different routes to changing a child’s care plan. Many mentioned that if it appeared that the child’s diagnosis or their treatment plan appeared to not suit the needs of the child, they would seek out a second opinion from another SLT or service. They also said that, if possible, they would try to offer more support to the child by retraining school staff and increasing the number and frequency of SLT

appointments. However, if it was not possible to offer more support or it was deemed that more support would not make a functional impact to the child's language outcomes clinicians would reduce the support they would offer and potentially discharge the child from services.

Based on clinicians' accounts of the typical diagnostic and treatment pathways that they implement in their settings, introducing a neuroimaging-based tool could be instrumental. Access to an objective tool that would be relatively cost effective could help address some of the barriers that clinicians are now facing when treating children with DLD. Importantly, such a tool could enable clinicians to provide a DLD diagnosis quicker, thus ensuring better allocation of resources and earlier access to support.

Identification Age

Currently DLD can be reliably diagnosed in children older than 5 years old (Sansavini et al. 2021). In this survey parents and clinicians were asked to comment on which age they considered ideal for DLD identification. Most participants in both groups would like to be able to identify a child with DLD before the age of 5. Parents advocated for the need to be able to diagnose DLD as early as possible and particularly by three years old. They explained that earlier identification could lead to earlier access to interventions and thus better future outcomes for the child. Investigations have shown that early interventions can be particularly effective for language development in children with language deficiencies (Kruythoff-Broekman et al. 2019, Rinaldi et al. 2021).

Additionally, both groups believed that earlier diagnosis would allow parents to better prepare themselves by researching the condition and creating a support system. This, in turn, would also allow them to be more involved in their child's care at critical stages for language development. Clinicians would be able to start allocating resources and monitoring the child's development early on.

Lastly, both sets of participants highlighted two important contingencies against early DLD identification. Firstly, most current interventions are designed and delivered to children above the age of 5, thus identifying DLD earlier would be futile since no treatment could be offered at that stage. However, as discussed earlier there is a wealth of evidence showing the benefits of parent-implemented therapies for language development (Roberts and Kaiser 2011, Levickis et al. 2014, Heidlage et al. 2020, Suttora et al. 2021). These treatments can be administered from infancy and can be highly adaptable to the child's need as they grow up (Roberts and Kaiser 2011, Levickis et al. 2014, Heidlage et al. 2020, Suttora et al. 2021). Secondly, clinicians and parents were concerned about the diagnosis's accuracy given that some toddlers with language delay tend to catch up to their peers. Evidence suggests that there are certain risk factors that indicate persistent language deficiencies that are less likely to resolve with age (Sansavini et al. 2021). However, in the absence of these factors it is currently impossible to predict future outcomes for children with early language delay. Consequently, clinicians have been reluctant to diagnose DLD to avoid causing unnecessary

parental anxiety, but also to preserve resources for children with more severe (and verified) needs.

Overall, parents and clinicians agreed that it would be desirable to be able to identify and diagnose DLD earlier than it is currently possible, demonstrating the need for a tool capable of delivering that. FNIRS could be ideal since it has been reliably used with children as young as infants to locate areas in the brain that process language and communication (Gervain 2014). Additionally, fNIRS could be used in adjunction to existing tools to monitor and adjust parent-implemented therapies.

Ideal characteristics of the neuroimaging-based tool

When considering the factors that would influence parents and clinicians to support a neuroimaging-based tool for DLD there were both overlaps as well as discrepancies. Both groups were concerned about how the findings of such tool would impact on the care a child receives. Specifically, parents would want to be sure that implementing a new tool would provide them with access to more support. Both groups highlighted that any new tool needs to satisfy certain practical conditions before they would feel confident endorsing it. Responders also commented that the tool would have to be comfortable for the child. Parents and clinicians would need to be reassured that any new assessment would be provided by a reliable service in adjunction to already validated measures for DLD. Furthermore, they stressed that parental input should be sought before using any tool. They also discussed the importance of the location where the test is carried out and the duration of the testing

paradigm. Regarding the test results, it would be important that they are easy to interpret and would not take long to acquire. Clinicians were particularly interested in a tool that would be cost effective and easy to use in a clinical setting. They also highlighted the importance of ensuring that the tool would be accessible to families with additional needs and families who had English as a second language. Currently the Royal College of Speech and Language Therapists recommends that all assessments must be carried out in all languages spoken by the child. However, they highlight that standardised assessments cannot adequately diagnose language difficulties in children with English as their second language and should thus be avoided. Thus, clinicians currently rely on informal assessments to assess a bilingual child's language skills (Stow and Pert, 2014). Parents stressed that the tool would have to be safe and non-invasive.

Lastly, parents and clinicians expressed that any new tool would have to be highly accurate, effective and evidence based. Given the barriers mentioned above with regards to limited resources, gaps between referral and diagnosis and wide variety of interventions, parents and clinicians would only endorse a tool that would be reliable and validated to ensure they do not add further burden to the children, their families or SLT services.

fNIRS is already used in clinical settings monitor overall brain state in intensive care patients (Gumulak et al. 2017). Currently, future applications are being developed for its clinical use in a wide range of conditions such as Alzheimer's disease, schizophrenia, epilepsy and post-neurosurgery assessments (Rahman

et al. 2020). As a clinical tool it already has many of the characteristics that parents and clinicians consider necessary. For instance, it is lightweight ensuring patient comfort, it is portable meaning that it can be implemented in any setting including the child's home or school (Chen et al. 2020, Rahman et al. 2020). It is also relatively cheap compared to other neuroimaging modalities and non-invasive (Chen et al. 2020, Rahman et al. 2020). Additionally, brain recordings can be acquired whilst the child is resting or completing a relatively simple task such as attempting to repeat sentences (Gallagher et al. 2012). As a result, the testing process can be non-demanding allowing it to be administered to children with complex needs and/or multilingual children. However, it is worth noting that more research needs to be conducted to determine the ideal task that would allow us to measure brain activity specific to children with DLD in order to provide an accurate diagnosis. Additionally, we need to work with clinical teams to ensure that any testing procedures that are developed utilising the neuroimaging tool are easy to implement. It would also be valuable to validate any test results acquired by the tool against current behavioural measures of language processing in children with DLD.

Changing the care plan

The last set of questions in the parental survey explored whether parents would be happy for their child's care plan to be changed if a neuroimaging tool was used to guide clinical decisions. Quantitative data showed that most parents would be in favour of changes in all cases. However, parents were

slightly more reluctant to accept changes if it meant that their child would "lose" their DLD diagnosis or that their child would remain on a treatment plan that was deemed effective based on the neuroimaging results but there were no immediate improvements in their day-to -day language performance. Further analysis of the qualitative data indicated that most parents would support any changes because ultimately, they wanted the best possible outcomes for their children. Parents also shared the sentiment that DLD is life-long condition and accepted that it would take trial and error to refine an effective treatment plan for their child. Additionally, parents expressed that they would trust the clinical team caring for their child, thus if the SLTs recommended any changes, they would be supportive. Lastly, some parents believed that employing new tools that would offer more information with regards to DLD would not only help their child but would also be consequential for raising more awareness of the condition in the long-term. This is a particularly important given that DLD is a relatively under researched disorder (Bishop 2010, McGregor 2020). Thus, it can be argued that investigating the neural basis of DLD could spark an interest in the condition that would lead to more visibility as well as funding for future research.

However, a lot of parents echoed their responses from previous questions that any new tool would need to satisfy certain conditions before it was used to affect their child's care plan. For instance, they repeated that the tool must be accurate, effective and evidence based. Another point that was raised was the consequences of the test results for access to support. Many would endorse changes to their child's care plan only if those led to more support

and/or more targeted interventions. Indeed, parents were concerned that if a new tool deemed the care plan as ineffective that could result in their child receiving less speech and language therapy and/or being discharged from the services.

Limitations

Participants in the clinicians' group had a wide range of years of experience with DLD and were occupied in both NHS as well as the private sector thus providing a wide range of views. However, all participants were SLTs and, even though they are the clinical group predominantly involved in the diagnosis and treatment of DLD, it would have been interesting to have responses from other types of clinicians, who are also involved in the care of a child with DLD, such as paediatricians and educational psychologists.

Additionally, there are some inherent limitations to surveys as research tools. The data presented were collected using an anonymised online survey and as such it is difficult to verify whether participants understood the questions as intended. To minimise this risk the questions were tested with clinicians, parents and members of the public. However, even though the survey included open ended questions where participants could explain their responses, it can be difficult to further explore participants' rational and conduct any follow ups. At this stage the scope of this work was to get an overview of participants' opinions on a new tool for DLD, but future work could incorporate focus groups and interviews for a more holistic approach.

7.5 Summary

The responses from the parents and clinicians offer an encouraging attitude towards the adoption of new tools based on neuroimaging for the diagnosis and monitoring of DLD. The next steps would be to continue researching suitable neural markers for DLD and conduct large scale clinical trials to prove the specificity and sensitivity of fNIRS as a tool for the identification of such markers. Additionally, ongoing advancements in fNIRS technology have resulted in new fNIRS systems that are wireless, light and low cost (Tsow et al. 2021). These developments further facilitate the capability of fNIRS to be incorporated in clinical practice. At the same time, it is imperative that any future plans are also discussed with stakeholders such as parents and clinicians to ensure that research priorities are in line with their interests.

8 Discussion

8.1 Research Aims

The overall aim of this thesis was to characterise neural patterns of language processing in typically developed children and adolescents and children and adolescents with DLD and subsequently explore whether such measures can predict language skills. To address this typically developed children and children with DLD underwent fNIRS imaging during rest and language tasks to measure cortical activity. Unfortunately, the outbreak of the coronavirus (SARS-CoV-2) caused a global public health emergency that overwhelmed the health services, led to significant barriers to non-essential treatments and halted face-to face research activity. However, to mitigate the effects of Covid-19 contingency plans were put in place. Those not only enhanced the scope of this thesis but also allowed for the development and implementation of new research skills.

To begin with the initial aim of this work was to explore the neural activations of the language network in typically developed children and adolescents in response to overt and covert language processing. A secondary aim was to investigate the suitability of using fNIRS and a high-level control condition to isolate the language-specific activations. Chapter three reports on those aims. Additionally, the association between age and cortical activations and the maturational changes that the language network undergoes during language processing are examined. The third aim of this thesis to investigate cortical activation in response to sentence repetition in children and adolescents with

DLD compared to a typically developed control group. Recruitment of both groups but particularly of children with DLD was severely impacted by Covid-19. Nonetheless, neural responses during sentence repetition and their association to language skills are reported for a small sample of typically developed adolescents in chapter four. It was not possible to conduct a formal statistical analysis for the DLD group due to the small sample size.

The next aim of this thesis was to examine the resting state connectivity patterns of the language network and their association with performance on standardised language assessments for the same cohort. Findings are reported in chapter 5. However, the limited number of participants prevented completion of this aim for the DLD group. The fifth aim described in chapter six was to explore the feasibility of measuring neural synchrony in mothers and their children during an unstructured free play paradigm using fNIRS. The last chapter of the thesis details a qualitative study that offered valuable insights into the opinions of parents and clinicians regarding the adoption of a neuroimaging-based tool for the diagnosis and monitoring of DLD.

8.2 Summary of findings

8.2.1 Chapter 3

1. The use of a combination of overt and covert language tasks was deemed an appropriate way to explore neural markers of language processing. Indeed, the observed overall left hemispheric lateralisation and left IFG lateralisation validates the use of such paradigm.

2. Greater cortical activity was identified in the left IFG in the language processing condition compared to the control condition, highlighting the feasibility of deploying a high-level baseline for the isolation of language specific responses.
3. Cortical activity over the right auditory cortex was associated with task performance and grammar proficiency as measured with a standardised language assessment. This indicates the feasibility of using neural markers measured by fNIRS to potentially predict language attainment in typically developed children and adolescents.

8.2.2 Chapter 4

1. Sentence repetition is a viable neural marker of language processing as measured with fNIRS that engages all cortical areas of the language network.
2. Activity over the left auditory cortex in response to sentence repetition was associated with reading outcomes in typically developed children.
3. Activity was not lateralised to the left hemisphere for either the sentence repetition or the NVWM tasks.

8.2.3 Chapter 5

1. Cortical responses revealed a left lateralised frontal to sensory resting state language network. Intrinsic activity was higher between bilateral auditory regions compared to homologue frontal regions

strengthening the theory that mature language networks are left lateralised and confined to temporal regions.

2. Age was associated with cortical connectivity from left hemisphere frontal and auditory regions towards right frontal regions, revealing decreased reliance on right frontal regions as age increases.
3. Reduced connectivity within right hemisphere was associated with reading outcomes in children and adolescents indicating the use of patterns of resting state connectivity within the language network to potentially predict language proficiency in typically developed children and adolescents.

8.2.4 Chapter 6

1. Increased neural synchrony in the interactive compared to the independent condition confirmed the feasibility of measuring neural synchrony patterns in an unstructured free play paradigm.
2. C2M synchrony was significantly higher in the interactive condition whereas M2C synchrony was not significantly different compared to the independent condition. The use of PTE to investigate the direction of the flow of information between mothers and children offered valuable preliminary insights into the underlying driving forces of neural synchrony.
3. Patterns of neural synchrony were associated with surgency levels in children indicating the feasibility of using hyperscanning as a marker of trait characteristics in children.

8.2.5 Chapter 7

1. The majority of clinicians and parents surveyed were supportive of a neuroimaging-based tool for the diagnosis and monitoring of DLD. Responders agreed that a tool that could diagnose DLD earlier than currently than possible would be extremely valuable.
2. Clinicians argued that accuracy and practical characteristics should be the focus for the development of a new tool. Specifically, the potential cost and time commitment were important considerations.
3. Parents stated that the impact of the results of any clinical assessment should be carefully accounted for as they could affect the care plans and overall support children with DLD have access to.

8.3 General Discussion

8.3.1 Neural markers of language processing in TD

Characterising patterns of cortical activations in the typically developed language network is an imperative step in identifying markers of atypical activity. As a result, a considerable portion of this thesis focused on exploring the task-driven and the resting state language network in typically developed children and adolescents. An additional goal was to examine the feasibility of using fNIRS for the purpose and to determine a suitable experimental set-up. The ideal paradigm would be capable of eliciting neural responses that would allow for isolation of language processing in the brain whilst being practical and comfortable for paediatric populations.

To accomplish that chapters three, four and five explored the language network at rest and during language processing. Most findings were in line with previous neuroimaging investigations. For instance, the left lateralisation of the language network demonstrated in chapters three and five has also been evidenced by considerable amount of both functional and structural neuroimaging investigations that have supported a left lateralization for language processing that is present at birth or that emerges shortly after (Holland et al. 2001, Brown et al. 2005, Kadis 2010, Wang et al. 2012, Gummadavelli et al. 2013, Yamasaki et al. 2013, Paquette et al. 2015). Additionally, the engagement of the right hemisphere in association to performance in both the online language tasks as well as the standardised language assessments, also highlights the establishments of the left lateralisation of the language network. Studies in adults have also shown that, they also recruit bilateral temporoparietal regions in response to semantic processing (Binder et al. 2009, Graves et al. 2010, Golestani et al. 2013, Price et al. 2015, Graessner et al. 2021) perhaps in response to increased task demands (Golestani et al. 2013, Rysop et al. 2022). These findings indicate that the recruitment of right temporoparietal regions in school-aged children could be due to task demands rather than a lack of hemispheric specialisation. A similar case can be argued for the role of the left IFG.

Even though left lateralisation appears to be established early in life, language networks continue to become more specialised throughout childhood and adolescence. Here we propose a timeline for the specialisation of the language network from late childhood to adolescence. To begin with, both

resting state connectivity as well task-related activations indicate a decreased reliance in right frontal regions, that, as shown in chapter five, is age dependant. This means that the decrease of connectivity between language areas of the language network and widespread bilateral connections described by others (Solé-Padullés et al. 2016, Xiao et al. 2016, Xiao et al. 2016) continues to take place even in adolescence, perhaps reaching full maturity in adulthood. Thus, further work may be required to evaluate the age at which lateralisation reaches adulthood and what drives this late maturation compared with other developmental processes.

Additionally, the lack of difference between left frontal and temporal regions seen in chapter three suggests that interhemispheric specialisation of the left language network continues across our age range. However, the resting state connectivity results showed a flow of information from frontal towards temporal regions as well as a stronger bilateral temporal connectivity compared to connectivity between frontal regions. Notably these were not age dependant, indicating that a shift in activation in more temporal regions might have already taken place by late childhood. A possible explanation for this discrepancy between the resting state connectivity and the task-driven activation patterns might lie in the specific task demands. During the resting state paradigm participants were required to relax and try thinking of nothing, whereas during the task paradigm, participants completed language tasks with phonological, semantic and grammatical demands. Previous literature has described the maturational changes in specific linguistic domains. For instance, even though infants respond to phonological stimuli in utero

(Hepper and Shahidullah 1994, Uchida-Ota et al. 2019) and to semantic cues from as early as six months of age (Bergelson and Swingley 2012) brain responses to semantic and phonological processing begin to be distinguishable at about 3-4 years of age (Skeide and Friederici 2016), becoming more specialised between the ages of 5-6 (Weiss et al. 2018, Wang et al. 2021). By that age, typically developed children exhibit left-lateralised activations in the left inferior frontal gyrus IFG and left temporal regions for phonological processing, whereas semantic processing elicited activations in the left IFG and bilateral temporoparietal regions (Mathur et al. 2020). Additionally, activations in response to semantic and syntactic processing are not separated and engage the IFG and temporal regions bilaterally in school-aged children. In contrast, adults show distinct activations only in the left temporal lobe (Brauer and Friederici 2007, Skeide et al. 2014). In late childhood, there appears to be specialisation between semantic and syntactic processing in the temporal lobe but not the frontal lobe (Wang et al. 2021). By adolescence semantic processing seems to have reached adult-like patterns whereas, specialisation for syntactic processing continues throughout adolescence (Schneider and Maguire 2019). Thus, it might be that the resting state language network in late childhood and adolescence resembles adult like patterns whereas, the task driven network matures at a slower pace.

The secondary goal of this body of work to establish a testing protocol for language processing was also accomplished. fNIRS was capable of recording reliably both the resting state connectivity patterns as well as task-driven cortical activations. The results presented within chapters three and four

suggest that fNIRS could be a suitable clinical tool to measure cortical responses during complex overt language production. The use of a combination of language tasks as an index of language processing proved to be a valid way of identifying language specific activations. Similarly, despite the small sample size that limited our ability to answer our questions sufficiently, the work presented in chapter four offers the first key step towards assessing if cortical responses in a sentence repetition task can be used as neural markers of language processing.

Additionally, our novel high-level control condition that combined two different types of tasks (i.e., time reversed speech and digit articulation) allowed for the isolation of language specific processing in the left IFG and the right auditory cortex. Choosing an appropriate control task has been a particularly challenging element of neuroimaging studies, as a task that is too easy would not be able separate whether activity is due to language processing or processing of non-linguistic elements (e.g., pitch and tonality of an auditory stimulus). Conversely, a control task that was too similar to the language task would not reveal any differences in neural activity (Bradshaw et al. 2017). In the present work, even though the control condition was not sufficient to discriminate language-related activity in the left temporal cortex, the paradigm used here is a significant step towards designing a suitable control task to contrast against an overt language processing.

8.3.2 Considerations for the development of an objective clinical tool for DLD

Overall, the findings presented in this thesis highlight the importance of early application of language interventions for children with DLD. The studies discussed in chapters three and five confirm that many aspects of the neural functions that support language processing appear to have matured by late childhood, thus it is imperative that treatment plans are put in place prior to that. Additionally, as shown in chapter seven both the families of children with DLD as well as the clinicians that work with them believed that earlier interventions would lead to better language development outcomes for the children. Needless to say, that early and accurate identification and diagnosis of DLD is an essential step to designing and offering the appropriate treatment plan in a timely manner. Another gap that needs to be addresses to achieve the goal of early intervention is the lack of evidence-based treatments.

Here we demonstrated that fNIRS has the potential to fulfil these requirements and become an effective and objective clinical tool that could help identify and monitor individuals with DLD, much earlier than is currently possible using behavioural techniques. To begin with, from a practical standpoint we confirmed that fNIRS is a tolerable technique for children of all ages that can be comfortably used for paradigms of varying lengths from 10 to 40 minutes. Additionally, the scientific and clinical community as well as the sample of responders in our survey recognised the importance of using neural markers in adjunction to behavioural standardised assessments as well proving that results from both are correlated. That is crucial to help validate

the neural markers measured and assess the relationship between neural markers and functional impact of the disorder. The association between the neural activity and scores on the TROG and the TOWRE seen in chapters three and five respectively indicate that fNIRS can measure clinically relevant differences in neural activations that correspond to real-life measures of language processing. This also proves that cortical activations measured using fNIRS could be used to assess language skills in younger children that cannot reliably complete standardised language assessments. Longitudinal investigations should be conducted to verify that.

It is also important to mention that fNIRS appears to also be capable of tracking the effectiveness of interventions for DLD. For instance, it could be used to track changes in neural networks during language processing whilst completing tasks similar to the ones described in chapter three. Additionally, fNIRS hyperscanning can be applied to assess the potential benefits of parent implemented therapies. Changes in neural synchrony between parents and children could be used as an adjunct to help guide parents and carers on how to interact more effectively with their children to help them improve their language development.

8.4 Limitations

8.4.1 Sampling

As reiterated throughout the thesis, investigation of patterns of cortical activations during language processing in children remains a novel field of research. Thus, it was not appropriate to conduct a formal sample size

calculation. The target of 25 participants per group was set based on previous test-retest reliability work conducted by our laboratory in adults that concluded that a sample size of N=24 was sufficient to produce fNIRS data of good-excellent reliability (Wiggins et al. 2016). Since then, a series of studies from our laboratory have published robust findings from paediatric studies with similar sample sizes (Mushtaq et al. 2019), (Lawrence et al. 2021). We aimed to recruit at least one more participant per group to account for the possibility of missing data. This was achieved in the first study (N=30), but not for the subsequent studies mainly due to the Covid-19 pandemic that led to extended closures of research facilities. Additionally, even after restrictions were lifted, Public Health England continued to advise for people to limit non-essential travel and self-isolate in case of contact with positive or suspected cases of Covid-19 (UKHSA 2022) resulting in reduced participation in voluntary research activities (second study: N=5 in the TD group and N=1 in the DLD group, hyperscanning study: N=12 pairs). Furthermore, during the pandemic, university resources were redirected towards Covid-19 related studies. That resulted in significant delays in acquiring ethical approvals and resuming research activities. Nevertheless, every effort was made to maximise recruitment. The recruitment phase of the second study remained open from April 2021, when Nottingham University Hospitals Research and Innovation Team approved the study, until March 2022 when it was the latest that was reasonably possible given the time constrains of this project. Additionally, new SLT centres in neighbouring geographical areas were added to aid with recruitment and extensive advertisement was conducted to local schools,

after-school youth groups and clubs, charitable organisations and private SLT practices.

8.4.2 Recruitment of DLD sample

Even though the impact of Covid-19 on the recruitment of the DLD sample cannot be denied, several other factors should also be considered. To begin with, DLD remains a relatively underdiagnosed and under researched disorder. Informal discussions with many professionals including SLTs and special education teachers revealed that there is still uncertainty regarding the terminology and diagnostic criteria for DLD. As a result, many hesitate to refer and/or diagnose children to avoid misdiagnosis, instead they adopt a "wait and see" approach to ensure difficulties persist and the diagnosis of another disorder is not appropriate. This leads to children with suspected "DLD" that might be monitored until they either receive a diagnosis or get discharged from the services. Several families of children with suspected "DLD" got in touch with regards to participating in the study, however these children unfortunately did not fit the eligibility criteria, as it was not possible to clinically assess them within the scope of this project.

Additionally, the complicated journey towards diagnosis and interventions detailed in chapter seven has led many seeking external assessments to aid access to resources. Thus, some families believed that participation in this research would provide them with results of clinical assessments such as brain scans. Parents and carers hoped that those could be used to advocate for increased support for their children. Unfortunately, that was also beyond the scope of this study and resulted in some families deciding not to participate.

Lastly, the SLT services in the UK and specifically in Nottinghamshire have been facing reductions in funding over the past couple of years (Wire 2020) that were only worsened by the Covid -19 pandemic. That has led to significant staffing shortages meaning that there were extended wating lists for children waiting for a diagnosis and less staff capacity to support research activities.

8.4.3 Methodological considerations

A cross-sectional approach was taken in all studies. This approach led to some valuable findings regarding the maturational trajectory of the language network and the relationship between cortical activations and language outcomes. However, it cannot offer any insights into causal relationships. Longitudinal investigations of language processing in young children with DLD would verify whether patterns of neural activations can reliably be used to predict language outcomes later in life. Particularly, in the case of DLD, there are currently no longitudinal neuroimaging studies thus there is a big gap that future research should address.

It is also important to mention that even though fNIRS was deemed a great tool to achieve the aims of this thesis, it does have drawbacks. To begin with, the relatively poor spatial resolution did not allow for detailed localisation of neural activity. fMRI investigations of the language network have described the finely tuned specialisation of both the temporo-parietal as well as frontal areas. For instance, Brodmann areas 47 and 45 of the IFG are preferentially involved in the analysis of semantic relations between words whereas

Brodmann area 44 of the IFG is recruited during the analysis of syntactic relations (Skeide and Friederici 2016). However, such explorations are not feasible using fNIRS. Furthermore, even though the choice of a priori ROIs in this study was usually verified by the group level cortical activation maps presented in chapter three and was based on extensive previous work in our lab, it is not possible to make definitive claims regarding which cortical regions are targeted. Additionally, this limitation is further exacerbated by the fact that the positioning of fNIRS headsets is usually guided by external reference points, and these points can vary from person to person. That might lead to variability in optode placement and as a result variability in the localisation of neural activity. possible mitigating solution of this problem could be the digital registration of fNIRS placement as described in section 3.2.4. Nonetheless, for enhanced precision in identifying ROIs, future research should consider the inclusion of a participant's MRI scan whenever feasible.

Neuroimaging findings presented in this thesis are limited to activations of the outer cortex, as it is not possible to image areas deeper than a few centimetres below that. Consequently, subcortical areas that are tightly linked to language processing such as the insula and the basal ganglia (Oh et al. 2014), (Weiss-Croft and Baldeweg 2015), (Krishnan et al. 2022) could not be targeted. Additionally, fNIRS measurements can be affected by scalp-related factors such as scalp-optode contact, hair density and cerebrospinal fluid. Other haemodynamic signals such as respiratory and cardiac signals can also interfere with the fNIRS measurements. To counteract this, the Yamada separation technique was added in the pre-processing procedure as described

in chapter three (Yamada et al. 2012). It is also important to mention that, completing overt tasks have been demonstrated to influence breathing rates. These effects vary and have different impacts on changes in HbO and HbR signals measured by fNIRS during the overt task (Zhang et al. 2017) (Scholkmann et al. 2013). The intricate interplay of speaking, breathing, and voluntary cognitive tasks complicates the interpretation of fNIRS signals (Zhang et al. 2017) (Scholkmann et al. 2013). To overcome this limitation, future studies could integrate pulse oximeters to record participants' breathing rates non-invasively, incorporate short channel separation channels that regress systemic responses from task-related responses and include simultaneous measurements of end-tidal CO_2 concentration in blood, which informs of the remaining levels of CO_2 in the exhaled breath at the end of a respiratory cycle (Zhang et al. 2017) (Scholkmann et al. 2013)

Lastly, even though fNIRS offers significant advantages with regards to participant comfort compared to other neuroimaging techniques, the two 3x5 arrays of the Hitachi ETG-4000 system used in this project became uncomfortable especially for some of the younger participants. To deal with that frequent breaks were offered to all participants to allow for them to rest. In the current studies, all of the participants were happy to complete all the experimental conditions, however there is no guarantee that this would always be the case.

8.5 Impact and future directions

The work presented in this thesis creates a strong foundation for the use of fNIRS as an adjunctive tool for the diagnosis and monitoring of DLD. Even though it was not possible to measure cortical activations in children with DLD, the findings acquired from imaging typically developed children offer important insights into the metrics that could form the basis of a clinical tool and should be further investigated. To begin with in agreement with previous work it appears that left hemispheric lateralisation in temporal regions is not a sufficient marker of language processing. In contrast focusing on frontal left activations might be a more appropriate approach to identifying neural responses to language processing. Additionally, the use of high-level control conditions that can isolate language specific activations can be instrumental in separating auditory processing, articulation processes and working memory demands from language processing bringing us closer to understanding the neural underpinnings of DLD. The feasibility of measuring language processing using a combination of tasks that targeted different linguistic modalities has great ecological validity and it is another avenue for future research as children with DLD often present a very heterogenous combination of deficiencies.

Both studies described in chapters three and five also offer exciting contributions to the understanding of the maturational trajectory of the language network. Findings suggest that a shift from widespread bilateral activations to more confined activation in the temporal regions has already

taken place by late childhood. This can be used as a neural marker to track the development of the language network in children with DLD.

Successfully recording patterns of neural synchrony using an unstructured free play paradigm is a milestone for the use of hyperscanning as a clinical tool to track child development. This is especially relevant for children with DLD given that many present with delays in acquiring speech and may have persistent difficulties that prevent them from completing complicated verbal tasks. This work has already been used to apply for a grant from the Efficacy and Mechanism Evaluation (EME) programme to explore the neural underpinning of the parent-child interaction therapy called It Takes Two to Talk in children with cochlear implants. The application has been successful at the first stage of assessment and at the time of submitting this thesis is under the second stage of consideration by the NIHR EME programme.

Future work should also take advantage of the developments in fNIRS equipment. High density fNIRS systems are capable of imaging subcortical structures and the introduction of caps with short separation channels allows for the regression of interfering signals from the scalp and the isolation of stimuli specific response. Lastly, the progress in lighter wearable fNIRS systems allows for the design of more naturalistic experiments that can be completed comfortably by participants of all ages in a wide variety of settings.

Additionally, as outlined in section 1.5, the reliability of fNIRS test-retest has been demonstrated to be strong in both adults (Wiggins et al., 2016) and infants (Blasi et al., 2014). This is especially true when focusing on specific

regions of interest and employing averaging across a limited number of channels (Plichta et al. 2006), (Schecklmann et al. 2008). However, these findings pertain to analyses conducted at the group level, and individual-level activations exhibit significant variability. To fully unlock the potential of fNIRS as a clinical tool, it is crucial that future investigations establish the test-retest reliability of fNIRS on an individual basis. This is particularly important in scenarios where participants and patients undergo multiple imaging sessions over a specific period to track changes in cortical activation stemming from developmental progress or clinical interventions. A methodological consideration for investigations of test-retest reliability in paediatric populations is a short test-retest interval, as test-retest reliability analyses depend on the assumption that the underlying processes remain consistent across different time points. Lastly, recruitment for this work focused on typically developed children and children with DLD without other neurodevelopmental disorders in order to create a more homogenous sample with less confounding factors. However, this line of research can be very beneficial to other clinical populations as well. In fact, children with DLD often have other comorbidities, such as emotional problems, ADHD, dyslexia, and autism (Westerlund et al. 2002, Nitin et al. 2022). Thus, assessments of the language skills that rely on neuroimaging and do not require behavioural responses can be used in the future to assess outcomes in children with complex needs.

8.6 Conclusion

The neural underpinning of language processing and the development of the language network remains elusive in typically developed children and especially in children with DLD. Previous work exploring the maturational changes in typical development indicate that advanced language skills are associated with left lateralised activations confined in temporal regions and reduced widespread connectivity across the language network. This work supports that hypothesis and offers a timeline for the establishment of this shift. Cortical activations during language processing and resting state connectivity patterns indicate that a shift in temporal regions has taken place by late childhood resulting in a network similar to the one found in adults. However, the long-range connections to right frontal regions are still decreasing as age increases, perhaps reaching maturation in adulthood. Additionally, cortical activations in the resting language network as well in response to linguistic stimuli can possibly predict language outcomes in typically developed children. Furthermore, findings presented in this thesis confirm that fNIRS hyperscanning recording can be measured successfully between mothers and toddlers in an unstructured free play paradigm regardless of the levels of verbal communication they engaged in. All of the above suggest that fNIRS is an adept tool for the imaging of the language network that possesses many characteristics that would allow for its use as clinical tool for DLD. Parents of children with DLD and professionals that work with children with DLD are in agreement regarding the need for the development of a neuroimaging-based tool for DLD that will be capable of

identifying DLD earlier than currently possible. However, future work should focus on honing the accuracy of measurements and their ability to predict language outcomes for children with DLD.

9 Appendix

9.1 Details of each participant's age, gender, cognitive assessment score and handedness (chapter three)

Participant ID	**Gender**	**CCC-2**	**TROG**	**TOWRESE**	**TOWEPE**	**PRI**	**FSIQ**
PT_01	Female	95	111	125	119	120	123
PT_02	Female	93	97	100	108	102	111
PT_03	Female	67	106	96	99	105	116
PT_04	Male	50	99	105	113	113	101
PT_05	Female	61	104	85	109	99	102
PT_06	Female	69	111	103	121	112	112
PT_07	Female	100	102	95	107	130	122
PT_08	Male	76	95	117	111	120	118
PT_09	Male	79	102	107	105	101	121
PT_10	Male	80	92	89	94	105	114
PT_11	Male	95	116	102	111	107	107
PT_12	Male	74	85	102	115	88	92
PT_13	Female	85	106	103	119	119	108
PT_14	Female	84	118	104	106	138	124
PT_15	Male	77	111	121	135	125	117
PT_16	Male	45	106	110	125	122	109
PT_17	Male	95	104	104	100	100	106
PT_18	Male	104	83	110	124	107	109
PT_19	Female	86	99	102	107	96	107
PT_20	Female	91	106	81	93	92	102
PT_21	Male	60	113	106	107	125	117
PT_22	Female	82	111	121	124	136	134
PT_23	Female	70	109	98	115	128	128
PT_24	Female	37	106	117	127	103	108
PT_25	Female	47	85	117	123	103	102
PT_26	Female	42	85	108	116	104	100

Appendix

PT_27	Female	39	92	113	126	98	103
PT_28	Female	83	111	106	112	126	131
PT_29	Male	99	97	114	119	106	113
PT_30	Female	89	97	84	97	107	100

The table above shows age, gender, handedness and age corrected scores in the CCC-2, TROG, TOWRE and WASI assessment details for each participant who took part in the study described in chapters three and five. Note that, participants highlighted in red were excluded form analysis in chapter five due to poor sculp-optode contact (PT_30 was also excluded from the analysis in chapter three).

9.2 Details of anatomical head landmarks of participants in the digitisation study (chapter 3)

Partcipant_ID	Left Tragus			Right Tragus			Nazion			Inion			Cz		
	x	y	z	x	y	z	x	y	z	x	y	z	x	y	z
DG_01	58.7	0.0	0.0	-60.2	0.0	0.0	0.0	-88.0	0.0	-6.4	79.1	40.1	-0.5	-19.6	130.6
DG_02	50.5	0.0	0.0	-63.6	0.0	0.0	0.0	-79.6	0.0	-8.4	88.7	18.1	-11.9	-0.6	124.2
DG_03	64.8	0.0	0.0	-66.0	0.0	0.0	0.0	-79.8	0.0	-0.3	70.2	17.5	4.8	-19.1	126.1
DG_04	64.1	0.0	0.0	-59.7	0.0	0.0	0.0	-75.9	0.0	1.5	74.5	27.8	-4.7	-15.4	130.0
DG_05	71.0	0.0	0.0	-71.1	0.0	0.0	0.0	-90.0	0.0	-1.8	78.1	34.8	-10.1	-15.8	137.6
DG_06	63.9	0.0	0.0	-65.1	0.0	0.0	0.0	-86.7	0.0	3.1	75.7	16.2	-12.1	-11.0	124.2
DG_07	64.1	0.0	0.0	-67.8	0.0	0.0	0.0	-92.4	0.0	-0.6	85.7	41.0	-7.9	-15.9	134.1
DG_08	65.4	0.0	0.0	-70.1	0.0	0.0	0.0	-97.7	0.0	-5.9	81.6	42.1	-17.6	-31.8	136.5
DG_09	70.3	0.0	0.0	-73.2	0.0	0.0	0.0	-96.5	0.0	-3.7	86.9	36.3	-9.2	-33.1	128.6
DG_10	57.9	0.0	0.0	-64.9	0.0	0.0	0.0	-85.0	0.0	-3.1	75.8	35.9	-20.6	-21.1	123.6
DG_11	60.6	0.0	0.0	-69.7	0.0	0.0	0.0	-94.8	0.0	-4.2	70.7	29.8	-11.8	-24.3	131.7
DG_12	62.6	0.0	0.0	-72.3	0.0	0.0	0.0	-96.7	0.0	-1.5	90.4	33.9	-5.4	-11.2	131.9

The table above shows the coordinate values in cm for the left and right tragus, the nazion, the inion and the Cz for each participant who took part in the digitisation study described in chapter three.

9.3 Details of beta values for all tasks, all conditions and all ROIs (Chapter3)

Verbal Fluency

Subject	LA_L_VF	RA_L_VF	LIFG_L_VF	RIFG_L_VF	RA_C_VF	LIFG_C_VF	RIFG_C_VF	LA_C_VF
1	-0.0172	-0.3911	-0.3370	-0.3042	-0.2360	-0.1858	-0.2348	-0.0671
2	-0.1108	-0.0204	0.0855	0.2087	-0.0047	-0.1474	-0.1339	-0.1359
3	0.0177	0.0152	-0.0067	-0.1105	0.0550	-0.0356	-0.0909	0.0515
4	0.3417	-0.0092	0.0895	-0.0224	-0.1259	-0.0552	-0.0133	0.1320
5	0.0426	0.0600	0.0415	0.0725	-0.0547	-0.0372	-0.0029	-0.0175
6	-0.0369	-0.0204	-0.1475	-0.0168	-0.0047	-0.3070	-0.0255	0.0356
7	-0.0369	0.0885	0.0179	-0.0571	-0.0883	0.0096	-0.0696	0.0356
8	-0.0369	-0.0204	0.0006	-0.0168	-0.0047	0.0028	-0.0255	0.0356
10	-0.0040	0.1677	-0.0067	0.1582	0.0863	-0.0356	0.0009	0.1582
11	-0.0369	-0.0204	-0.0067	-0.1083	-0.0047	-0.0356	-0.0058	0.0356
12	-0.0603	0.0083	-0.1429	0.1646	-0.1044	-0.2993	-0.0230	-0.2096
13	-0.0369	-0.2541	-0.0067	-0.0014	-0.0737	-0.0356	0.0015	0.0356
14	-0.0369	-0.0568	-0.1428	-0.0167	-0.0108	-0.0354	0.0171	0.0356
15	-0.0205	-0.3316	-0.0934	-0.1767	-0.0635	0.0130	0.0296	0.0442
16	0.0125	-0.0529	-0.0744	-0.0666	-0.0600	-0.1251	-0.1765	-0.0212
17	-0.0794	-0.0170	-0.0416	0.0003	-0.0218	0.0811	0.0277	0.1390
18	-0.0369	-0.0185	0.2746	-0.0224	-0.0066	-0.0623	-0.0319	0.0356
19	-0.0848	-0.0204	-0.0139	-0.0393	-0.0047	-0.0891	0.0269	0.0319
20	-0.0719	0.0119	-0.0183	-0.1506	-0.0157	-0.4168	-0.3630	0.0393
21	-0.0117	0.0513	0.3640	0.3058	0.1382	0.2478	0.1033	0.0830
22	-0.0534	-0.0227	-0.0543	0.0356	0.0842	0.0167	-0.0397	0.0058
23	-0.2385	-0.0204	-0.0985	-0.0823	-0.0047	0.0314	-0.0749	0.1870
24	-0.0369	-0.0751	0.0910	0.0273	0.0013	0.0233	-0.0281	0.0356
25	-0.0369	-0.1503	-0.0309	-0.1413	0.1654	-0.4644	-0.0678	0.0356
26	-0.0761	-0.0520	-0.0067	-0.0169	0.0915	-0.0356	0.1796	-0.0023
27	-0.2875	-0.0223	0.0286	-0.0047	0.2579	-0.0792	-0.0772	0.2030
28	0.0683	-0.0371	0.0808	0.0727	0.1381	-0.0217	-0.0172	-0.0211
29	-0.0607	0.0563	0.1063	0.1021	-0.0027	-0.0356	-0.0857	-0.0135
30	0.0154	-0.0655	0.0594	-0.1022	0.3327	0.2755	0.0065	0.2762

The table above shows beta values for each participant who took part in the verbal fluency task described in chapter three. LA and RA stand for left and right auditory cortex respectively, LIFG and RIFG stand for left and right inferior frontal gyrus respectively. L stands for the language condition and C stands for the control condition.

Appendix

Sentence Repetition

Subject	LA_L_SR	RA_L_SR	LIFG_L_SR	RIFG_L_SR	RA_C_SR	LIFG_C_SR	RIFG_C_SR	LA_C_SR
1	0.2144	0.0845	0.1167	0.2145	0.0509	-0.2187	-0.0693	0.0527
2	-0.1182	0.0874	0.0143	-0.0043	0.0467	0.0444	-0.1032	0.1581
3	0.0876	0.0874	-0.2177	-0.0966	0.0467	-0.0649	-0.0803	0.0664
4	0.0084	-0.0371	0.1033	0.0272	-0.0130	0.0878	-0.0170	0.1048
5	0.0806	0.0490	0.1782	0.0709	0.0937	0.0253	0.1056	0.0977
6	0.2544	0.0039	0.0232	-0.0765	-0.0001	-0.0632	-0.0197	-0.2191
7	0.0876	0.0678	0.3503	0.0328	-0.0145	0.2600	-0.0706	0.0664
8	0.0433	0.3624	0.1147	-0.0076	-0.0520	0.1969	0.1606	0.0341
10	0.0670	0.1165	0.0232	0.0337	0.1622	-0.0632	0.0724	0.1250
11	0.0876	0.0017	0.3175	0.0548	0.0006	0.0900	0.0225	0.0664
12	-0.0171	0.1674	-0.1527	-0.0196	0.0625	-0.2867	-0.0161	-0.0351
13	0.1238	0.0409	0.0232	-0.0006	0.1940	-0.0632	-0.0018	0.2571
14	0.0876	0.1435	0.2474	0.2367	0.0798	-0.0614	-0.1611	0.0664
15	0.0561	-0.0214	-0.1321	-0.1802	-0.1017	-0.1487	-0.0908	-0.1419
16	0.2086	0.1497	0.0080	0.1524	0.0073	-0.2228	-0.0632	0.0652
17	0.1382	0.0736	-0.0015	0.0120	-0.0950	-0.1497	-0.0344	-0.0625
18	-0.0147	-0.0229	-0.1490	-0.1023	-0.0897	-0.1756	-0.0870	0.0255
19	0.0775	0.0874	0.0211	0.0455	0.0467	-0.0122	0.0058	0.0676
20	0.0876	0.0874	0.0612	-0.1823	0.0353	-0.1863	-0.1393	0.0664
21	0.2364	0.1746	0.2092	0.0724	0.0999	0.2514	-0.0232	0.2794
22	0.1302	0.1720	-0.0818	-0.0649	0.0592	-0.2263	-0.0886	0.1308
23	0.1493	-0.1491	-0.1428	-0.1546	-0.0797	-0.0831	-0.0707	-0.0329
24	0.0876	0.2480	0.0729	0.1636	0.0714	0.1684	0.1795	0.0664
25	0.0876	0.5478	-0.0670	0.0193	0.2279	-0.1159	-0.0232	0.0664
26	0.0908	0.0507	0.0232	0.0730	0.0467	-0.0632	-0.0317	0.1695
27	-0.0178	-0.0705	0.0232	0.0664	0.1053	-0.0632	0.0882	0.2075
28	0.1070	0.1647	0.0241	-0.0063	-0.0023	0.0230	0.0551	0.0498
29	0.0844	0.1367	0.0223	0.0193	-0.0196	-0.2458	-0.0626	-0.0106
30	0.2207	0.3490	0.0976	0.0005	0.4477	0.1190	0.3817	0.3769

The table above shows beta values for each participant who took part in the sentence repetition task described in chapter three. LA and RA stand for left and right auditory cortex respectively, LIFG and RIFG stand for left and right inferior frontal gyrus respectively. L stands for the language condition and C stands for the control condition.

Appendix

Syntactic Comprehension

Subject	LA_L_RSyn	RA_L_RSyn	LIFG_L_RSyn	RIFG_L_RSyn	RA_C_RSyn	LIFG_C_RSyn	RIFG_C_RSyn	LA_C_RSyn
1	0.0351	-0.1126	0.0835	-0.1980	0.0132	0.0077	0.0154	0.0616
2	0.1009	0.0145	-0.1465	-0.0782	0.1396	0.0909	0.0789	0.0240
3	0.0351	-0.0020	0.3770	0.0503	0.0433	0.0650	-0.0825	0.0616
4	-0.1842	-0.0780	-0.1298	0.0223	-0.0488	0.1819	-0.0343	0.0633
5	0.0671	-0.0543	0.0230	-0.0240	0.0525	-0.0078	-0.0352	0.0730
6	0.0351	-0.0020	0.0497	-0.0093	0.0433	-0.3407	-0.0009	0.0616
7	-0.0736	0.0337	0.0396	0.0385	-0.0115	0.2602	0.0466	0.1720
8	-0.0874	-0.1196	-0.0470	-0.1572	0.3699	0.3734	0.0485	0.1320
10	0.0705	0.0436	0.0385	-0.0541	0.0614	-0.1265	-0.0414	-0.1138
11	0.0351	0.0698	-0.0329	-0.1039	0.0528	0.0187	0.0544	0.0616
12	0.2332	0.2706	0.1617	-0.0043	0.1998	0.2175	0.0093	0.2588
13	0.3027	0.0569	0.0307	0.0006	0.1239	-0.0084	-0.0008	0.0993
14	-0.0231	-0.0228	0.0206	0.1225	0.0389	-0.0791	0.1426	-0.0422
15	-0.0943	-0.1027	-0.0151	-0.1437	-0.0879	-0.1040	-0.0067	-0.0912
16	0.0234	-0.1478	0.0207	-0.0118	-0.0138	-0.0307	-0.0382	0.1304
17	0.0184	0.0249	-0.0679	-0.0253	-0.0024	-0.0966	-0.1109	-0.0849
18	0.0320	0.1934	0.0548	-0.0675	0.0158	-0.0491	-0.0326	0.1317
19	-0.0603	-0.0020	-0.0151	-0.1703	0.0433	-0.1260	-0.0684	-0.0655
20	0.0351	-0.0122	0.1758	0.1476	0.0493	0.0715	0.0715	0.0616
21	0.2426	-0.0020	0.0443	0.0272	-0.0584	-0.0068	0.1577	0.0195
22	0.0300	-0.0926	0.0672	-0.0230	-0.0945	0.0003	-0.0792	-0.0079
23	0.1209	-0.0020	-0.0526	0.0316	0.0433	0.1232	0.0221	0.2891
24	0.0351	0.0164	0.0155	0.0178	0.1091	-0.2068	-0.1529	0.0616
25	0.0351	-0.3164	0.5486	-0.0069	0.0882	-0.0851	-0.0010	0.0616
26	0.1207	-0.0149	0.0307	0.1350	0.0433	-0.0084	-0.0677	0.0537
27	-0.0924	-0.0585	0.0307	-0.0409	0.3490	-0.0084	0.0848	0.3228
28	0.0456	0.0006	-0.1550	-0.0248	0.0066	-0.0090	-0.0355	0.0360
29	0.0382	0.0057	0.1517	0.0023	0.0055	-0.0593	0.0769	0.0598
30	0.1119	0.0075	0.1067	0.1119	0.1778	-0.0194	0.1295	0.1867

The table above shows beta values for each participant who took part in the syntactic comprehension task described in chapter three. LA and RA stand for left and right auditory cortex respectively, LIFG and RIFG stand for left and right inferior frontal gyrus respectively. L stands for the language condition and C stands for the control condition.

Appendix

Semantic Comprehension

Subject	LA_L_RSem	RA_L_RSem	LIFG_L_RSem	RIFG_L_RSem	RA_C_RSem	LIFG_C_RSem	RIFG_C_RSem	LA_C_RSem
1	0.0011	0.0368	-0.0996	0.0151	-0.1241	0.0358	-0.0716	-0.0802
2	0.0072	0.0173	-0.0086	0.1242	0.0268	0.0091	-0.0220	0.0478
3	0.0150	0.0173	0.1085	0.0801	0.0268	0.0760	0.0250	0.0421
4	-0.1182	-0.1607	-0.0002	-0.0165	-0.0791	-0.1343	-0.0705	0.0311
5	0.0228	-0.0434	-0.0801	-0.0411	0.0465	0.0989	0.0157	0.0345
6	0.0150	0.0173	-0.1535	0.0236	0.0268	-0.0522	-0.0072	0.0421
7	0.0400	0.0150	0.0932	0.0115	-0.0294	0.1121	-0.0072	0.2916
8	-0.0060	-0.0218	0.0106	0.1327	-0.0678	0.0992	-0.0976	-0.0136
10	0.0669	-0.0100	-0.0229	-0.0136	0.1679	-0.0474	-0.0127	0.0547
11	0.0150	0.0173	-0.0002	0.0295	0.0268	0.0082	0.0236	0.0421
12	0.1859	0.2021	0.2657	0.0872	0.2024	0.0082	0.0408	0.1737
13	0.0333	0.1980	-0.0002	-0.0025	0.0932	0.0082	-0.0025	0.2377
14	0.0150	0.0705	0.0008	0.1100	-0.0542	0.0728	-0.0303	0.0421
15	-0.0413	0.0287	0.0363	0.0236	-0.0439	0.0269	-0.0772	0.0508
16	0.0530	-0.0910	-0.0091	-0.0448	-0.0240	-0.2031	0.0368	-0.0052
17	0.1086	-0.0006	-0.0360	-0.0865	-0.0181	0.0521	0.3143	0.0267
18	0.0150	0.0081	0.0523	0.0534	-0.0700	-0.1267	0.1475	0.0421
19	-0.0114	-0.0006	0.0397	-0.0462	-0.0014	-0.0273	-0.0127	0.0980
20	0.2460	0.0599	-0.1206	-0.1889	0.2009	-0.1516	-0.1988	0.2826
21	-0.0308	-0.1482	0.0457	-0.0849	0.0864	-0.0595	-0.0608	0.0365
22	-0.0841	0.1095	0.3054	0.1682	0.1335	0.2445	0.1389	0.1734
23	-0.1350	0.0173	0.0007	0.0383	0.0268	-0.0514	0.0350	0.0345
24	0.0150	-0.0137	-0.0146	0.0666	0.0490	-0.0664	0.0190	0.0421
25	0.0150	0.0910	-0.3914	0.0236	0.1748	0.5317	-0.0072	0.0421
26	0.0573	0.0801	-0.0002	0.0439	0.2298	0.0082	-0.0331	0.0834
27	-0.0294	0.3073	-0.0002	0.1029	0.3515	0.0082	0.0865	0.1496
28	0.0553	0.0195	-0.0276	-0.0271	-0.1568	-0.0626	-0.0188	-0.0075
29	-0.0673	-0.0135	-0.0182	-0.0279	0.0071	-0.1439	-0.0388	-0.0379
30	0.2452	0.1865	0.1041	0.2294	0.1588	0.2973	0.0150	0.0321

The table above shows beta values for each participant who took part in the semantic comprehension task described in chapter three. LA and RA stand for left and right auditory cortex respectively, LIFG and RIFG stand for left and right inferior frontal gyrus respectively. L stands for the language condition and C stands for the control condition.

Appendix

Phonological Awareness

Subject	LA_L_PA	RA_L_PA	LIFG_L_PA	RIFG_L_PA	RA_C_PA	LIFG_C_PA	RIFG_C_PA	LA_C_PA
1	0.0659	0.0615	-0.0993	-0.0653	0.0713	-0.2276	-0.0309	0.0298
2	0.0469	0.0300	0.0137	-0.0315	0.0541	0.0273	-0.0252	0.0414
3	0.0271	0.0326	0.0852	-0.0248	0.0015	0.0081	-0.1079	0.0215
4	0.1059	0.0481	0.1527	0.0851	0.0063	0.2679	0.0341	0.0781
5	0.0766	-0.0041	0.0635	0.0655	-0.0452	0.0069	0.0423	0.0805
6	0.3355	-0.0007	0.0852	0.0966	0.0008	0.0087	-0.0698	-0.0219
7	0.0659	0.0638	0.1182	0.0091	0.1284	0.0093	0.1833	0.0298
8	0.0659	0.0473	-0.0013	0.0076	0.0588	-0.0003	-0.0166	0.0298
10	0.0342	0.1104	0.0852	-0.1304	-0.1645	0.0087	-0.0954	-0.0617
11	0.0659	0.0473	0.0852	0.0061	0.0588	0.0087	0.1292	0.0298
12	0.2160	0.0825	0.2059	0.0837	0.1565	0.0250	0.0115	0.0914
13	0.0659	0.2224	0.0852	-0.0023	-0.0785	0.0087	0.0013	0.0298
14	-0.0283	-0.0202	0.1695	-0.0137	0.0831	-0.0158	-0.1147	-0.0244
15	0.0490	0.0465	-0.1372	-0.2059	-0.0460	-0.1748	-0.0996	-0.0356
16	0.0712	-0.0201	0.0908	-0.0107	-0.0450	0.0344	-0.0080	-0.0028
17	-0.0275	0.0076	0.0510	-0.0093	0.1118	0.2382	0.0094	0.2119
18	-0.0222	-0.0492	0.1008	0.0237	0.0746	0.0498	0.0567	0.0072
19	0.0751	0.0003	0.0796	-0.0628	-0.0003	-0.0267	0.0154	0.0563
20	0.1675	0.0665	-0.1013	-0.1044	-0.0083	0.1477	0.0238	0.0568
21	0.0397	-0.0726	0.1813	0.0735	0.1332	-0.0163	-0.0701	0.1277
22	0.1910	0.0954	0.2588	0.0167	0.0635	0.0240	-0.1565	-0.0048
23	0.0607	0.0572	0.1416	0.0570	0.2044	-0.0263	-0.1572	0.0381
24	0.0659	-0.0376	-0.2190	-0.1577	-0.0215	0.0317	-0.0589	0.0298
25	0.0659	0.2484	-0.0302	0.0076	0.2956	0.1168	-0.0166	0.0298
26	0.1855	0.1858	0.0852	0.0528	0.1480	0.0087	0.1221	0.0533
27	0.2400	0.3362	0.1112	0.1129	0.1380	-0.0909	-0.0522	0.1758
28	0.0077	-0.0430	0.0290	0.0306	0.0524	-0.0435	0.0184	-0.0013
29	0.0016	-0.0112	0.2202	-0.0328	0.1965	-0.0158	-0.0292	-0.0622
30	0.1915	0.0535	0.2240	0.0827	0.0466	0.1847	-0.0821	0.0173

The table above shows beta values for each participant who took part in the phonological awareness task described in chapter three. LA and RA stand for left and right auditory cortex respectively, LIFG and RIFG stand for left and right inferior frontal gyrus respectively. L stands for the language condition and C stands for the control condition.

9.4 Relationship between neural activity and performance during language processing tasks

Verbal Fluency		
Age	F (3,78) = .623	p > .05
Performance	F (3,78) = .446	p > .05
Sentence Repetition		
Age	F (3,78) = 1.003	p > .05
Performance	F (3,78) = 2.292	p > .05
Syntactic Comprehension		
Age	F (3,78) = .449	p > .05
Performance	F (3,78) = 1.247	p > .05
Semantic Comprehension		
Age	F (3,78) = 1.144	p > .05
Performance	F (3,78) = 2.987	p > .05
Phonological Awareness		
Age	F (3,78) = .629	p > .05
Performance	F (3,78) = .748	p > .05

The table shows the results of 1-way ANOVAs with ROI as the dependant variable and age and performance as covariate for each task. No interaction reached statistical significance with p>.05.

9.5 Details of each participant's age, gender, handedness and cognitive assessment score (chapter four)

Participant ID	**Gender**	**CCC-2**	**TROG**	**TOWRESE**	**TOWEPE**	**PRI**	**FSIQ**
TD_01	Male	74	116	119	104	108	120
TD_02	Female	72	102	100	100	109	109
TD_03	Female	84	104	92	106	91	107
TD_04	Female	85	106	82	86	86	85
TD_05	Female	55	74	95	100	86	95
DLD_06	Female	13	76	124	114	85	70

The table above shows age, gender, handedness and age corrected scores in the CCC-2, TROG, TOWRE and WASI assessment details for each participant who took part in the study described in chapters four and five. Note that, participants highlighted in red were excluded form analysis in chapter five due to poor sculp-optode contact. Participant DLD_01 was not included in the analysis of chapter five since they were the only participant of their group.

9.6 Details of each dyad's; child and mother age, child gender, and behavioural assessment scores (chapter six)

Dyad ID	**Child Gender**	**Surgency**	**Negative affect**	**Effortful Control**	**ERQ_CR**	**ERQ_ES**
NS_01	Male	5.67	2.58	5.30	4.33	2.00
NS_02	Female	4.89	3.27	5.91	6.00	6.00
NS_03	Male	5.42	2.83	5.25	4.83	1.25
NS_04	Male	4.30	2.17	5.33	5.33	2.25
NS_05	Male	5.75	5.09	4.82	4.67	1.00
NS_06	Female	5.73	2.45	4.83	4.17	1.75
NS_07	Female	5.42	1.58	6.36	5.33	3.25
NS_08	Female	5.67	3.83	4.75	5.50	1.00
NS_09	Male	5.92	1.64	6.00	4.17	3.00
NS_10	Male	6.08	2.75	6.33	5.33	3.00
NS_11	Female	6.00	2.20	5.00	3.83	4.00
NS_12	Male	6.58	3.67	5.42	6.17	5.00

The table above shows child's age and gender, mother's age and scores on the Children's behaviour questionnaire (surgency, negative affect and effortful control) and the emotion regulation questionnaire (CR: cognitive reappraisal and ES: expressive suppression) for each dyad who took part in the study described in chapter six.

9.7 Survey of parents and clinicians (chapter seven)

9.7.1 Parental Survey

University of Nottingham
UK | CHINA | MALAYSIA

Parental opinions of a clinical tool for DLD: an online survey

Page 1

Research Team: Tia Papoutselou, PhD Student, Professor Douglas Hartley and Dr Ian Wiggins, Academic Supervisors, Samantha Harrison, collaborating PhD Student, Hearing Sciences, Division of Clinical Neuroscience, School of Medicine at the University of Nottingham.

Research Ethics Ref: FMHS 37-0620

The aim of this study is to assess the acceptability of using a predictive measure of language processing in children that have Developmental Language Disorder (DLD), by asking both parents and language professionals about the subject.

We appreciate your interest in taking part in this online survey. **You have been invited to participate as you are a parent (18+ years) with a child who has DLD** formerly known as specific language impairment (SLI). Please read through this information before agreeing to participate by ticking the 'yes' box below. You may ask any questions before taking part by contacting the researcher, Tia Papoutselou (details below). Taking part is voluntary.

What will I be asked to do?

You will be asked to provide some basic demographic information (i.e. gender, job, education). You will then be presented with a questionnaire. It should take you about 20 minutes to complete. However, you can take as much time as your need to answer all questions. You can withdraw at any point during the questionnaire for any reason, before submitting your answers by clicking the Exit button/closing the browser. The data will only be uploaded on completion of the questionnaire by clicking the SUBMIT button on the final page. At this point it will not be possible to withdraw your answers.

1 / 19

Who will know I have taken part in the study?

No one will know you have taken part in this study because we will not ask for your name or any other personal ID during this questionnaire. Your IP address will not be visible to or stored by the research team because an online survey platform is being used which receives and stores an IP address but enables this detail to be filtered out before it is transferred to the research team. As with any online related activity the risk of breach is possible but this risk is being minimized by using a platform that sits on an encrypted webpage. For further information about the online survey tool security please see https://www.onlinesurveys.ac.uk/security/

What will happen to your data?

When you have clicked the submit button at the end of the questionnaire, it will be uploaded into a password protected database with a code number. The research team will not be able to see who it is from and for this reason it will not possible to withdraw the data at this point. Your data (research data) will be stored in a password-protected folder sitting on a restricted access server at the University under the terms of its data protection policy. Data is kept for a minimum of 7 years and then destroyed.

This questionnaire is part of a PhD research project and the answers received from all participants will be combined in a password protected database ready for analysis. The results will be written up as part of a thesis and may be used in academic publications and presentations. The overall anonymised data from this study may be shared for use in future research and teaching (with research ethics approval).

The only personal data we will receive is your e-mail if you contact us to ask further questions. This will be received and handled separately from your completed questionnaire. Your e-mail address will only be kept as long as needed to resolve your query. It will then be deleted. For further information about how the university processes personal data please see: https://www.nottingham.ac.uk/utilities/privacy.aspx/

Who will have access to your data?

The University of Nottingham is the data controller (legally responsible for data security) and the Supervisor of this study (named above) is the data custodian (manages access to the data) and as such will determine how your data is used in the study. Your research and personal data will be used for the purposes of the research only. Research is a task that we perform in the public interest.

Responsible members of the University of Nottingham may be given access to data for

2 / 19

monitoring and/or audit of the study to ensure it is being carried out correctly.

What if there is a problem?

If you have any concerns about any aspect about this project, please contact the researcher or their supervisor:

Tia Papoutselou: efstratia.papoutselou@nottingham.ac.uk
Professor Douglas Hartley (supervisor): douglas.hartley@nottingham.ac.uk

The researcher should acknowledge your concern and give you an indication of how they intend to deal with it.

If you remain unhappy and wish to complain formally, you should then contact the FMHS Research Ethics Committee Administrator E-mail: FMHS-ResearchEthics@nottingham.ac.uk

Declaration

- I have read and understood the above information.
- I confirm that I am 18 years old or older.
- I confirm that I have a child or children who have developmental language disorder
- I understand that my participation is voluntary, and I can end the study at any time and withdraw my data by clicking the EXIT button or closing the browser.
- I understand the anonymised data from this study may be used in the future for research and/or teaching purposes.

By clicking "Next" below, you are consenting to take part in this study.

3 / 19

Demographics

What is your age (in years)?

Which gender best describes you?

- Female
- Male
- Non-binary
- Prefer to self-describe
- Prefer not to say

If you selected Prefer to self-describe, please state:

What is the highest level of education you have completed?

- No formal education
- Secondary education (e.g. GCSE/O Level or equivalent)
- Further education (A-level, BTEC or equivalent)
- Bachelor's degree
- Master's degree
- Doctorate (PhD or equivalent)
- Prefer not to say
- Other

4 / 19

If you selected Other, please specify:

Which of the following best describes your current main daily responsibilities?

- Working full-time
- Working part-time
- Unemployed
- Keeping house or raising children full-time
- Retired
- Student
- Temporarily out of work due to covid-19
- Other

If you selected Other, please specify:

Which best described your main daily activities before the covid-19 pandemic?

- Working full-time
- Working part-time
- Prefer not to say

5 / 19

Your child/children and their DLD

Questions in this section refer to you child/ children that have been diagnosed with DLD. If you have more than one children with DLD, answer this set of questions again for your eldest child first. Then click yes to final question and answer this set of questions again for your second oldest and so on.

Approximately how old was your child when you noticed that they might have difficulties with speech and language (in years and months)?

Approximately how old was your child when you sought professional help for their language difficulties (in years and months)?

For approximately how long has your child had their DLD diagnosis (in years and months)?

How old is your child currently (in years and months)?

6 / 19

Do you have another child with DLD?

- Yes
- No

7 / 19

Your child/children and their DLD

Questions in this section refer to your second eldest child that has been diagnosed with DLD.

Approximately how old was your child when you noticed that they might have difficulties with speech and language (in years and months)?

Approximately how old was your child when you sought professional help for their language difficulties (in years and months)?

For approximately how long has your child had their DLD diagnosis (in years and months)?

How old is your child currently (in years and months)?

Do you have another child with DLD?

8 / 19

Yes
No

9 / 19

Your child/children and their DLD

Questions in this section refer to your third eldest child that has been diagnosed with DLD.

Approximately how old was your child when you noticed that they might have difficulties with speech and language (in years and months)?

Approximately how old was your child when you sought professional help for their language difficulties (in years and months)? * Required

For approximately how long has your child had their DLD diagnosis (in years and months)?

For approximately how long has your child had their DLD diagnosis (in years and months)?

10 / 19

Do you have another child with DLD?

Yes
No

11 / 19

Your child/children and their DLD

Questions in this section refer to your fourth eldest child that has been diagnosed with DLD.

Approximately how old was your child when you noticed that they might have difficulties with speech and language (in years and months)?

Approximately how old was your child when you sought professional help for their language difficulties (in years and months)?

For approximately how long has your child had their DLD diagnosis (in years and months)?

For approximately how long has your child had their DLD diagnosis (in years and months)?

12 / 19

A diagnostic test

DLD looks different across people who have it and the language of a person with DLD might be similar in some ways to the language of someone who is younger or someone who is learning a new language. That makes it particularly tricky for clinicians to give a diagnosis of DLD especially to younger children that cannot complete lengthy language tests that assess their language and communication skills. Additionally, even though it is thought that the earlier a child with DLD receives treatment, the better their future outcomes are, many children may wait a long time for speech-language therapy assessment. This means the children who have DLD might be unidentified for up to a few years.

Questions in this section of the survey refer to "a diagnostic test". By this, we mean a test which can be used to identify signs of language disorder. Such a test may involve the child listening to different sounds, watching videos or speaking whilst being with their parent or caregiver, wearing a headset similar to that seen in the picture below. This headset shines harmless light through the scalp and skull to the outer area of the brain, where it measures brain activity. The headset is suitable for use from birth and so the test could be conducted long before a patient is old enough to complete the behaviour-based language assessments currently used in clinical settings.

If it were possible to identify patients who may struggle with language and communication earlier on, they could potentially access rehabilitation and support earlier than is currently possible to improve their future outcomes.

Would you have found it beneficial to know whether your child was likely to have DLD before they were old enough to demonstrate their language abilities behaviourally?

- ○ Yes
- ○ No
- ○ I don't know

Please elaborate:

13 / 19

- ○ Yes
- ○ No

Please explain why:

If a diagnostic test, such as the one described above, identified your child as likely to NOT have DLD, would you be happy for their care plan in clinic to be altered accordingly?

- ○ Yes
- ○ No

Please explain why:

What key factors or features might encourage you, as a parent, to support the use of a diagnostic test for the identification of DLD (e.g. time from testing to diagnosis, accuracy of diagnosis etc.)?

15 / 19

At what stage of a child's development would it be most beneficial to you, as a parent, to know whether your child has DLD?

- ○ Between 0-18 months – when the child begins to understand produce their first words
- ○ Between 18-36 months – when the child begins forming sentences
- ○ Between 3-5 years old – when language skills expand rapidly
- ○ At 5 to 6 years old- when the child enters formal education
- ○ After 6 years old – after the child has entered formal education
- ○ Other

If you selected Other, please specify:

Please explain why:

If a diagnostic test, such as the one described above, identified your child as likely to have DLD, would you be happy for their care plan in clinic to be altered accordingly?

14 / 19

What key factors or features might discourage you, as a parent, from supporting the use of a diagnostic test for the identification of DLD (e.g. additional clinic appointments etc.)?

Please use the box below for any other comments you may have regarding a diagnostic tool: *Optional*

16 / 19

A monitoring tool

Questions in this section of the survey refer to "a monitoring test". By this, we mean a test which can be used to monitor the effectiveness of interventions and treatment. The same tool described above could be used to assess whether the chosen treatment plan is successful or not. This could help clinicians better evaluate the child's progress, and personalise therapy to ensure better outcomes for the child.

If a monitoring test, such as the one described above, identified that your child's treatment plan is not effective, would you be happy for their care plan in clinic to be altered accordingly?

- Yes
- No

Please elaborate:

If a monitoring test, such as the one described above, identified that your child's treatment plan is effective even though you might not be seeing results in the short-term, would you be happy for their care plan in clinic to remain the same?

- Yes
- No

Please elaborate:

What key factors or features might encourage you, as a parent, to support the use of a tool to monitor the effectiveness of treatment plans for DLD (e.g. accuracy of findings etc.)?

What key factors or features might discourage you, as a parent, from supporting the use of a tool to monitor the effectiveness of treatment plans for DLD (e.g. additional examinations etc.)?

Please use the box below for any other comments you may have regarding a monitoring tool:

Final page

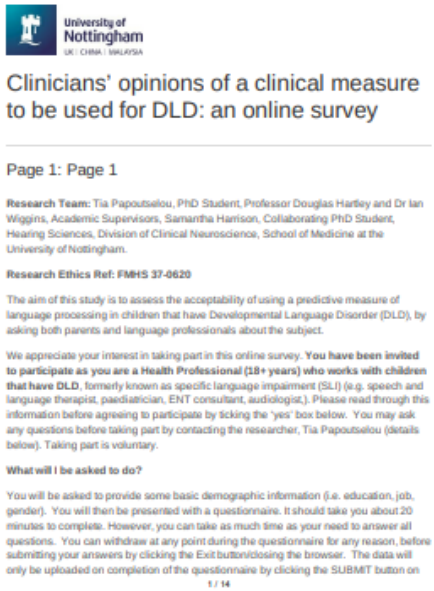
Thank you for taking the time to complete this survey. We truly value the information you have provided.

If you have any comments on the survey or the project, please contact Tia Papoutselou (mszep9@nottingham.ac.uk)

Many thanks,

The research team

9.7.2 Clinicians' Survey



University of Nottingham
UK | CHINA | MALAYSIA

Clinicians' opinions of a clinical measure to be used for DLD: an online survey

Page 1: Page 1

Research Team: Tia Papoutselou, PhD Student, Professor Douglas Hartley and Dr Ian Wiggins, Academic Supervisors, Samantha Harrison, Collaborating PhD Student, Hearing Sciences, Division of Clinical Neuroscience, School of Medicine at the University of Nottingham.

Research Ethics Ref: FMHS 37-0620

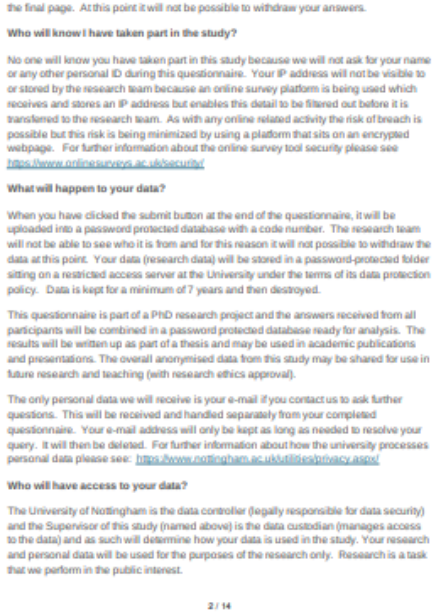
The aim of this study is to assess the acceptability of using a predictive measure of language processing in children that have Developmental Language Disorder (DLD), by asking both parents and language professionals about the subject.

We appreciate your interest in taking part in this online survey. **You have been invited to participate as you are a Health Professional (18+ years) who works with children that have DLD**, formerly known as specific language impairment (SLI) (e.g. speech and language therapist, paediatrician, ENT consultant, audiologist,). Please read through this information before agreeing to participate by ticking the 'yes' box below. You may ask any questions before taking part by contacting the researcher, Tia Papoutselou (details below). Taking part is voluntary.

What will I be asked to do?

You will be asked to provide some basic demographic information (i.e. education, job, gender). You will then be presented with a questionnaire. It should take you about 20 minutes to complete. However, you can take as much time as your need to answer all questions. You can withdraw at any point during the questionnaire for any reason, before submitting your answers by clicking the Exit button/closing the browser. The data will only be uploaded on completion of the questionnaire by clicking the SUBMIT button on

1 / 14



the final page. At this point it will not be possible to withdraw your answers.

Who will know I have taken part in the study?

No one will know you have taken part in this study because we will not ask for your name or any other personal ID during this questionnaire. Your IP address will not be visible to or stored by the research team because an online survey platform is being used which receives and stores an IP address but enables this detail to be filtered out before it is transferred to the research team. As with any online related activity the risk of breach is possible but this risk is being minimized by using a platform that sits on an encrypted webpage. For further information about the online survey tool security please see https://www.onlinesurveys.ac.uk/security/

What will happen to your data?

When you have clicked the submit button at the end of the questionnaire, it will be uploaded into a password protected database with a code number. The research team will not be able to see who it is from and for this reason it will not possible to withdraw the data at this point. Your data (research data) will be stored in a password-protected folder sitting on a restricted access server at the University under the terms of its data protection policy. Data is kept for a minimum of 7 years and then destroyed.

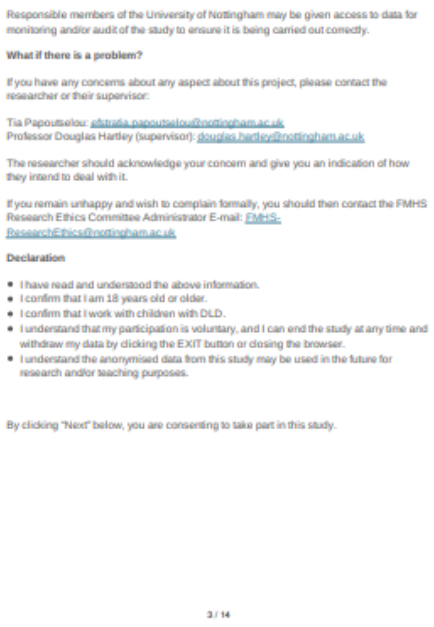
This questionnaire is part of a PhD research project and the answers received from all participants will be combined in a password protected database ready for analysis. The results will be written up as part of a thesis and may be used in academic publications and presentations. The overall anonymised data from this study may be shared for use in future research and teaching (with research ethics approval).

The only personal data we will receive is your e-mail if you contact us to ask further questions. This will be received and handled separately from your completed questionnaire. Your e-mail address will only be kept as long as needed to resolve your query. It will then be deleted. For further information about how the university processes personal data please see: https://www.nottingham.ac.uk/utilities/privacy.aspx/

Who will have access to your data?

The University of Nottingham is the data controller (legally responsible for data security) and the Supervisor of this study (named above) is the data custodian (manages access to the data) and as such will determine how your data is used in the study. Your research and personal data will be used for the purposes of the research only. Research is a task that we perform in the public interest.

2 / 14



Responsible members of the University of Nottingham may be given access to data for monitoring and/or audit of the study to ensure it is being carried out correctly.

What if there is a problem?

If you have any concerns about any aspect about this project, please contact the researcher or their supervisor:

Tia Papoutselou: efstratia.papoutselou@nottingham.ac.uk
Professor Douglas Hartley (supervisor): douglas.hartley@nottingham.ac.uk

The researcher should acknowledge your concern and give you an indication of how they intend to deal with it.

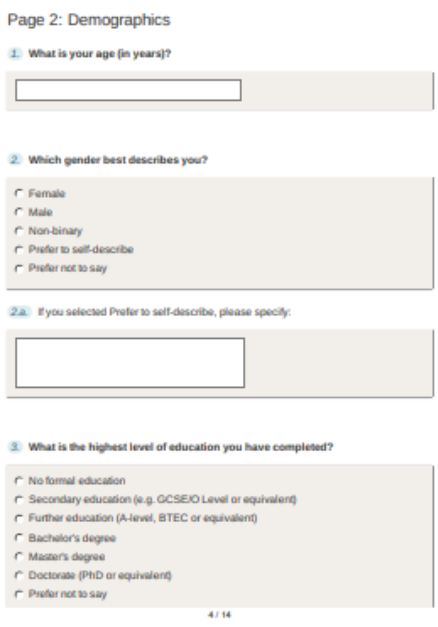
If you remain unhappy and wish to complain formally, you should then contact the FMHS Research Ethics Committee Administrator E-mail: FMHS-ResearchEthics@nottingham.ac.uk

Declaration

- I have read and understood the above information.
- I confirm that I am 18 years old or older.
- I confirm that I work with children with DLD.
- I understand that my participation is voluntary, and I can end the study at any time and withdraw my data by clicking the EXIT button or closing the browser.
- I understand the anonymised data from this study may be used in the future for research and/or teaching purposes.

By clicking "Next" below, you are consenting to take part in this study.

3 / 14



Page 2: Demographics

1. **What is your age (in years)?**

2. **Which gender best describes you?**

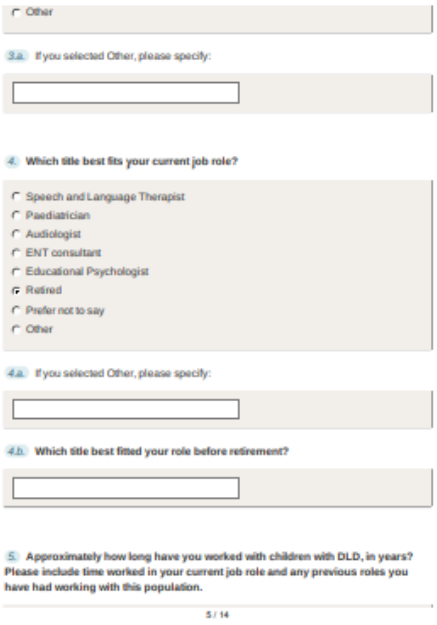
- Female
- Male
- Non-binary
- Prefer to self-describe
- Prefer not to say

2.a. If you selected Prefer to self-describe, please specify:

3. **What is the highest level of education you have completed?**

- No formal education
- Secondary education (e.g. GCSE/O Level or equivalent)
- Further education (A-level, BTEC or equivalent)
- Bachelor's degree
- Master's degree
- Doctorate (PhD or equivalent)
- Prefer not to say

4 / 14



Other

3.a. If you selected Other, please specify:

4. **Which title best fits your current job role?**

- Speech and Language Therapist
- Paediatrician
- Audiologist
- ENT consultant
- Educational Psychologist
- Retired
- Prefer not to say
- Other

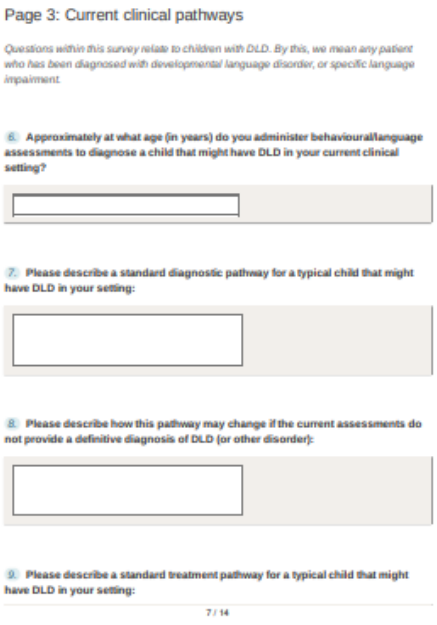
4.a. If you selected Other, please specify:

4.b. **Which title best fitted your role before retirement?**

5. **Approximately how long have you worked with children with DLD, in years? Please include time worked in your current job role and any previous roles you have had working with this population.**

5 / 14

6 / 14



Page 3: Current clinical pathways

Questions within this survey relate to children with DLD. By this, we mean any patient who has been diagnosed with developmental language disorder, or specific language impairment.

6. **Approximately at what age (in years) do you administer behavioural/language assessments to diagnose a child that might have DLD in your current clinical setting?**

7. **Please describe a standard diagnostic pathway for a typical child that might have DLD in your setting:**

8. **Please describe how this pathway may change if the current assessments do not provide a definitive diagnosis of DLD (or other disorder):**

9. **Please describe a standard treatment pathway for a typical child that might have DLD in your setting:**

7 / 14

10. **Please describe how this pathway may change if the given treatment is not effective for that child:**

8 / 14

Page 4: A diagnostic tool

Questions in this section of the survey refer to "a diagnostic test". By this, we mean a test which can be used to identify signs of language disorder. Such a test may involve a patient listening to different sounds, watching videos or speaking whilst being with their parent or caregiver, wearing a headset similar to that seen in the picture below. This headset shines harmless light through the scalp and skull to the outer area of the brain, where it measures brain activity. The headset is suitable for use from birth and so the test could be conducted long before a patient is old enough to complete the behaviour-based language assessments currently used in clinical settings.

If it were possible to identify patients who may struggle with language and communication earlier on using an objective tool, they could potentially access rehabilitation and support earlier than is currently possible to improve their future outcomes.

11. **Do you think it would be beneficial to identify children with DLD before they are old enough to undergo standardised language/behavioural testing, either with a test such as the one described above or by other means?**

- (•) Yes
- ( ) No

11.a. Please explain:

12. **At what stage of a child's development would it be most beneficial to you, as a clinician, to know whether a child has DLD?**

- ( ) Between 0-18 months – when the child begins to understand and produce their first words
- ( ) Between 18-36 months – when the child begins forming sentences
- ( ) Between 3-5 years old – when language skills expand rapidly
- ( ) At 5 to 6 years old- when the child enters formal education
- ( ) After 6 years old – after the child has entered formal education
- ( ) Other

12.a. If you selected Other, please specify:

12.b. Please explain why: * *Required*

13. **What key factors or features might encourage you to use a diagnostic test in your clinic (e.g. length of examination appointment, time from testing to diagnosis, accuracy of diagnosis etc.?**

14. **What key factors or features might discourage you from using a diagnostic tool in your clinic (e.g. cost, need for additional training, disseminating results to patients and their families etc.)?**

14.a. **Would the factors or features that you identified above still discourage you if another service could provide this test for your patients?**

- ( ) Yes
- ( ) No

14.a.i. If yes, please elaborate:

15. **Please use the box below for any other comments you may have regarding a diagnostic tool:** *Optional*

Page 5: A monitoring tool

Questions in this section of the survey refer to "a monitoring test". By this, we mean a test which can be used to monitor the effectiveness of interventions and treatment. The same tool described above could be used to assess whether the chosen treatment plan is successful or not. This could help clinicians better evaluate the child's progress, and personalise therapy to ensure better outcomes for the child.

16. **What key factors or features might encourage you to use a monitoring test in your clinic (e.g. length of examination appointment, time from testing to diagnosis, accuracy of diagnosis etc.)?**

17. **What key factors or features might discourage you from using a monitoring tool in your clinic (e.g. cost, need for additional training, disseminating results to patients and their families etc.)?**

17.a. **Would the factors or features that you identified above still discourage you if another service could provide this test for your patients?**

- ( ) Yes
- ( ) No

17.a.i. If yes, please elaborate:

18. **Please use the box below for any other comments you may have regarding a monitoring tool:** *Optional*

Page 6: Final page

Thank you for taking the time to complete this survey. We truly value the information you have provided.

If you have any comments on the survey or the project, please contact Tia Papoutselou (msxep9@nottingham.ac.uk)

Many thanks,

The research team

10 References

Aasted, C. M., M. A. Yücel, R. J. Cooper, J. Dubb, D. Tsuzuki, L. Becerra, M. P. Petkov, D. Borsook, I. Dan and D. A. Boas (2015). "Anatomical guidance for functional near-infrared spectroscopy: AtlasViewer tutorial." Neurophotonics **2**(2): 020801.

Aguilar-Mediavilla, E., L. Buil-Legaz, R. López-Penadés, V. A. Sanchez-Azanza and D. Adrover-Roig (2019). "Academic outcomes in bilingual children with developmental language disorder: a longitudinal study." Frontiers in psychology **10**: 531.

Aguilar-Mediavilla, E., L. Buil-Legaz, R. López-Penadés, V. A. Sanchez-Azanza and D. Adrover-Roig (2019). "Academic Outcomes in Bilingual Children With Developmental Language Disorder: A Longitudinal Study." Front Psychol **10**: 531.

Ahn, S., H. Cho, M. Kwon, K. Kim, H. Kwon, B. S. Kim, W. S. Chang, J. W. Chang and S. C. Jun (2018). "Interbrain phase synchronization during turn-taking verbal interaction-a hyperscanning study using simultaneous EEG/MEG." Hum Brain Mapp **39**(1): 171-188.

Ailion, A. S., X. You, J. S. Mbwana, E. J. Fanto, M. Krishnamurthy, C. J. Vaidya, L. N. Sepeta, W. D. Gaillard and M. M. Berl (2022). "Functional Connectivity as a Potential Mechanism for Language Plasticity." Neurology **98**(3): e249-e259.

Alcauter, S., L. García-Mondragón, Z. Gracia-Tabuenca, M. B. Moreno, J. J. Ortiz and F. A. Barrios (2017). "Resting state functional connectivity of the anterior striatum and prefrontal cortex predicts reading performance in school-age children." Brain and Language **174**: 94-102.

Ali, N., D. W. Green, F. Kherif, J. T. Devlin and C. J. Price (2010). "The role of the left head of caudate in suppressing irrelevant words." J Cogn Neurosci **22**(10): 2369-2386.

Allen, J. and C. R. Marshall (2011). "Parent–Child Interaction Therapy (PCIT) in school-aged children with specific language impairment." International Journal of Language & Communication Disorders **46**(4): 397-410.

Alpert, C. L. and A. P. Kaiser (1992). "Training parents as milieu language teachers." Journal of Early intervention **16**(1): 31-52.

Alt, M. (2011). "Phonological working memory impairments in children with specific language impairment: where does the problem lie?" Journal of communication disorders **44**(2): 173-185.

Anderson, C. A., I. M. Wiggins, P. T. Kitterick and D. E. Hartley (2017). "Adaptive benefit of cross-modal plasticity following cochlear implantation in deaf adults." Proceedings of the National Academy of Sciences **114**(38): 10256-10261.

Anderson, C. A., I. M. Wiggins, P. T. Kitterick and D. E. H. Hartley (2019). "Pre-operative Brain Imaging Using Functional Near-Infrared Spectroscopy Helps Predict Cochlear Implant Outcome in Deaf Adults." J Assoc Res Otolaryngol **20**(5): 511-528.

Andrés-Roqueta, C., J. E. Adrian, R. A. Clemente and L. Villanueva (2016). "Social cognition makes an independent contribution to peer relations in children with Specific Language Impairment." Research in Developmental Disabilities **49-50**: 277-290.

Andreu, L., M. Sanz-Torrent, L. B. Legaz and B. Macwhinney (2012). "Effect of verb argument structure on picture naming in children with and without specific language impairment (SLI)." Int J Lang Commun Disord **47**(6): 637-653.

Annett, M. (2003). "Cerebral asymmetry in twins: predictions of the right shift theory." Neuropsychologia **41**(4): 469-479.

Arbel, Y. and E. Donchin (2014). "Error and performance feedback processing by children with Specific Language Impairment--an ERP study." Biol Psychol **99**: 83-91.

Archibald, L. M. and S. E. Gathercole (2006). "Short-term and working memory in specific language impairment." International Journal of Language & Communication Disorders **41**(6): 675-693.
Archibald, L. M. and S. E. Gathercole (2007). "The complexities of complex memory span: Storage and processing deficits in specific language impairment." Journal of memory and language **57**(2): 177-194.
Archibald, L. M. and M. F. Joanisse (2009). "On the sensitivity and specificity of nonword repetition and sentence recall to language and memory impairments in children." J Speech Lang Hear Res **52**(4): 899-914.
Argyropoulos, G. P., P. Tremblay and S. L. Small (2013). "The neostriatum and response selection in overt sentence production: an fMRI study." Neuroimage **82**: 53-60.
Arsalidou, M. and M. J. Taylor (2011). "Is 2+2=4? Meta-analyses of brain areas needed for numbers and calculations." NeuroImage **54**(3): 2382-2393.
Arun, K. M., K. A. Smitha, P. G. Rajesh and C. Kesavadas (2018). "Functional near-infrared spectroscopy is in moderate accordance with functional MRI in determining lateralisation of frontal language areas." Neuroradiol J **31**(2): 133-141.
Atzil, S. and M. Gendron (2017). "Bio-behavioral synchrony promotes the development of conceptualized emotions." Current Opinion in Psychology **17**: 162-169.
Avram, L., A. Sevcenco and I. Stoicescu (2013). Clinical markers of specific language impairment and developmental dyslexia in Romanian: The case of Accusative clitics'**:** 129-159.
Azhari, A., A. Bizzego and G. Esposito (2021). "Father-child dyads exhibit unique inter-subject synchronization during co-viewing of animation video stimuli." Soc Neurosci **16**(5): 522-533.
Azhari, A., G. Gabrieli, A. Bizzego, M. H. Bornstein and G. Esposito (2020). "Probing the association between maternal anxious attachment style and mother-child brain-to-brain coupling during passive co-viewing of visual stimuli." Attach Hum Dev: 1-16.
Azhari, A., W. Q. Leck, G. Gabrieli, A. Bizzego, P. Rigo, P. Setoh, M. H. Bornstein and G. Esposito (2019). "Parenting Stress Undermines Mother-Child Brain-to-Brain Synchrony: A Hyperscanning Study." Scientific Reports **9**(1): 11407.
Azhari, A., W. Q. Leck, G. Gabrieli, A. Bizzego, P. Rigo, P. Setoh, M. H. Bornstein and G. Esposito (2019). "Parenting Stress Undermines Mother-Child Brain-to-Brain Synchrony: A Hyperscanning Study." Sci Rep **9**(1): 11407.
Babaeeghazvini, P., L. M. Rueda-Delgado, J. Gooijers, S. P. Swinnen and A. Daffertshofer (2021). "Brain Structural and Functional Connectivity: A Review of Combined Works of Diffusion Magnetic Resonance Imaging and Electro-Encephalography." Front Hum Neurosci **15**: 721206.
Badcock, N. A., D. V. Bishop, M. J. Hardiman, J. G. Barry and K. E. Watkins (2012). "Co-localisation of abnormal brain structure and function in specific language impairment." Brain Lang **120**(3): 310-320.
Baddeley, A., S. Gathercole and C. Papagno (1998). "The phonological loop as a language learning device." Psychol Rev **105**(1): 158-173.
Badre, D. and A. D. Wagner (2007). "Left ventrolateral prefrontal cortex and the cognitive control of memory." (0028-3932 (Print)).
Bartha-Doering, L., K. Kollndorfer, G. Kasprian, A. Novak, A. L. Schuler, F. P. S. Fischmeister, J. Alexopoulos, W. D. Gaillard, D. Prayer, R. Seidl and M. M. Berl (2018). "Weaker semantic language lateralization associated with better semantic language performance in healthy right-handed children." Brain Behav **8**(11): e01072.
Basu, M., A. Krishnan and C. Weber-Fox (2010). "Brainstem correlates of temporal auditory processing in children with specific language impairment." Dev Sci **13**(1): 77-91.

Baumwell, L., C. S. Tamis-LeMonda and M. H. Bornstein (1997). "Maternal verbal sensitivity and child language comprehension." Infant behavior and Development **20**(2): 247-258.
Bavin, E. L., P. H. Wilson, P. Maruff and F. Sleeman (2005). "Spatio-visual memory of children with specific language impairment: evidence for generalized processing problems." International journal of language & communication disorders **40**(3): 319-332.
Beitchman, J. H., B. Wilson, C. J. Johnson, L. Atkinson, A. Young, E. Adlaf, M. Escobar and L. Douglas (2001). "Fourteen-Year Follow-up of Speech/Language-Impaired and Control Children: Psychiatric Outcome." Journal of the American Academy of Child & Adolescent Psychiatry **40**(1): 75-82.
Bell, M. A. and K. Cuevas (2012). "Using EEG to Study Cognitive Development: Issues and Practices." Journal of Cognition and Development **13**(3): 281-294.
Bembich, S., A. Saksida, S. Mastromarino, L. Travan, G. Di Risio, G. Cont and S. Demarini (2022). "Empathy at birth: Mother's cortex synchronizes with that of her newborn in pain." Eur J Neurosci **55**(6): 1519-1531.
Benischek, A., X. Long, C. S. Rohr, S. Bray, D. Dewey and C. Lebel (2020). "Pre-reading language abilities and the brain's functional reading network in young children." Neuroimage **217**: 116903.
Benjamini, Y. and Y. Hochberg (1995). "Controlling the false discovery rate: a practical and powerful approach to multiple testing." Journal of the Royal statistical society: series B (Methodological) **57**(1): 289-300.
Benke, T., B. Köylü, P. Visani, E. Karner, C. Brenneis, L. Bartha, E. Trinka, T. Trieb, S. Felber, G. Bauer, A. Chemelli and K. Willmes (2006). "Language lateralization in temporal lobe epilepsy: a comparison between fMRI and the Wada Test." Epilepsia **47**(8): 1308-1319.
Berdan, L. E., S. P. Keane and S. D. Calkins (2008). "Temperament and externalizing behavior: social preference and perceived acceptance as protective factors." Developmental psychology **44**(4): 957.
Beres, A. M. (2017). "Time is of the Essence: A Review of Electroencephalography (EEG) and Event-Related Brain Potentials (ERPs) in Language Research." Appl Psychophysiol Biofeedback **42**(4): 247-255.
Bergelson, E. and D. Swingley (2012). "At 6–9 months, human infants know the meanings of many common nouns." Proceedings of the National Academy of Sciences **109**(9): 3253-3258.
Berglund-Barraza, A., F. Tian, C. Basak, J. Hart and J. L. Evans (2020). "Tracking Changes in Frontal Lobe Hemodynamic Response in Individual Adults With Developmental Language Disorder Following HD tDCS Enhanced Phonological Working Memory Training: An fNIRS Feasibility Study." Front Hum Neurosci **14**: 362.
Berl, M. M., J. Mayo, E. N. Parks, L. R. Rosenberger, J. VanMeter, N. B. Ratner, C. J. Vaidya and W. D. Gaillard (2014). "Regional differences in the developmental trajectory of lateralization of the language network." Human Brain Mapping **35**(1): 270-284.
Berthier, M. L., M. A. Lambon Ralph, J. Pujol and C. Green (2012). "Arcuate fasciculus variability and repetition: the left sometimes can be right." Cortex **48**(2): 133-143.
Besle, J., O. Bertrand and M. H. Giard (2009). "Electrophysiological (EEG, sEEG, MEG) evidence for multiple audiovisual interactions in the human auditory cortex." Hear Res **258**(1-2): 143-151.
Binder, J. R., R. H. Desai, W. W. Graves and L. L. Conant (2009). "Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies." Cerebral cortex **19**(12): 2767-2796.

Binder, J. R., R. H. Desai, W. W. Graves and L. L. Conant (2009). "Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies." Cereb Cortex **19**(12): 2767-2796.
Bishop, D., J. Chan, J. Hartley and F. Weir (1998). "When a nod is as good as a word: Form-function relationships between questions and their responses." Applied Psycholinguistics **19**(3): 415-432.
Bishop, D. V. (2006). "What causes specific language impairment in children?" Current directions in psychological science **15**(5): 217-221.
Bishop, D. V. (2010). "Which neurodevelopmental disorders get researched and why?" PLoS One **5**(11): e15112.
Bishop, D. V. (2013). "Cerebral asymmetry and language development: cause, correlate, or consequence?" Science **340**(6138): 1230531.
Bishop, D. V. (2014). "Problems with tense marking in children with specific language impairment: not how but when." Philos Trans R Soc Lond B Biol Sci **369**(1634): 20120401.
Bishop, D. V., R. P. Carlyon, J. M. Deeks and S. J. Bishop (1999). "Auditory temporal processing impairment: neither necessary nor sufficient for causing language impairment in children." J Speech Lang Hear Res **42**(6): 1295-1310.
Bishop, D. V., M. Hardiman, R. Uwer and W. von Suchodoletz (2007). "Atypical long-latency auditory event-related potentials in a subset of children with specific language impairment." Dev Sci **10**(5): 576-587.
Bishop, D. V., G. Holt, A. J. Whitehouse and M. Groen (2014). "No population bias to left-hemisphere language in 4-year-olds with language impairment." PeerJ **2**: e507.
Bishop, D. V., T. North and C. Donlan (1995). "Genetic basis of specific language impairment: evidence from a twin study." Dev Med Child Neurol **37**(1): 56-71.
Bishop, D. V. M., M. J. Snowling, P. A. Thompson, T. Greenhalgh and a. t. C.-. consortium (2017). "Phase 2 of CATALISE: a multinational and multidisciplinary Delphi consensus study of problems with language development: Terminology." Journal of Child Psychology and Psychiatry **58**(10): 1068-1080.
Bishop, D. V. M., M. J. Snowling, P. A. Thompson, T. Greenhalgh and C. consortium (2016). "CATALISE: A Multinational and Multidisciplinary Delphi Consensus Study. Identifying Language Impairments in Children." PLOS ONE **11**(7): e0158753.
Blasi, A., S. Lloyd-Fox, M. H. Johnson and C. Elwell (2014). "Test-retest reliability of functional near infrared spectroscopy in infants." Neurophotonics **1**(2): 025005.
Boas, D. A., A. M. Dale and M. A. Franceschini (2004). "Diffuse optical imaging of brain activation: approaches to optimizing image sensitivity, resolution, and accuracy." NeuroImage **23**: S275-S288.
Borjkhani, H. and S. K. Setarehdan (2020). "Performance assessment of high-density diffuse optical topography regarding source-detector array topology." PLoS One **15**(3): e0230206.
Bornstein, M. H. and C. S. Tamis-LeMonda (1989). "Maternal responsiveness and cognitive development in children." New Dir Child Dev(43): 49-61.
Bortfeld, H. (2019). "Functional near-infrared spectroscopy as a tool for assessing speech and spoken language processing in pediatric and adult cochlear implant users." Dev Psychobiol **61**(3): 430-443.
Boudreau, D. M. and N. L. Hedberg (1999). "A comparison of early literacy skills in children with specific language impairment and their typically developing peers." American Journal of Speech-Language Pathology **8**(3): 249-260.
Bradshaw, A. R., P. A. Thompson, A. C. Wilson, D. V. M. Bishop and Z. V. J. Woodhead (2017). "Measuring language lateralisation with different language tasks: a systematic review." PeerJ **5**: e3929.

Brauer, J. and A. D. Friederici (2007). "Functional neural networks of semantic and syntactic processes in the developing brain." Journal of cognitive neuroscience **19**(10): 1609-1623.
Braun, V. and V. Clarke (2006). "Using thematic analysis in psychology." Qualitative Research in Psychology **3**(2): 77-101.
Briscoe, J., D. V. Bishop and C. F. Norbury (2001). "Phonological processing, language, and literacy: a comparison of children with mild-to-moderate sensorineural hearing loss and those with specific language impairment." J Child Psychol Psychiatry **42**(3): 329-340.
Brown, T., M. Erhart, D. Avesar, A. Dale, E. Halgren and J. Evans (2014). "Atypical Right Hemisphere Specialization for Object Representations in an Adolescent with Specific Language Impairment." Frontiers in Human Neuroscience **8**.
Brown, T. T. (2017). "Individual differences in human brain development." Wiley Interdiscip Rev Cogn Sci **8**(1-2).
Brown, T. T., H. M. Lugar, R. S. Coalson, F. M. Miezin, S. E. Petersen and B. L. Schlaggar (2005). "Developmental changes in human cerebral functional organization for word generation." Cerebral Cortex **15**(3): 275-290.
Bruchhage, M. M. K., G. C. Ngo, N. Schneider, V. D'Sa and S. C. L. Deoni (2020). "Functional connectivity correlates of infant and early childhood cognitive development." Brain Struct Funct **225**(2): 669-681.
Bryan, K., G. Garvani, J. Gregory and K. Kilner (2015). "Language difficulties and criminal justice: The need for earlier identification." International Journal of Language & Communication Disorders **50**(6): 763-775.
BSA (2018). Recommended Procedure Pure Tone Audiometry. B. S. o. Audiology. Bathgate.
Buchsbaum, B. R., R. K. Olsen, P. Koch and K. F. Berman (2005). "Human dorsal and ventral auditory streams subserve rehearsal-based and echoic processes during verbal working memory." Neuron **48**(4): 687-697.
Burgoyne, K., R. Gardner, H. Whiteley, M. J. Snowling and C. Hulme (2018). "Evaluation of a parent-delivered early language enrichment programme: Evidence from a randomised controlled trial." Journal of Child Psychology and Psychiatry **59**(5): 545-555.
Button, K. S., J. P. Ioannidis, C. Mokrysz, B. A. Nosek, J. Flint, E. S. Robinson and M. R. Munafò (2013). "Power failure: why small sample size undermines the reliability of neuroscience." Nat Rev Neurosci **14**(5): 365-376.
Calder, S. D., M. Claessen, S. Leitão and S. Ebbels (2022). "A profile of expressive inflectional morphology in early school-age children with developmental language disorder." Clin Linguist Phon **36**(4-5): 341-358.
Cao, J., X. Wang, H. Liu and G. Alexandrakis (2018). "Directional changes in information flow between human brain cortical regions after application of anodal transcranial direct current stimulation (tDCS) over Broca's area." Biomed Opt Express **9**(11): 5296-5317.
Cardy, J. E., R. Tannock, A. M. Johnson and C. J. Johnson (2010). "The contribution of processing impairments to SLI: insights from attention-deficit/hyperactivity disorder." J Commun Disord **43**(2): 77-91.
Carollo, A., M. Lim, V. Aryadoust and G. Esposito (2021). "Interpersonal Synchrony in the Context of Caregiver-Child Interactions: A Document Co-citation Analysis." Frontiers in Psychology **12**.
Cartmill, E. A., B. F. Armstrong III, L. R. Gleitman, S. Goldin-Meadow, T. N. Medina and J. C. Trueswell (2013). "Quality of early parent input predicts child vocabulary 3 years later." Proceedings of the National Academy of Sciences **110**(28): 11278-11283.

Catts, H. W., M. E. Fey, J. B. Tomblin and X. Zhang (2002). "A longitudinal investigation of reading outcomes in children with language impairments."
Chaddock-Heyman, L., T. B. Weng, C. Kienzler, K. I. Erickson, M. W. Voss, E. S. Drollette, L. B. Raine, S. C. Kao, C. H. Hillman and A. F. Kramer (2018). "Scholastic performance and functional connectivity of brain networks in children." PLoS One **13**(1): e0190073.
Chang, S. E., H. M. Chow, E. A. Wieland and J. D. McAuley (2016). "Relation between functional connectivity and rhythm discrimination in children who do and do not stutter." Neuroimage Clin **12**: 442-450.
Chen, W. L., J. Wagner, N. Heugel, J. Sugar, Y. W. Lee, L. Conant, M. Malloy, J. Heffernan, B. Quirk, A. Zinos, S. A. Beardsley, R. Prost and H. T. Whelan (2020). "Functional Near-Infrared Spectroscopy and Its Clinical Application in the Field of Neuroscience: Advances and Future Directions." Front Neurosci **14**: 724.
Cheng, H. C., R. J. Cherng and P. Y. Yang (2022). "Rapid automatic naming and phonological awareness deficits in preschool children with probable developmental coordination disorder." Front Pediatr **10**: 957823.
Cheng, X., X. Li and Y. Hu (2015). "Synchronous brain activity during cooperative exchange depends on gender of partner: A fNIRS-based hyperscanning study." Hum Brain Mapp **36**(6): 2039-2048.
Cheng, Y. Y., H. C. Wu, H. Y. Shih, P. W. Yeh, H. L. Yen and C. Y. Lee (2021). "Deficits in Processing of Lexical Tones in Mandarin-Speaking Children With Developmental Language Disorder: Electrophysiological Evidence." J Speech Lang Hear Res **64**(4): 1176-1188.
Chilosi, A. M., P. Brovedani, P. Cipriani and C. Casalini (2021). "Sex differences in early language delay and in developmental language disorder." Journal of Neuroscience Research **n/a**(n/a).
Chinn, L. K., M. A. Zhukova, R. J. Kroeger, L. M. Ledesma, J. E. Cavitt and E. L. Grigorenko (2022). "Auditory brainstem response deficits in learning disorders and developmental language disorder: a systematic review and meta-analysis." Sci Rep **12**(1): 20124.
Chou, T. L., J. R. Booth, D. D. Burman, T. Bitan, J. D. Bigio, D. Lu and N. E. Cone (2006). "Developmental changes in the neural correlates of semantic processing." Neuroimage **29**(4): 1141-1149.
Claessen, M., S. Leitão, R. Kane and C. Williams (2013). "Phonological processing skills in specific language impairment." Int J Speech Lang Pathol **15**(5): 471-483.
Collins, D. L., A. P. Zijdenbos, V. Kollokian, J. G. Sled, N. J. Kabani, C. J. Holmes and A. C. Evans (1998). "Design and construction of a realistic digital brain phantom." IEEE transactions on medical imaging **17**(3): 463-468.
Conant, L. L., E. Liebenthal, A. Desai and J. R. Binder (2017). "The relationship between maternal education and the neural substrates of phoneme perception in children: Interactions between socioeconomic status and proficiency level." Brain Lang **171**: 14-22.
Confederation, N. (2022). Hidden waits: the lasting impact of the pandemic on children's services in the community. N. Providers.
Conti-Ramsden, G. and N. Botting (1999). "Classification of children with specific language impairment: Longitudinal considerations." Journal of Speech, Language, and Hearing Research **42**(5): 1195-1204.
Conti-Ramsden, G., P. L. Mok, A. Pickles and K. Durkin (2013). "Adolescents with a history of specific language impairment (SLI): Strengths and difficulties in social, emotional and behavioral functioning." Research in developmental disabilities **34**(11): 4161-4169.
Conti-Ramsden, G., M. T. Ullman and J. A. G. Lum (2015). "The relation between receptive grammar and procedural, declarative, and working memory in specific language impairment." Frontiers in psychology **6**: 1090-1090.

Cooke, A., E. B. Zurif, C. DeVita, D. Alsop, P. Koenig, J. Detre, J. Gee, M. Pinãngo, J. Balogh and M. Grossman (2002). "Neural basis for sentence comprehension: grammatical and short-term memory components." Hum Brain Mapp **15**(2): 80-94.
Cooke, J. E., L. B. Kochendorfer, K. L. Stuart-Parrigon, A. J. Koehn and K. A. Kerns (2019). "Parent-child attachment and children's experience and regulation of emotion: A meta-analytic review." Emotion **19**(6): 1103-1126.
Corp, I. (2020). IBM SPSS Statistics for Windows. I. Corp. Armonk, NY, IBM Corp.
Crow, T. J., L. R. Crow, D. J. Done and S. Leask (1998). "Relative hand skill predicts academic ability: global deficits at the point of hemispheric indecision." Neuropsychologia **36**(12): 1275-1282.
Crowe, L. K., J. A. Norris and P. R. Hoffman (2004). "Training caregivers to facilitate communicative participation of preschool children with language impairment during storybook reading." Journal of Communication Disorders **37**(2): 177-196.
Cui, X., S. Bray, D. M. Bryant, G. H. Glover and A. L. Reiss (2011). "A quantitative comparison of NIRS and fMRI across multiple cognitive tasks." Neuroimage **54**(4): 2808-2821.
Curtin, F. and P. Schulz (1998). "Multiple correlations and Bonferroni's correction." Biol Psychiatry **44**(8): 775-777.
Curtin, M., E. Dirks, M. Cruice, R. Herman, L. Newman, L. Rodgers and G. Morgan (2021). "Assessing Parent Behaviours in Parent-Child Interactions with Deaf and Hard of Hearing Infants Aged 0-3 Years: A Systematic Review." J Clin Med **10**(15).
Czeszumski, A., S. Eustergerling, A. Lang, D. Menrath, M. Gerstenberger, S. Schuberth, F. Schreiber, Z. Z. Rendon and P. König (2020). "Hyperscanning: A Valid Method to Study Neural Inter-brain Underpinnings of Social Interaction." Front Hum Neurosci **14**: 39.
D'Souza, H. and A. Karmiloff-Smith (2017). "Neurodevelopmental disorders." Wiley Interdisciplinary Reviews: Cognitive Science **8**(1-2): e1398.
Davies, D. J., M. Clancy, D. Lighter, G. M. Balanos, S. J. E. Lucas, H. Dehghani, Z. Su, M. Forcione and A. Belli (2017). "Frequency-domain vs continuous-wave near-infrared spectroscopy devices: a comparison of clinically viable monitors in controlled hypoxia." J Clin Monit Comput **31**(5): 967-974.
Davis, M., J. Bilms and C. Suveg (2017). "In sync and in control: A meta-analysis of parent–child positive behavioral synchrony and youth self-regulation." Family process **56**(4): 962-980.
Davis, M., K. West, J. Bilms, D. Morelen and C. Suveg (2018). "A systematic review of parent–child synchrony: It is more than skin deep." Developmental Psychobiology **60**(6): 674-691.
Dawes, P. and D. Bishop (2009). "Auditory processing disorder in relation to developmental disorders of language, communication and attention: a review and critique." Int J Lang Commun Disord **44**(4): 440-465.
De Fossé, L., S. M. Hodge, N. Makris, D. N. Kennedy, V. S. Caviness, Jr., L. McGrath, S. Steele, D. A. Ziegler, M. R. Herbert, J. A. Frazier, H. Tager-Flusberg and G. J. Harris (2004). "Language-association cortex asymmetry in autism and specific language impairment." Ann Neurol **56**(6): 757-766.
de Guibert, C., C. Maumet, P. Jannin, J. C. Ferré, C. Tréguier, C. Barillot, E. Le Rumeur, C. Allaire and A. Biraben (2011). "Abnormal functional lateralization and activity of language brain areas in typical specific language impairment (developmental dysphasia)." Brain **134**(Pt 10): 3044-3058.
Delage, H. and U. H. Frauenfelder (2020). "Relationship between working memory and complex syntax in children with Developmental Language Disorder." J Child Lang **47**(3): 600-632.

Delaherche, E., M. Chetouani, A. Mahdhaoui, C. Saint-georges, S. Viaux and D. Cohen (2012). "Interpersonal Synchrony: A Survey of Evaluation Methods across Disciplines." IEEE Transactions on Affective Computing **3**: 349-365.
Desmottes, L., T. Meulemans and C. Maillart (2016). "Later learning stages in procedural memory are impaired in children with Specific Language Impairment." Res Dev Disabil **48**: 53-68.
Dibbets, P., K. Bakker and J. Jolles (2006). "Functional MRI of task switching in children with Specific Language Impairment (SLI)." Neurocase **12**(1): 71-79.
Dick, F., B. Wulfeck, M. Krupa-Kwiatkowski and E. Bates (2004). "The development of complex sentence interpretation in typically developing children compared with children with specific language impairments or early unilateral focal lesions." Dev Sci **7**(3): 360-377.
Dietrich, S., H. Ackermann, D. P. Szameitat and K. Alter (2006). "Psychoacoustic studies on the processing of vocal interjections: how to disentangle lexical and prosodic information?" Prog Brain Res **156**: 295-302.
Djalovski, A., G. Dumas, S. Kinreich and R. Feldman (2021). "Human attachments shape interbrain synchrony toward efficient performance of social goals." NeuroImage **226**: 117600.
Dockrell, J. E. and D. Messer (2007). "Language profiles and naming in children with word finding difficulties." Folia Phoniatrica et Logopaedica **59**(6): 318-323.
Dockrell, J. E., J. Ricketts, T. Charman and G. Lindsay (2014). "Exploring writing products in students with language impairments and autism spectrum disorders." Learning and Instruction **32**: 81-90.
Doesburg, S. M., K. Tingling, M. J. MacDonald and E. W. Pang (2016). "Development of Network Synchronization Predicts Language Abilities." J Cogn Neurosci **28**(1): 55-68.
Dollar, J. M. and C. A. Stifter (2012). "Temperamental surgency and emotion regulation as predictors of childhood social competence." J Exp Child Psychol **112**(2): 178-194.
Dravida, S., J. A. Noah, X. Zhang and J. Hirsch (2020). "Joint Attention During Live Person-to-Person Contact Activates rTPJ, Including a Sub-Component Associated With Spontaneous Eye-to-Eye Contact." Front Hum Neurosci **14**: 201.
Duan, L., Y. J. Zhang and C. Z. Zhu (2012). "Quantitative comparison of resting-state functional connectivity derived from fNIRS and fMRI: a simultaneous recording study." Neuroimage **60**(4): 2008-2018.
Duinmeijer, I. (2013). "Persistent problems in SLI: which grammatical problems remain when children grow older?" Linguistics in Amsterdam **6**: 28-48.
Dumas, G., J. Nadel, R. Soussignan, J. Martinerie and L. Garnero (2010). "Inter-Brain Synchronization during Social Interaction." PLOS ONE **5**(8): e12166.
Durkin, K. and G. Conti-Ramsden (2010). "Young people with specific language impairment: A review of social and emotional functioning in adolescence." Child Language Teaching and Therapy **26**: 105-121.
Ebbels, S. (2007). "Teaching grammar to school-aged children with specific language impairment using Shape Coding." Child Language Teaching & Therapy - CHILD LANG TEACH THER **23**.
Ebbels, S. (2014). "Introducing the SLI debate." International Journal of Language & Communication Disorders **49**(4): 377.
Ebbels, S. H., E. McCartney, V. Slonims, J. E. Dockrell and C. F. Norbury (2019). "Evidence-based pathways to intervention for children with language disorders." International Journal of Language & Communication Disorders **54**(1): 3-19.
Ellis Weismer, S. (2013). "Developmental Language Disorders: Challenges and Implications of Cross-Group Comparisons." Folia Phoniatrica et Logopaedica **65**(2): 68-77.

Ellis Weismer, S., M. M. Davidson, I. Gangopadhyay, H. Sindberg, H. Roebuck and M. Kaushanskaya (2017). "The role of nonverbal working memory in morphosyntactic processing by children with specific language impairment and autism spectrum disorders." Journal of neurodevelopmental disorders **9**: 28-28.
Ellis Weismer, S., E. Plante, M. Jones and J. B. Tomblin (2005). "A functional magnetic resonance imaging investigation of verbal working memory in adolescents with specific language impairment." J Speech Lang Hear Res **48**(2): 405-425.
Ellis Weismer, S., J. B. Tomblin, X. Zhang, P. Buckwalter, J. G. Chynoweth and M. Jones (2000). "Nonword repetition performance in school-age children with and without language impairment." J Speech Lang Hear Res **43**(4): 865-878.
Elmahallawi, T. H., T. A. Gabr, M. E. Darwish and F. M. Seleem (2022). "Children with developmental language disorder: a frequency following response in the noise study." Braz J Otorhinolaryngol **88**(6): 954-961.
Engel de Abreu, P. M., A. Cruz-Santos and M. L. Puglisi (2014). "Specific language impairment in language-minority children from low-income families." Int J Lang Commun Disord **49**(6): 736-747.
Eriksson, J., E. K. Vogel, A. Lansner, F. Bergström and L. Nyberg (2015). "Neurocognitive Architecture of Working Memory." Neuron **88**(1): 33-46.
Evans, J. L., M. J. Maguire and M. L. Sizemore (2022). "Neural patterns elicited by lexical processing in adolescents with specific language impairment: support for the procedural deficit hypothesis?" J Neurodev Disord **14**(1): 20.
Factor, L. and L. Goffman (2022). "Phonological characteristics of novel gesture production in children with developmental language disorder: Longitudinal findings." Appl Psycholinguist **43**(2): 333-362.
Fan, S., B. Ma, X. Song and Y. Wang (2022). "Effect of language therapy alone for developmental language disorder in children: A meta-analysis." Front Psychol **13**: 922866.
Farah, R., J. Dudley, J. S. Hutton, P. Greenwood, S. Holland and T. Horowitz-Kraus (2021). "Maternal depression is associated with decreased functional connectivity within semantics and phonology networks in preschool children." Depress Anxiety **38**(8): 826-835.
Farquharson, K., T. M. Centanni, C. E. Franzluebbers and T. P. Hogan (2014). "Phonological and lexical influences on phonological awareness in children with specific language impairment and dyslexia." Front Psychol **5**: 838.
Farran, D. C. and C. Kasari (1990). "A longitudinal analysis of the development of synchrony in mutual gaze in mother-child dyads." Journal of Applied Developmental Psychology **11**(4): 419-430.
Feldman, R. (2007). "Parent–infant synchrony: Biological foundations and developmental outcomes." Current directions in psychological science **16**(6): 340-345.
Ferrari, M. and V. Quaresima (2012). "A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application." Neuroimage **63**(2): 921-935.
Finke, K., P. Bublak and J. Zihl (2006). "Visual spatial and visual pattern working memory: neuropsychological evidence for a differential role of left and right dorsal visual brain." Neuropsychologia **44**(4): 649-661.
Fitton, L., R. Hoge, Y. Petscher and C. Wood (2019). "Psychometric Evaluation of the Bilingual English-Spanish Assessment Sentence Repetition Task for Clinical Decision Making." J Speech Lang Hear Res **62**(6): 1906-1922.
Fraschini, M. H., Arjan (2017). Phase Transfer Entropy in Matlab., figshare.
Friston, K., R. Moran and A. K. Seth (2013). "Analysing connectivity with Granger causality and dynamic causal modelling." Curr Opin Neurobiol **23**(2): 172-178.

Frizelle, P., A. K. Tolonen, J. Tulip, C. A. Murphy, D. Saldana and C. McKean (2021). "The Influence of Quantitative Intervention Dosage on Oral Language Outcomes for Children With Developmental Language Disorder: A Systematic Review and Narrative Synthesis." Lang Speech Hear Serv Sch **52**(2): 738-754.
Fu, G., N. J. Wan, J. M. Baker, J. W. Montgomery, J. L. Evans and R. B. Gillam (2016). "A proof of concept study of function-based statistical analysis of fNIRS data: syntax comprehension in children with specific language impairment compared to typically-developing controls." Frontiers in Behavioral Neuroscience **10**: 108.
Fukui, Y., Y. Ajichi and E. Okada (2003). "Monte Carlo prediction of near-infrared light propagation in realistic adult and neonatal head models." Appl Opt **42**(16): 2881-2887.
Fuster, J. M. (2001). "The prefrontal cortex--an update: time is of the essence." Neuron **30**(2): 319-333.
Gabrielsen, T. P., J. S. Anderson, K. G. Stephenson, J. Beck, J. B. King, R. Kellems, D. N. Top, Jr., N. C. C. Russell, E. Anderberg, R. A. Lundwall, B. Hansen and M. South (2018). "Functional MRI connectivity of children with autism and low verbal and cognitive performance." Mol Autism **9**: 67.
Gallagher, A., R. Béland and M. Lassonde (2012). "The contribution of functional near-infrared spectroscopy (fNIRS) to the presurgical assessment of language function in children." Brain and language **121**(2): 124-129.
Gallagher, A., J. Tremblay and P. Vannasing (2016). "Language mapping in children using resting-state functional connectivity: comparison with a task-based approach." J Biomed Opt **21**(12): 125006.
Gathercole, S. E. and A. D. Baddeley (1990). "Phonological memory deficits in language disordered children: Is there a causal connection?" Journal of Memory and Language **29**(3): 336-360.
Gaudet, I., A. Hüsser, P. Vannasing and A. Gallagher (2020). "Functional Brain Connectivity of Language Functions in Children Revealed by EEG and MEG: A Systematic Review." Frontiers in human neuroscience **14**: 62-62.
Gervain, J. (2014). "Near-infrared spectroscopy: recent advances in infant speech perception and language acquisition research." Front Psychol **5**: 916.
Gibson, S. (2015). Special educational needs in England: January 2015. D. f. Education.
Gilkerson, J., J. A. Richards, S. F. Warren, D. K. Oller, R. Russo and B. Vohr (2018). "Language Experience in the Second Year of Life and Language Outcomes in Late Childhood." Pediatrics **142**(4).
Gillam, R. B., S. Serang, J. W. Montgomery and J. L. Evans (2021). "Cognitive Processes Related to Memory Capacity Explain Nearly All of the Variance in Language Test Performance in School-Age Children With and Without Developmental Language Disorder." Front Psychol **12**: 724356.
Girbau-Massana, D., G. Garcia-Marti, L. Marti-Bonmati and R. G. Schwartz (2014). "Gray-white matter and cerebrospinal fluid volume differences in children with Specific Language Impairment and/or Reading Disability." Neuropsychologia **56**: 90-100.
Golestani, N., A. Hervais-Adelman, J. Obleser and S. K. Scott (2013). "Semantic versus perceptual interactions in neural processing of speech-in-noise." NeuroImage **79**: 52-61.
Graessner, A., E. Zaccarella and G. Hartwigsen (2021). "Differential contributions of left-hemispheric language regions to basic semantic composition." Brain Structure and Function **226**(2): 501-518.
Granger, C. W. J. (1969). "Investigating Causal Relations by Econometric Models and Cross-spectral Methods." Econometrica **37**(3): 424-438.

Graves, W. W., J. R. Binder, R. H. Desai, L. L. Conant and M. S. Seidenberg (2010). "Neural correlates of implicit and explicit combinatorial semantic processing." Neuroimage **53**(2): 638-646.
Groba, A., A. De Houwer, H. Obrig and S. Rossi (2019). "Bilingual and Monolingual First Language Acquisition Experience Differentially Shapes Children's Property Term Learning: Evidence from Behavioral and Neurophysiological Measures." Brain Sci **9**(2).
Grol, R. and M. Wensing (2004). "What drives change? Barriers to and incentives for achieving evidence-based practice." Medical Journal of Australia **180**(S6): S57-S60.
Gross, J. J. and O. P. John (2003). "Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being." J Pers Soc Psychol **85**(2): 348-362.
Gummadavelli, A., Y. Wang, X. Guo, M. Pardos, H. Chu, Y. Liu, P. Horn, F. Zhang and J. Xiang (2013). "Spatiotemporal and frequency signatures of word recognition in the developing brain: a magnetoencephalographic study." Brain Res **1498**: 20-32.
Gumulak, R., L. C. Lucanova and M. Zibolen (2017). "Use of near-infrared spectroscopy (NIRS) in cerebral tissue oxygenation monitoring in neonates." Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub **161**(2): 128-133.
Gunnar, M. R., A. M. Sebanc, K. Tout, B. Donzella and M. M. Van Dulmen (2003). "Peer rejection, temperament, and cortisol activity in preschoolers." Developmental Psychobiology: The Journal of the International Society for Developmental Psychobiology **43**(4): 346-368.
Gvirts, H. Z. and R. Perlmutter (2020). "What Guides Us to Neurally and Behaviorally Align With Anyone Specific? A Neurobiological Model Based on fNIRS Hyperscanning Studies." Neuroscientist **26**(2): 108-116.
Hage, S. V. R., L. Y. Sawasaki, Y. Hyter and F. D. M. Fernandes (2021). "Social Communication and pragmatic skills of children with Autism Spectrum Disorder and Developmental Language Disorder." Codas **34**(2): e20210075.
Haghighat, H., M. Mirzarezaee, B. N. Araabi and A. Khadem (2021). "Functional Networks Abnormalities in Autism Spectrum Disorder: Age-Related Hypo and Hyper Connectivity." Brain Topography **34**(3): 306-322.
Harrison, S. and D. Hartley (2019). "Shedding Light On The Human Auditory Cortex: A Review Of The Advances In Near Infrared Spectroscopy (NIRS)." Reports in Medical Imaging **Volume 12**: 31-42.
Harrist, A. W. and R. M. Waugh (2002). "Dyadic synchrony: Its structure and function in children's development." Developmental review **22**(4): 555-592.
Hartley, D. E., P. R. Hill and D. R. Moore (2003). "The auditory basis of language impairments: temporal processing versus processing efficiency hypotheses." Int J Pediatr Otorhinolaryngol **67 Suppl 1**: S137-142.
Hartwigsen, G., N. E. Neef, J. A. Camilleri, D. S. Margulies and S. B. Eickhoff (2019). "Functional Segregation of the Right Inferior Frontal Gyrus: Evidence From Coactivation-Based Parcellation." Cerebral Cortex **29**(4): 1532-1546.
Hasson, U., A. A. Ghazanfar, B. Galantucci, S. Garrod and C. Keysers (2012). "Brain-to-brain coupling: a mechanism for creating and sharing a social world." Trends Cogn Sci **16**(2): 114-121.
Heather, K. J. v. D. L. and B. Jackie (2003). "WH-Movement in Children with Grammatical SLI: A Test of the RDDR Hypothesis." Language **79**(1): 153-181.
Heidlage, J. K., J. E. Cunningham, A. P. Kaiser, C. M. Trivette, E. E. Barton, J. R. Frey and M. Y. Roberts (2020). "The effects of parent-implemented language interventions on child linguistic outcomes: A meta-analysis." Early Childhood Research Quarterly **50**: 6-23.

Helenius, P., P. Sivonen, T. Parviainen, P. Isoaho, S. Hannus, T. Kauppila, R. Salmelin and L. Isotalo (2014). "Abnormal functioning of the left temporal lobe in language-impaired children." Brain Lang **130**: 11-18.
Henry, L. A., D. J. Messer and G. Nash (2012). "Executive functioning in children with specific language impairment." Journal of child psychology and psychiatry **53**(1): 37-45.
Henry, L. A., D. J. Messer and G. Nash (2012). "Executive functioning in children with specific language impairment." J Child Psychol Psychiatry **53**(1): 37-45.
Hepper, P. G. and B. S. Shahidullah (1994). "Development of fetal hearing." Arch Dis Child Fetal Neonatal Ed **71**(2): F81-87.
Hesketh, A. and G. Conti-Ramsden (2013). "Memory and language in middle childhood in individuals with a history of specific language impairment." PLoS One **8**(2): e56314.
Hickok, G., B. Buchsbaum, C. Humphries and T. Muftuler (2003). "Auditory-motor interaction revealed by fMRI: speech, music, and working memory in area Spt." J Cogn Neurosci **15**(5): 673-682.
Hickok, G. and D. Poeppel (2004). "Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language." Cognition **92**(1-2): 67-99.
Hickok, G. and D. Poeppel (2007). "The cortical organization of speech processing." Nat Rev Neurosci **8**(5): 393-402.
Hirsch, J., X. Zhang, J. A. Noah and Y. Ono (2017). "Frontal temporal and parietal systems synchronize within and across brains during live eye-to-eye contact." Neuroimage **157**: 314-330.
Hoehl, S., M. Fairhurst and A. Schirmer (2020). "Interactional synchrony: signals, mechanisms and benefits." Social Cognitive and Affective Neuroscience **16**(1-2): 5-18.
Hoff, G. E. A.-J., M. Van Den Heuvel, M. J. N. L. Benders, K. J. Kersbergen and L. S. de Vries (2013). "On development of functional brain connectivity in the young brain." Frontiers in Human Neuroscience **7**(650).
Holland, S. K., E. Plante, A. W. Byars, R. H. Strawsburg, V. J. Schmithorst and W. S. Ball Jr (2001). "Normal fMRI brain activation patterns in children performing a verb generation task." Neuroimage **14**(4): 837-843.
Holland, S. K., J. Vannest, M. Mecoli, L. M. Jacola, J. M. Tillema, P. R. Karunanayaka, V. J. Schmithorst, W. Yuan, E. Plante and A. W. Byars (2007). "Functional MRI of language lateralization during development in children." Int J Audiol **46**(9): 533-551.
Hollenstein, T., A. B. Tighe and J. P. Lougheed (2017). "Emotional development in the context of mother-child relationships." Curr Opin Psychol **17**: 140-144.
Hollo, A. and J. Chow (2015). "Communicative Functions of Problem Behavior for Students with High-Incidence Disabilities." Beyond Behavior **24**(3): 23-30.
Horowitz-Kraus, T. and S. K. Holland (2015). "Greater functional connectivity between reading and error-detection regions following training with the reading acceleration program in children with reading difficulties." Ann Dyslexia **65**(1): 1-23.
Horowitz-Kraus, T., J. J. Vannest, D. Kadis, N. Cicchino, Y. Y. Wang and S. K. Holland (2014). "Reading acceleration training changes brain circuitry in children with reading difficulties." Brain Behav **4**(6): 886-902.
Hosomi, A., Y. Nagakane, K. Yamada, N. Kuriyama, T. Mizuno, T. Nishimura and M. Nakagawa (2009). "Assessment of arcuate fasciculus with diffusion-tensor tractography may predict the prognosis of aphasia in patients with left middle cerebral artery infarcts." Neuroradiology **51**(9): 549-555.
Hoyniak, C. P., L. E. Quiñones-Camacho, M. C. Camacho, J. H. Chin, E. M. Williams, L. S. Wakschlag and S. B. Perlman (2021). "Adversity is Linked with Decreased Parent-Child Behavioral and Neural Synchrony." Dev Cogn Neurosci **48**: 100937.

Hsu, H. J. and D. V. Bishop (2014). "Training understanding of reversible sentences: a study comparing language-impaired children with age-matched and grammar-matched controls." PeerJ **2**: e656.
Hu, X. S., K. S. Hong and S. S. Ge (2012). "fNIRS-based online deception decoding." J Neural Eng **9**(2): 026012.
Huang, Y., M. Mao, Z. Zhang, H. Zhou, Y. Zhao, L. Duan, U. Kreplin, X. Xiao and C. Zhu (2017). "Test-retest reliability of the prefrontal response to affective pictures based on functional near-infrared spectroscopy." J Biomed Opt **22**(1): 16011.
Hugdahl, K., H. Gundersen, C. Brekke, T. Thomsen, L. M. Rimol, L. Ersland and J. Niemi (2004). "FMRI brain activation in a finnish family with specific language impairment compared with a normal control group." J Speech Lang Hear Res **47**(1): 162-172.
Huppert, T. J., S. G. Diamond, M. A. Franceschini and D. A. Boas (2009). "HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain." Applied optics **48**(10): D280-D298.
Hwang, J. W., J. B. Lee, B. N. Kim, H. Y. Lee, D. S. Lee, M. S. Shin and S. C. Cho (2006). "Regional cerebral perfusion abnormalities in developmental language disorder. Statistical parametric mapping analysis." Eur Arch Psychiatry Clin Neurosci **256**(3): 131-137.
Im-Bolter, N., J. Johnson and J. Pascual-Leone (2006). "Processing limitations in children with specific language impairment: The role of executive function." Child development **77**(6): 1822-1841.
Im, S.-H., E. S. Park, D. Y. Kim, D. H. Song and J. D. Lee (2007). "The Neuroradiological Findings of Children with Developmental Language Disorder." ymj **48**(3): 405-411.
Irimia, A., M. J. Erhart and T. T. Brown (2014). "Variability of magnetoencephalographic sensor sensitivity measures as a function of age, brain volume and cortical area." Clin Neurophysiol **125**(10): 1973-1984.
Jasper, H. H. (1958). "The ten-twenty electrode system of the International Federation." Electroencephalogr. Clin. Neurophysiol. **10**: 370-375.
Jeong, J., E. E. Franchett, C. V. Ramos de Oliveira, K. Rehmani and A. K. Yousafzai (2021). "Parenting interventions to promote early child development in the first three years of life: A global systematic review and meta-analysis." PLoS Med **18**(5): e1003602.
Jiang, J., K. Borowiak, L. Tudge, C. Otto and K. von Kriegstein (2017). "Neural mechanisms of eye contact when listening to another person talking." Soc Cogn Affect Neurosci **12**(2): 319-328.
Jiang, J., B. Dai, D. Peng, C. Zhu, L. Liu and C. Lu (2012). "Neural synchronization during face-to-face communication." J Neurosci **32**(45): 16064-16069.
Johnson, C. J., J. H. Beitchman and E. Brownlie (2010). "Twenty-year follow-up of children with and without speech-language impairments: Family, educational, occupational, and quality of life outcomes."
Jokihaka, S., M. Laasonen, P. Lahti-Nuuttila, S. Smolander, S. Kunnari, E. Arkkila, A. K. Pesonen and K. Heinonen (2022). "Cross-Sectional and Longitudinal Associations Between Quality of Parent-Child Interaction and Language Ability in Preschool-Age Children With Developmental Language Disorder." J Speech Lang Hear Res **65**(6): 2258-2271.
Justice, L. M., H. Jiang, K. M. Purtell, K. Schmeer, K. Boone, R. Bates and P. J. Salsberry (2019). "Conditions of Poverty, Parent-Child Interactions, and Toddlers' Early Language Skills in Low-Income Families." Matern Child Health J **23**(7): 971-978.
Justice, L. M., J. Kaderavek, R. Bowles and K. Grimm (2005). "Language impairment, parent—child shared reading, and phonological awareness: a feasibility study." Topics in Early Childhood Special Education **25**(3): 143-156.
Kadis, D. (2010). Developmental plasticity of language representation in healthy subjects and children with medically intractable epilepsy.

Kadis, D. S., A. Dimitrijevic, C. A. Toro-Serey, M. L. Smith and S. K. Holland (2016). "Characterizing Information Flux Within the Distributed Pediatric Expressive Language Network: A Core Region Mapped Through fMRI-Constrained MEG Effective Connectivity Analyses." Brain Connect **6**(1): 76-83.
Kambanaros, M. and K. K. Grohmann (2015). "Grammatical Class Effects Across Impaired Child and Adult Populations." Front Psychol **6**: 1670.
Kamhi, A. G. (2004). "A meme's eye view of speech-language pathology."
Kamran, M. A., M. M. Mannan and M. Y. Jeong (2016). "Cortical Signal Analysis and Advances in Functional Near-Infrared Spectroscopy Signal: A Review." Front Hum Neurosci **10**: 261.
Katsos, N., C. A. Roqueta, R. A. Estevan and C. Cummins (2011). "Are children with Specific Language Impairment competent with the pragmatics and logic of quantification?" Cognition **119**(1): 43-57.
Kelley, M. S., J. A. Noah, X. Zhang, B. Scassellati and J. Hirsch (2020). "Comparison of Human Social Brain Activity During Eye-Contact With Another Human and a Humanoid Robot." Front Robot AI **7**: 599581.
Kempler, D. and M. Goral (2011). "A comparison of drill- and communication-based treatment for aphasia." Aphasiology **25**(11): 1327-1346.
Kennan, R. P., D. Kim, A. Maki, H. Koizumi and R. T. Constable (2002). "Non-invasive assessment of language lateralization by transcranial near infrared optical topography and functional MRI." Hum Brain Mapp **16**(3): 183-189.
Kinreich, S., A. Djalovski, L. Kraus, Y. Louzoun and R. Feldman (2017). "Brain-to-Brain Synchrony during Naturalistic Social Interactions." Scientific Reports **7**(1): 17060.
Klem, M., M. Melby-Lervåg, B. Hagtvet, S. A. Lyster, J. E. Gustafsson and C. Hulme (2015). "Sentence repetition is a measure of children's language skills rather than working memory limitations." Dev Sci **18**(1): 146-154.
Knowland, V. C. P., D. H. Baker, M. G. Gaskell, E. van Rijn, S. A. Walker, C. F. Norbury and L. M. Henderson (2022). "Neural Responses to Novel and Existing Words in Children with Autism Spectrum and Developmental Language Disorder." J Cogn **5**(1): 14.
Knox, E. and G. Conti-Ramsden (2003). "Bullying risks of 11-year-old children with specific language impairment (SLI): Does school placement matter?" International Journal of Language & Communication Disorders **38**(1): 1-12.
Koenigs, M., A. K. Barbey, B. R. Postle and J. Grafman (2009). "Superior parietal cortex is critical for the manipulation of information in working memory." J Neurosci **29**(47): 14980-14986.
Koly, K. N., S. P. Martin-Herz, M. S. Islam, N. Sharmin, H. Blencowe and A. Naheed (2021). "Parent mediated intervention programmes for children and adolescents with neurodevelopmental disorders in South Asia: A systematic review." PLoS One **16**(3): e0247432.
Kopton, I. M. and P. Kenning (2014). "Near-infrared spectroscopy (NIRS) as a new tool for neuroeconomic research." Front Hum Neurosci **8**: 549.
Kornilov, S. A., J. S. Magnuson, N. Rakhlin, N. Landi and E. L. Grigorenko (2015). "Lexical processing deficits in children with developmental language disorder: An event-related potentials study." Development and psychopathology **27**(2): 459-476.
Kornilov, S. A., J. S. Magnuson, N. Rakhlin, N. Landi and E. L. Grigorenko (2015). "Lexical processing deficits in children with developmental language disorder: An event-related potentials study." Dev Psychopathol **27**(2): 459-476.
Kovelman, I., M. H. Shalinsky, M. S. Berens and L. A. Petitto (2014). "Words in the bilingual brain: an fNIRS brain imaging investigation of lexical processing in sign-speech bimodal bilinguals." Front Hum Neurosci **8**: 606.

Koyama, M. S., A. Di Martino, X. N. Zuo, C. Kelly, M. Mennes, D. R. Jutagir, F. X. Castellanos and M. P. Milham (2011). "Resting-state functional connectivity indexes reading competence in children and adults." J Neurosci **31**(23): 8617-8624.
Krishnan, S., S. S. Asaridou, G. J. Cler, H. J. Smith, H. E. Willis, M. P. Healy, P. A. Thompson, D. V. M. Bishop and K. E. Watkins (2021). "Functional organisation for verb generation in children with developmental language disorder." Neuroimage **226**: 117599.
Krishnan, S., G. J. Cler, H. J. Smith, H. E. Willis, S. S. Asaridou, M. P. Healy, D. Papp and K. E. Watkins (2022). "Quantitative MRI reveals differences in striatal myelin in children with DLD." Elife **11**: e74242.
Kruppa, J. A., V. Reindl, C. Gerloff, E. Oberwelland Weiss, J. Prinz, B. Herpertz-Dahlmann, K. Konrad and M. Schulte-Rüther (2021). "Brain and motor synchrony in children and adolescents with ASD-a fNIRS hyperscanning study." Soc Cogn Affect Neurosci **16**(1-2): 103-116.
Kruythoff-Broekman, A., C. Wiefferink, C. Rieffe and N. Uilenburg (2019). "Parent-implemented early language intervention programme for late talkers: parental communicative behaviour change and child language outcomes at 3 and 4 years of age." International Journal of Language & Communication Disorders **54**(3): 451-464.
Lakens, D. and E. R. Evers (2014). "Sailing From the Seas of Chaos Into the Corridor of Stability: Practical Recommendations to Increase the Informational Value of Studies." Perspect Psychol Sci **9**(3): 278-292.
Lara-Díaz, M. F., A. Mateus-Moreno and J. C. Beltrán-Rojas (2021). "Reading and Oral Language Skills in Children With Developmental Language Disorder: Influence of Socioeconomic, Educational, and Family Variables." Front Psychol **12**: 718988.
Lavelli, M., C. Barachetti, M. Majorano, E. Florit, C. Brotto and P. Miottello (2019). "Impacts of a shared book-reading intervention for Italian-speaking children with developmental language disorder." International Journal of Language & Communication Disorders **54**(4): 565-579.
Law, J., J. Charlton, J. Dockrell, M. Gascoigne, C. McKean and A. Theakston (2017). "Early Language Development: Needs, provision and intervention for pre-school children from socio-economically disadvantaged backgrounds. London Education Endowment Foundation."
Law, J., Z. Garrett and C. Nye (2003). "Speech and language therapy interventions for children with primary speech and language delay or disorder." Cochrane Database of Systematic Reviews(3).
Law, J., P. Levickis, I. R. Rodríguez-Ortiz, A. Matić, R. Lyons, C. Messarra, E. Kouba Hreich and M. Stankova (2019). "Working with the parents and families of children with developmental language disorders: An international perspective." J Commun Disord **82**: 105922.
Lawrence, R. J., I. M. Wiggins, C. A. Anderson, J. Davies-Thompson and D. E. H. Hartley (2018). "Cortical correlates of speech intelligibility measured using functional near-infrared spectroscopy (fNIRS)." Hear Res **370**: 53-64.
Lawrence, R. J., I. M. Wiggins, J. C. Hodgson and D. E. H. Hartley (2021). "Evaluating cortical responses to speech in children: A functional near-infrared spectroscopy (fNIRS) study." Hearing Research **401**: 108155.
Leclercq, A. L., P. Quémart, D. Magis and C. Maillart (2014). "The sentence repetition task: a powerful diagnostic tool for French children with specific language impairment." Res Dev Disabil **35**(12): 3423-3430.
Leclère, C., S. Viaux, M. Avril, C. Achard, M. Chetouani, S. Missonnier and D. Cohen (2014). "Why synchrony matters during mother-child interactions: a systematic review." PloS one **9**(12): e113571.

Lee, S. M. and G. McCarthy (2016). "Functional Heterogeneity and Convergence in the Right Temporoparietal Junction." Cereb Cortex **26**(3): 1108-1116.
Lemos, C. d., A. Kranios, R. Beauchamp-Whitworth, A. Chandwani, N. Gilbert, A. Holmes, A. Pender, C. Whitehouse and N. Botting (2022). "Awareness of developmental language disorder amongst workplace managers." Journal of Communication Disorders **95**: 106165.
Leonard, L. B. (2009). "Is expressive language disorder an accurate diagnostic category?" Am J Speech Lang Pathol **18**(2): 115-123.
Leonard, L. B. (2009). "Is expressive language disorder an accurate diagnostic category?".
Leonard, L. B. (2010). "Language combinations, subtypes, and severity in the study of bilingual children with specific language impairment." Applied psycholinguistics **31**(2): 310-315.
Leonard, L. B., S. Ellis Weismer, C. A. Miller, D. J. Francis, J. B. Tomblin and R. V. Kail (2007). "Speed of processing, working memory, and language impairment in children." J Speech Lang Hear Res **50**(2): 408-428.
Leonard, M. K., C. Torres, K. E. Travis, T. T. Brown, D. J. Hagler, Jr., A. M. Dale, J. L. Elman and E. Halgren (2011). "Language proficiency modulates the recruitment of non-classical language areas in bilinguals." PLoS One **6**(3): e18240.
Leong, V., E. Byrne, K. Clackson, S. Georgieva, S. Lam and S. Wass (2017). "Speaker gaze increases information coupling between infant and adult brains." Proceedings of the National Academy of Sciences **114**(50): 13290-13295.
Leppänen, P. H. and H. Lyytinen (1997). "Auditory event-related potentials in the study of developmental language-related disorders." Audiol Neurootol **2**(5): 308-340.
Leroy, S., C. Parisse and C. Maillart (2012). "Analogical reasoning in children with specific language impairment." Clin Linguist Phon **26**(4): 380-395.
Levelt, W. J. (2001). "Spoken word production: a theory of lexical access." Proc Natl Acad Sci U S A **98**(23): 13464-13471.
Levickis, P., S. Reilly, L. Girolametto, O. C. Ukoumunne and M. Wake (2014). "Maternal behaviors promoting language acquisition in slow-to-talk toddlers: prospective community-based study." Journal of Developmental & Behavioral Pediatrics **35**(4): 274-281.
Lévy-Rueff, M., M. Bourgeois, A. Assous, B. Beauquier-Maccota, E. Boucheron, C. Clouard, S. Dondé, O. Fostini, P. Pinot, A. Mosser, G. Rittori, C. Soufflet, L. Vaivre-Douret, B. Golse and L. Robel (2012). "[Abnormal electroencephalography results and specific language impairment: towards a theoretical neurodevelopmental model?]." Encephale **38**(4): 318-328.
Lewis, B. A., E. Patton, L. Freebairn, J. Tag, S. K. Iyengar, C. M. Stein and H. G. Taylor (2016). "Psychosocial co-morbidities in adolescents and adults with histories of communication disorders." Journal of Communication Disorders **61**: 60-70.
Li, Y., L. Zhang, Z. Xia, J. Yang, H. Shu and P. Li (2017). "The Relationship between Intrinsic Couplings of the Visual Word Form Area with Spoken Language Network and Reading Ability in Children and Adults." Front Hum Neurosci **11**: 327.
Liao, Y., Z. A. Acar, S. Makeig and G. Deak (2015). "EEG imaging of toddlers during dyadic turn-taking: Mu-rhythm modulation while producing or observing social actions." NeuroImage **112**: 52-60.
Liégeois, F., A. Mayes and A. Morgan (2014). "Neural Correlates of Developmental Speech and Language Disorders: Evidence from Neuroimaging." Current developmental disorders reports **1**(3): 215-227.
Liégeois, F. J., J. Butler, A. T. Morgan, J. D. Clayden and C. A. Clark (2016). "Anatomy and lateralization of the human corticobulbar tracts: an fMRI-guided tractography study." Brain Struct Funct **221**(6): 3337-3345.

Lin, Y.-A. (2006). "Against the Deficit in Computational Grammatical Complexity Hypothesis: A Corpus-Based Study." Concentric: Studies in Linguistics **32**.
Liu, D., B. Wang, Y. Zhang, T. Pan, Y. Liu and F. Gao (2020). Improving temporal resolution of fNIRS-DOT by the guidance of data-reduced pre-OT, SPIE.
Liu, G., E. Huo, H. Liu, G. Jia, Y. Zhi, Q. Dong and H. Niu (2022). "Development and emergence of functional network asymmetry in 3- to 9-month-old infants." Cortex **154**: 390-404.
Lobier, M., F. Siebenhühner, S. Palva and J. M. Palva (2014). "Phase transfer entropy: a novel phase-based measure for directed connectivity in networks coupled by oscillatory interactions." Neuroimage **85 Pt 2**: 853-872.
Logothetis, N. K. (2008). "What we can do and what we cannot do with fMRI." Nature **453**(7197): 869-878.
Longfield, A. (2019). Children's Commissioner for England Annual Report and Accounts 2018-19. C. s. Commissioner. London, House of Commons.
Lorusso, M. L., M. Burigo, V. Borsa and M. Molteni (2015). "Processing Sentences with Literal versus Figurative Use of Verbs: An ERP Study with Children with Language Impairments, Nonverbal Impairments, and Typical Development." Behav Neurol **2015**: 475271.
Lum, J. A. and D. Bleses (2012). "Declarative and procedural memory in Danish speaking children with specific language impairment." J Commun Disord **45**(1): 46-58.
Lum, J. A. G., G. M. Clark, F. J. Bigelow and P. G. Enticott (2022). "Resting state electroencephalography (EEG) correlates with children's language skills: Evidence from sentence repetition." Brain Lang **230**: 105137.
Lum, J. A. G., M. T. Ullman and G. Conti-Ramsden (2015). "Verbal declarative memory impairments in specific language impairment are related to working memory deficits." Brain and language **142**: 76-85.
Lyons, E. R., A. K. Nekkanti, B. W. Funderburk and E. A. Skowron (2022). "Parent-Child Interaction Therapy Supports Healthy Eating Behavior in Child Welfare-Involved Children." Int J Environ Res Public Health **19**(17).
Macoir, J., V. Martel-Sauvageau, L. Bouvier, R. Laforce and L. Monetta (2021). "Heterogeneity of repetition abilities in logopenic variant primary progressive aphasia." Dement Neuropsychol **15**(3): 405-412.
Majerus, S. (2013). "Language repetition and short-term memory: an integrative framework." Front Hum Neurosci **7**: 357.
Marinellie, S. A. (2004). "Complex syntax used by school-age children with specific language impairment (SLI) in child-adult conversation." J Commun Disord **37**(6): 517-533.
Marinellie, S. A. and C. J. Johnson (2002). "Definitional skill in school-age children with specific language impairment." J Commun Disord **35**(3): 241-259.
Marriott Haresign, I., E. A. M. Phillips, M. Whitehorn, L. Goupil, V. Noreika, V. Leong and S. V. Wass (2022). "Measuring the temporal dynamics of inter-personal neural entrainment in continuous child-adult EEG hyperscanning data." Dev Cogn Neurosci **54**: 101093.
Martínez-Cancino, R., A. Delorme, J. Wagner, K. Kreutz-Delgado, R. C. Sotero and S. Makeig (2020). "What Can Local Transfer Entropy Tell Us about Phase-Amplitude Coupling in Electrophysiological Signals?" Entropy (Basel) **22**(11).
Marton, K. (2008). "Visuo-spatial processing and executive functions in children with specific language impairment." International Journal of Language & Communication Disorders **43**(2): 181-200.
Mascelloni, M., R. Zamparelli, F. Vespignani, T. Gruber and J. L. Mueller (2019). "Distinct Neural Processes for Memorizing Form and Meaning Within Sentences." Front Hum Neurosci **13**: 412.

Mathur, A., D. Schultz and Y. Wang (2020). "Neural Bases of Phonological and Semantic Processing in Early Childhood." Brain Connect **10**(5): 212-223.
Matthews, P. H. (2014). The Concise Oxford Dictionary of Linguistics, OUP Oxford.
Maximo, J. O., D. L. Murdaugh, S. O'Kelley and R. K. Kana (2017). "Changes in intrinsic local connectivity after reading intervention in children with autism." Brain Lang **175**: 11-17.
Mayes, A. K., S. Reilly and A. T. Morgan (2015). "Neural correlates of childhood language disorder: a systematic review." Dev Med Child Neurol **57**(8): 706-717.
Mayor-Dubois, C., P. Zesiger, M. Van der Linden and E. Roulet-Perez (2014). "Nondeclarative learning in children with specific language impairment: predicting regularities in the visuomotor, phonological, and cognitive domains." Child Neuropsychol **20**(1): 14-22.
McArthur, C., Y. Bai, P. Hewston, L. Giangregorio, S. Straus and A. Papaioannou (2021). "Barriers and facilitators to implementing evidence-based guidelines in long-term care: a qualitative evidence synthesis." Implement Sci **16**(1): 70.
McArthur, G., C. Atkinson and D. Ellis (2009). "Atypical brain responses to sounds in children with specific language and reading impairments." Dev Sci **12**(5): 768-783.
McArthur, G. M. and D. V. Bishop (2004). "Frequency discrimination deficits in people with specific language impairment: reliability, validity, and linguistic correlates." J Speech Lang Hear Res **47**(3): 527-541.
McArthur, G. M. and D. V. Bishop (2005). "Speech and non-speech processing in people with specific language impairment: a behavioural and electrophysiological study." Brain Lang **94**(3): 260-273.
McArthur, G. M. and J. H. Hogben (2001). "Auditory backward recognition masking in children with a specific language impairment and children with a specific reading disability." The Journal of the Acoustical Society of America **109**(3): 1092-1100.
McCartney, E., J. Boyle, S. Ellis, S. Bannatyne and M. Turnbull (2015). "Indirect language therapy for children with persistent language impairment in mainstream primary schools: outcomes from a cohort intervention." International journal of language & communication disorders: 1-9.
McConachie, H. and T. Diggle (2007). "Parent implemented early intervention for young children with autism spectrum disorder: a systematic review." J Eval Clin Pract **13**(1): 120-129.
McDaniel, D., H. S. Cairns and C. McKee (1998). Methods for assessing children's syntax, Mit Press.
McGregor, K. K. (2020). "How We Fail Children With Developmental Language Disorder." Lang Speech Hear Serv Sch **51**(4): 981-992.
Mehta, R. K. and R. Parasuraman (2013). "Neuroergonomics: a review of applications to physical and cognitive work." Front Hum Neurosci **7**: 889.
Meltzer, J. A., A. Kielar, L. Panamsky, K. A. Links, T. Deschamps and R. C. Leigh (2017). "Electrophysiological signatures of phonological and semantic maintenance in sentence repetition." NeuroImage **156**: 302-314.
Mengisidou, M. and C. R. Marshall (2019). "Deficient Explicit Access to Phonological Representations Explains Phonological Fluency Difficulties in Greek Children With Dyslexia and/or Developmental Language Disorder." Front Psychol **10**: 638.
Mengler, E. D., J. H. Hogben, P. Michie and D. V. Bishop (2005). "Poor frequency discrimination is related to oral language disorder in children: a psychoacoustic study." Dyslexia **11**(3): 155-173.
Messer, D. and J. E. Dockrell (2006). "Children's naming and word-finding difficulties: descriptions and explanations." J Speech Lang Hear Res **49**(2): 309-324.

Miles, L. K., L. K. Nind and C. N. Macrae (2009). "The rhythm of rapport: Interpersonal synchrony and social perception." Journal of Experimental Social Psychology **45**(3): 585-589.
Miller, P. Vrtička, X. Cui, S. Shrestha, S. H. Hosseini, J. M. Baker and A. L. Reiss (2019). "Inter-brain synchrony in mother-child dyads during cooperation: an fNIRS hyperscanning study." Neuropsychologia **124**: 117-124.
Miller, C. A., L. B. Leonard and D. Finneran (2008). "Grammaticality judgements in adolescents with and without language impairment." Int J Lang Commun Disord **43**(3): 346-360.
Minagawa-Kawai, Y., K. Mori, J. C. Hebden and E. Dupoux (2008). "Optical imaging of infants' neurocognitive development: recent advances and perspectives." Dev Neurobiol **68**(6): 712-728.
Minagawa-Kawai, Y., H. van der Lely, F. Ramus, Y. Sato, R. Mazuka and E. Dupoux (2011). "Optical brain imaging reveals general auditory and language-specific processing in early infant development." Cereb Cortex **21**(2): 254-261.
Molavi, B. and G. A. Dumont (2012). "Wavelet-based motion artifact removal for functional near-infrared spectroscopy." Physiological measurement **33**(2): 259.
Montague, P. R., G. S. Berns, J. D. Cohen, S. M. McClure, G. Pagnoni, M. Dhamala, M. C. Wiest, I. Karpov, R. D. King, N. Apple and R. E. Fisher (2002). "Hyperscanning: simultaneous fMRI during linked social interactions." Neuroimage **16**(4): 1159-1164.
Montgomery, J. W. and J. L. Evans (2009). "Complex sentence comprehension and working memory in children with specific language impairment." J Speech Lang Hear Res **52**(2): 269-288.
Monticelli, M., P. Zeppa, M. Mammi, F. Penner, A. Melcarne, F. Zenga and D. Garbossa (2021). "Where We Mentalize: Main Cortical Areas Involved in Mentalization." Frontiers in Neurology **12**.
Morgan, A. T., M. Su, S. Reilly, G. Conti-Ramsden, A. Connelly and F. J. Liégeois (2018). "A Brain Marker for Developmental Speech Disorders." J Pediatr **198**: 234-239.e231.
Moritz-Gasser, S. and H. Duffau (2013). "The anatomo-functional connectivity of word repetition: insights provided by awake brain tumor surgery." Front Hum Neurosci **7**: 405.
Mushtaq, F., I. M. Wiggins, P. T. Kitterick, C. A. Anderson and D. E. Hartley (2019). "Evaluating time-reversed speech and signal-correlated noise as auditory baselines for isolating speech-specific processing using fNIRS." PLoS One **14**(7): e0219927.
Mushtaq, F., I. M. Wiggins, P. T. Kitterick, C. A. Anderson and D. E. H. Hartley (2019). "Evaluating time-reversed speech and signal-correlated noise as auditory baselines for isolating speech-specific processing using fNIRS." PLoS One **14**(7): e0219927.
Nasr, J. T., L. Gabis, M. Savatic and M. R. Andriola (2001). "The Electroencephalogram in Children with Developmental Dysphasia." Epilepsy Behav **2**(2): 115-118.
Newbury, D. F. and A. P. Monaco (2010). "Genetic advances in the study of speech and language disorders." Neuron **68**(2): 309-320.
Nguyen, T., H. Schleihauf, E. Kayhan, D. Matthes, P. Vrtička and S. Hoehl (2020). "The effects of interaction quality on neural synchrony during mother-child problem solving." Cortex **124**: 235-249.
Nguyen, T., H. Schleihauf, M. Kungl, E. Kayhan, S. Hoehl and P. Vrtička (2021). "Interpersonal Neural Synchrony During Father-Child Problem Solving: An fNIRS Hyperscanning Study." Child Dev **92**(4): e565-e580.
NICE (2011). Autism spectrum disorder in under 19s: recognition, referral and diagnosis N. I. o. H. a. C. Excellence, National Institute of Health and Care Excellence.
Nilsson, K. K. and K. J. de Lopez (2016). "Theory of mind in children with specific language impairment: A systematic review and meta-analysis." Child development **87**(1): 143-153.

Nippold, M. A., T. C. Mansfield, J. L. Billow and J. B. Tomblin (2008). "Expository discourse in adolescents with language impairments: examining syntactic development." Am J Speech Lang Pathol **17**(4): 356-366.
Nishiyori, R. (2016). "fNIRS: An Emergent Method to Document Functional Cortical Activity during Infant Movements." Front Psychol **7**: 533.
Nitin, R., D. M. Shaw, D. B. Rocha, C. E. Walters, Jr., C. F. Chabris, S. M. Camarata, R. L. Gordon and J. E. Below (2022). "Association of Developmental Language Disorder With Comorbid Developmental Conditions Using Algorithmic Phenotyping." JAMA Network Open **5**(12): e2248060-e2248060.
Nivetha Saravanan, E. P., Samantha Harisson, Guangting Mai, Bryoni Buck, Ian Wiggins, Douglas Hartley (In Preperation). Neural Sychrony between billingual mother-child pairs, a fNIRS hyperscanning study.
Noah, J. A., X. Zhang, S. Dravida, Y. Ono, A. Naples, J. C. McPartland and J. Hirsch (2020). "Real-Time Eye-to-Eye Contact Is Associated With Cross-Brain Neural Coupling in Angular Gyrus." Front Hum Neurosci **14**: 19.
Noah, J. A., X. Zhang, S. Dravida, Y. Ono, A. Naples, J. C. McPartland and J. Hirsch (2020). "Real-Time Eye-to-Eye Contact Is Associated With Cross-Brain Neural Coupling in Angular Gyrus." Frontiers in Human Neuroscience **14**.
Norbury, C. (2017). "Developmental Language Disorder: The most common childhood condition you've never heard of." The Guardian.
Norbury, C. F., D. Gooch, C. Wray, G. Baird, T. Charman, E. Simonoff, G. Vamvakas and A. Pickles (2016). "The impact of nonverbal ability on prevalence and clinical presentation of language disorder: evidence from a population study." J Child Psychol Psychiatry **57**(11): 1247-1257.
Northam, G. B., S. Adler, K. C. J. Eschmann, W. K. Chong, F. M. Cowan and T. Baldeweg (2018). "Developmental conduction aphasia after neonatal stroke." Ann Neurol **83**(4): 664-675.
Norton, E. S., B. L. Manning, E. M. Harriott, J. I. Nikolaeva, O. S. Nyabingi, K. M. Fredian, J. M. Page, S. McWeeny, S. Krogh-Jespersen, L. A. MacNeill, M. Y. Roberts and L. S. Wakschlag (2022). "Social EEG: A novel neurodevelopmental approach to studying brain-behavior links and brain-to-brain synchrony during naturalistic toddler–parent interactions." Developmental Psychobiology **64**(3): e22240.
Novick, J. M., S. L. Trueswell Jc Fau - Thompson-Schill and S. L. Thompson-Schill (2005). "Cognitive control and parsing: reexamining the role of Broca's area in sentence comprehension." (1530-7026 (Print)).
Obrig, H. (2014). "NIRS in clinical neurology - a 'promising' tool?" Neuroimage **85 Pt 1**: 535-546.
Oh, A., E. G. Duerden and E. W. Pang (2014). "The role of the insula in speech and language processing." Brain Lang **135**: 96-103.
Oldehinkel, A. J., C. A. Hartman, A. F. De Winter, R. Veenstra and J. Ormel (2004). "Temperament profiles associated with internalizing and externalizing problems in preadolescence." Development and psychopathology **16**(2): 421-440.
Oldfield, R. C. (1971). "The assessment and analysis of handedness: the Edinburgh inventory." Neuropsychologia **9**(1): 97-113.
Osterling, J. A., G. Dawson and J. A. Munson (2002). "Early recognition of 1-year-old infants with autism spectrum disorder versus mental retardation." Development and psychopathology **14**(2): 239-251.
Ota, T., K. Kamada, K. Kawai, M. Yumoto, S. Aoki and N. Saito (2011). "Refined analysis of complex language representations by non-invasive neuroimaging techniques." Br J Neurosurg **25**(2): 197-202.
Pan, Y., X. Cheng, Z. Zhang, X. Li and Y. Hu (2017). "Cooperation in lovers: an f NIRS-based hyperscanning study." Human brain mapping **38**(2): 831-841.

Paquette, N., M. Lassonde, P. Vannasing, J. Tremblay, B. González-Frankenberger, O. Florea, R. Béland, F. Lepore and A. Gallagher (2015). "Developmental patterns of expressive language hemispheric lateralization in children, adolescents and adults using functional near-infrared spectroscopy." Neuropsychologia **68**: 117-125.
Parviainen, T., E. Poskiparta, P. Niemi and R. Salmelin (2011). "Speech Perception in the Child Brain: Cortical Timing and its Relevance to Literacy Acquisition." Human brain mapping **32**: 2193-2206.
Pavelko, S. L., R. J. Lieberman, J. Schwartz and D. Hahs-Vaughn (2018). "The Contributions of Phonological Awareness, Alphabet Knowledge, and Letter Writing to Name Writing in Children With Specific Language Impairment and Typically Developing Children." Am J Speech Lang Pathol **27**(1): 166-180.
Peelle, J. E. (2012). "The hemispheric lateralization of speech processing depends on what "speech" is: a hierarchical perspective." Front Hum Neurosci **6**: 309.
Pei, X., E. C. Leuthardt, C. M. Gaona, P. Brunner, J. R. Wolpaw and G. Schalk (2011). "Spatiotemporal dynamics of electrocorticographic high gamma activity during overt and covert word repetition." Neuroimage **54**(4): 2960-2972.
Pentimonti, J. M., K. A. Murphy, L. M. Justice, J. A. Logan and J. N. Kaderavek (2016). "School readiness of children with language impairment: predicting literacy skills from pre-literacy and social–behavioural dimensions." International Journal of Language & Communication Disorders **51**(2): 148-161.
Perani, D., M. C. Saccuman, P. Scifo, A. Anwander, D. Spada, C. Baldoli, A. Poloniato, G. Lohmann and A. D. Friederici (2011). "Neural language networks at birth." Proceedings of the National Academy of Sciences **108**(38): 16056-16061.
Pereira, T. and M. Lousada (2022). "Psychometric Properties of Standardized Instruments that are Used to Measure Pragmatic Intervention Effects in Children with Developmental Language Disorder: A Systematic Review." J Autism Dev Disord.
Pérez, A., G. Dumas, M. Karadag and J. A. Duñabeitia (2019). "Differential brain-to-brain entrainment while speaking and listening in native and foreign languages." Cortex **111**: 303-315.
Pergher, V., B. Wittevrongel, J. Tournoy, B. Schoenmakers and M. M. Van Hulle (2019). "Mental workload of young and older adults gauged with ERPs and spectral power during N-Back task performance." Biol Psychol **146**: 107726.
Peter, V., U. Goswami, D. Burnham and M. Kalashnikova (2022). "Impaired neural entrainment to low frequency amplitude modulations in English-speaking children with dyslexia or dyslexia and DLD." Brain Lang **236**: 105217.
Pham, G. and K. D. Ebert (2020). "Diagnostic Accuracy of Sentence Repetition and Nonword Repetition for Developmental Language Disorder in Vietnamese." J Speech Lang Hear Res **63**(5): 1521-1536.
Phan, P., D. Highton, J. Lai, M. Smith, C. Elwell and I. Tachtsidis (2016). "Multi-channel multi-distance broadband near-infrared spectroscopy system to measure the spatial response of cellular oxygen metabolism and tissue oxygenation." Biomedical optics express **7**(11): 4424-4440.
Piazza, E. A., L. Hasenfratz, U. Hasson and C. Lew-Williams (2019). "Infant and Adult Brains Are Coupled to the Dynamics of Natural Communication." Psychological Science **31**(1): 6-17.
Piazza, E. A., L. Hasenfratz, U. Hasson and C. Lew-Williams (2020). "Infant and Adult Brains Are Coupled to the Dynamics of Natural Communication." Psychol Sci **31**(1): 6-17.
Pigdon, L., C. Willmott, S. Reilly, G. Conti-Ramsden, C. Gaser, A. Connelly and A. T. Morgan (2019). "Grey matter volume in developmental speech and language disorder." Brain Struct Funct **224**(9): 3387-3398.

Pigdon, L., C. Willmott, S. Reilly, G. Conti-Ramsden, F. Liegeois, A. Connelly and A. T. Morgan (2020). "The neural basis of nonword repetition in children with developmental speech or language disorder: An fMRI study." Neuropsychologia **138**: 107312.
Pijnacker, J., N. Davids, M. van Weerdenburg, L. Verhoeven, H. Knoors and P. van Alphen (2017). "Semantic Processing of Sentences in Preschoolers With Specific Language Impairment: Evidence From the N400 Effect." J Speech Lang Hear Res **60**(3): 627-639.
Pinti, P., I. Tachtsidis, A. Hamilton, J. Hirsch, C. Aichelburg, S. Gilbert and P. W. Burgess (2020). "The present and future use of functional near-infrared spectroscopy (fNIRS) for cognitive neuroscience." Ann N Y Acad Sci **1464**(1): 5-29.
Plichta, M. M., M. J. Herrmann, C. G. Baehne, A. C. Ehlis, M. M. Richter, P. Pauli and A. J. Fallgatter (2006). "Event-related functional near-infrared spectroscopy (fNIRS): are the measurements reliable?" Neuroimage **31**(1): 116-124.
Plichta, M. M., M. J. Herrmann, C. G. Baehne, A. C. Ehlis, M. M. Richter, P. Pauli and A. J. Fallgatter (2007). "Event-related functional near-infrared spectroscopy (fNIRS) based on craniocerebral correlations: reproducibility of activation?" Hum Brain Mapp **28**(8): 733-741.
Ploeg, J., B. Davies, N. Edwards, W. Gifford and P. E. Miller (2007). "Factors influencing best-practice guideline implementation: lessons learned from administrators, nursing staff, and project leaders." Worldviews Evid Based Nurs **4**(4): 210-219.
Poblano, A., E. Castro-Sierra, C. Arteaga and S. J. Pérez-Ruiz (2016). "Lexical tonal discrimination in Zapotec children. A study of the theta rhythm." Bol Med Hosp Infant Mex **73**(2): 84-89.
Polišenská, K., S. Chiat and P. Roy (2015). "Sentence repetition: what does the task measure?" Int J Lang Commun Disord **50**(1): 106-118.
Pollonini, L., C. Olds, H. Abaya, H. Bortfeld, M. S. Beauchamp and J. S. Oghalai (2014). "Auditory cortex activation to natural speech and simulated cochlear implant speech measured with functional near-infrared spectroscopy." Hearing research **309**: 84-93.
Price, A. R., M. F. Bonner, J. E. Peelle and M. Grossman (2015). "Converging evidence for the neuroanatomic basis of combinatorial semantics in the angular gyrus." Journal of Neuroscience **35**(7): 3276-3284.
Price, C. J. (2010). "The anatomy of language: a review of 100 fMRI studies published in 2009." Ann N Y Acad Sci **1191**: 62-88.
Price, C. J. (2012). "A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading." Neuroimage **62**(2): 816-847.
Putnam, L. Ellis and M. Rothbart (2001). The structure of temperament from infancy through adolescence**:** 165-182.
Putnam, S. P., L. K. Ellis, M. K. Rothbart, A. Eliasz and A. Angleitner (2001). "Advances in research on temperament." Lengerich, Germany, Pabst Science: 165-182.
Putnam, S. P. and M. K. Rothbart (2006). "Development of short and very short forms of the Children's Behavior Questionnaire." J Pers Assess **87**(1): 102-112.
Putnam, S. P. and C. A. Stifter (2005). "Behavioral approach–inhibition in toddlers: Prediction from infancy, positive and negative affective components, and relations with behavior problems." Child Development **76**(1): 212-226.
Qi, T., G. Schaadt and A. D. Friederici (2021). "Associated functional network development and language abilities in children." Neuroimage **242**: 118452.
Quaresima, V., S. Bisconti and M. Ferrari (2012). "A brief review on the use of functional near-infrared spectroscopy (fNIRS) for language imaging studies in human newborns and adults." Brain Lang **121**(2): 79-89.

Quaresima, V. and M. Ferrari (2019). "Functional Near-Infrared Spectroscopy (fNIRS) for Assessing Cerebral Cortex Function During Human Behavior in Natural/Social Situations: A Concise Review." Organizational Research Methods **22**(1): 46-68.

Quiñones-Camacho, L. E., F. A. Fishburn, K. Belardi, D. L. Williams, T. J. Huppert and S. B. Perlman (2021). "Dysfunction in interpersonal neural synchronization as a mechanism for social impairment in autism spectrum disorder." Autism Research **14**(8): 1585-1596.

Quiñones-Camacho, L. E., F. A. Fishburn, M. C. Camacho, C. O. Hlutkowsky, T. J. Huppert, L. S. Wakschlag and S. B. Perlman (2020). "Parent–child neural synchrony: a novel approach to elucidating dyadic correlates of preschool irritability." Journal of Child Psychology and Psychiatry **61**(11): 1213-1223.

Rahman, M. A., A. B. Siddik, T. K. Ghosh, F. Khanam and M. Ahmad (2020). "A Narrative Review on Clinical Applications of fNIRS." J Digit Imaging **33**(5): 1167-1184.

Ramanan, S., L. Marstaller, J. R. Hodges, O. Piguet and M. Irish (2020). "Understanding the neural basis of episodic amnesia in logopenic progressive aphasia: A multimodal neuroimaging study." Cortex **125**: 272-287.

Ramos, M. N., P. Collins and E. D. Peña (2022). "Sharpening Our Tools: A Systematic Review to Identify Diagnostically Accurate Language Sample Measures." J Speech Lang Hear Res **65**(10): 3890-3907.

Raye, C. L., M. K. Johnson, K. J. Mitchell, J. A. Reeder and E. J. Greene (2002). "Neuroimaging a Single Thought: Dorsolateral PFC Activity Associated with Refreshing Just-Activated Information." NeuroImage **15**(2): 447-453.

Reilly, S., B. Tomblin, J. Law, C. McKean, F. K. Mensah, A. Morgan, S. Goldfeld, J. M. Nicholson and M. Wake (2014). "Specific language impairment: a convenient label for whom?" International Journal of Language & Communication Disorders **49**(4): 416-451.

Reilly, S., M. Wake, O. C. Ukoumunne, E. Bavin, M. Prior, E. Cini, L. Conway, P. Eadie and L. Bretherton (2010). "Predicting language outcomes at 4 years of age: findings from Early Language in Victoria Study." Pediatrics **126**(6): e1530-e1537.

Reindl, V., C. Gerloff, W. Scharke and K. Konrad (2018). "Brain-to-brain synchrony in parent-child dyads and the relationship with emotion regulation revealed by fNIRS-based hyperscanning." NeuroImage **178**: 493-502.

Ren, Z., Y. Zhang, H. He, Q. Feng, T. Bi and J. Qiu (2019). "The Different Brain Mechanisms of Object and Spatial Working Memory: Voxel-Based Morphometry and Resting-State Functional Connectivity." Front Hum Neurosci **13**: 248.

Rescorla, L. (2011). "Late Talkers: Do Good Predictors of Outcome Exist?" Developmental Disabilities Research Reviews **17**(2): 141-150.

Reynolds, J. E., X. Long, M. N. Grohs, D. Dewey and C. Lebel (2019). "Structural and functional asymmetry of the language network emerge in early childhood." Dev Cogn Neurosci **39**: 100682.

Rice, M. L. and J. V. Bode (1993). "GAPS in the verb lexicons of children with specific language impairment." First Language **13**(37): 113-131.

Rice, M. L. and L. Hoffman (2015). "Predicting vocabulary growth in children with and without specific language impairment: A longitudinal study from 2; 6 to 21 years of age." Journal of Speech, Language, and Hearing Research **58**(2): 345-359.

Rice, M. L., S. M. Redmond and L. Hoffman (2006). "Mean length of utterance in children with specific language impairment and in younger control children shows concurrent validity and stable and parallel growth trajectories." J Speech Lang Hear Res **49**(4): 793-808.

Rice, M. L., J. B. Tomblin, L. Hoffman, W. A. Richman and J. Marquis (2004). "Grammatical tense deficits in children with SLI and nonspecific language impairment: relationships with nonverbal IQ over time." J Speech Lang Hear Res **47**(4): 816-834.

Rice, M. L., K. Wexler and P. L. Cleave (1995). "Specific language impairment as a period of extended optional infinitive." J Speech Hear Res **38**(4): 850-863.
Richardson, F. M., M. S. Thomas and C. J. Price (2010). "Neuronal activation for semantically reversible sentences." Journal of cognitive neuroscience **22**(6): 1283-1298.
Rieth, S. R., R. Haine-Schlagel, M. Burgeson, K. Searcy, K. S. Dickson and A. C. Stahmer (2018). "Integrating a Parent-Implemented Blend of Developmental and Behavioral Intervention Strategies into Speech-Language Treatment for Toddlers at Risk for Autism Spectrum Disorder." Semin Speech Lang **39**(2): 114-124.
Rimm-Kaufman, S. E. and J. Kagan (2005). "Infant predictors of kindergarten behavior: The contribution of inhibited and uninhibited temperament types." Behavioral Disorders **30**(4): 331-347.
Rinaldi, S., M. C. Caselli, V. Cofelice, S. D'Amico, A. G. De Cagno, G. Della Corte, M. V. Di Martino, B. Di Costanzo, M. C. Levorato, R. Penge, T. Rossetto, A. Sansavini, S. Vecchi and P. Zoccolotti (2021). "Efficacy of the Treatment of Developmental Language Disorder: A Systematic Review." Brain Sci **11**(3).
Rinker, T., K. Hartmann, E. Smith, R. Reiter, P. Alku, M. Kiefer and S. Brosch (2014). "[Children with specific language impairment: electrophysiological and pedaudiological findings]." Laryngorhinootologie **93**(8): 521-527.
Roa-Rojas, P., J. Grinstead, J. Silva-Pereyra, T. Fernández and M. Rodríguez-Camacho (2021). "Syntactic Gender Agreement Processing on Direct-Object Clitics by Spanish-Speaking Children with Developmental Language Disorder: Evidence from ERP." Children (Basel) **8**(3).
Roberts, M. Y., P. R. Curtis, B. J. Sone and L. H. Hampton (2019). "Association of Parent Training With Child Language Development: A Systematic Review and Meta-analysis." JAMA Pediatr **173**(7): 671-680.
Roberts, M. Y. and A. P. Kaiser (2011). "The effectiveness of parent-implemented language interventions: A meta-analysis."
Rogalsky, C., T. Poppa, K. H. Chen, S. W. Anderson, H. Damasio, T. Love and G. Hickok (2015). "Speech repetition as a window on the neurobiology of auditory-motor integration for speech: A voxel-based lesion symptom mapping study." Neuropsychologia **71**: 18-27.
Romeo, R. R., J. A. Leonard, S. T. Robinson, M. R. West, A. P. Mackey, M. L. Rowe and J. D. E. Gabrieli (2018). "Beyond the 30-Million-Word Gap: Children's Conversational Exposure Is Associated With Language-Related Brain Function." Psychol Sci **29**(5): 700-710.
Roos, E. M. and S. E. Weismer (2008). "Language Outcomes of Late Talking Toddlers at Preschool and Beyond." Perspect Lang Learn Educ **15**(3): 119-126.
Rosen, S. (2003). "Auditory processing in dyslexia and specific language impairment: is there a deficit? What is its nature? Does it explain anything?" Journal of Phonetics **31**(3): 509-527.
Rossi, M., C. F. Tirotta, R. G. Lagueruela and D. Madril (2007). "Diminished Blalock-Taussig shunt flow detected by cerebral oximetry." Paediatr Anaesth **17**(1): 72-74.
Rota-Donahue, C., R. G. Schwartz, V. Shafer and E. S. Sussman (2016). "Perception of Small Frequency Differences in Children with Auditory Processing Disorder or Specific Language Impairment." J Am Acad Audiol **27**(6): 489-497.
Rubia, K. (2013). "Functional brain imaging across development." Eur Child Adolesc Psychiatry **22**(12): 719-731.
Rudolph, J. M. and L. B. Leonard (2016). "Early Language Milestones and Specific Language Impairment." Journal of Early Intervention **38**(1): 41-58.

Rysop, A. U., L. M. Schmitt, J. Obleser and G. Hartwigsen (2022). "Age-related differences in the neural network interactions underlying the predictability gain." Cortex **154**: 269-286.
Saager, R. and A. Berger (2008). "Measurement of layer-like hemodynamic trends in scalp and cortex: implications for physiological baseline suppression in functional near-infrared spectroscopy." J Biomed Opt **13**(3): 034017.
Sabisch, B., A. Hahne, E. Glass, W. von Suchodoletz and A. D. Friederici (2006). "Lexical-semantic processes in children with specific language impairment." Neuroreport **17**(14): 1511-1514.
Sabisch, B., C. A. Hahne, E. Glass, W. von Suchodoletz and A. D. Friederici (2009). "Children with specific language impairment: the role of prosodic processes in explaining difficulties in processing syntactic information." Brain Res **1261**: 37-44.
Sair, H. I., S. Agarwal and J. J. Pillai (2017). "Application of Resting State Functional MR Imaging to Presurgical Mapping: Language Mapping." Neuroimaging Clin N Am **27**(4): 635-644.
Sanjeevan, T. and E. Mainela-Arnold (2019). "Characterizing the Motor Skills in Children with Specific Language Impairment." Folia Phoniatr Logop **71**(1): 42-55.
Sansavini, A., M. E. Favilla, M. T. Guasti, A. Marini, S. Millepiedi, M. V. Di Martino, S. Vecchi, N. Battajon, L. Bertolo, O. Capirci, B. Carretti, M. P. Colatei, C. Frioni, L. Marotta, S. Massa, L. Michelazzo, C. Pecini, S. Piazzalunga, M. Pieretti, P. Rinaldi, R. Salvadorini, C. Termine, M. Zuccarini, S. D'Amico, A. G. De Cagno, M. C. Levorato, T. Rossetto and M. L. Lorusso (2021) "Developmental Language Disorder: Early Predictors, Age for the Diagnosis, and Diagnostic Tools. A Scoping Review." Brain Sciences **11** DOI: 10.3390/brainsci11050654.
Santamaria, L., V. Noreika, S. Georgieva, K. Clackson, S. Wass and V. Leong (2020). "Emotional valence modulates the topology of the parent-infant inter-brain network." Neuroimage **207**: 116341.
Sato, H., M. Kiguchi, A. Maki, Y. Fuchino, A. Obata, T. Yoro and H. Koizumi (2006). "Within-subject reproducibility of near-infrared spectroscopy signals in sensorimotor activation after 6 months." J Biomed Opt **11**(1): 014021.
Satterthwaite, T. D., D. H. Wolf, D. R. Roalf, K. Ruparel, G. Erus, S. Vandekar, E. D. Gennatas, M. A. Elliott, A. Smith, H. Hakonarson, R. Verma, C. Davatzikos, R. E. Gur and R. C. Gur (2015). "Linked Sex Differences in Cognition and Functional Connectivity in Youth." Cereb Cortex **25**(9): 2383-2394.
Saur, D., B. W. Kreher, S. Schnell, D. Kümmerer, P. Kellmeyer, M. S. Vry, R. Umarova, M. Musso, V. Glauche, S. Abel, W. Huber, M. Rijntjes, J. Hennig and C. Weiller (2008). "Ventral and dorsal pathways for language." Proc Natl Acad Sci U S A **105**(46): 18035-18040.
Schecklmann, M., A. C. Ehlis, M. M. Plichta and A. J. Fallgatter (2008). "Functional near-infrared spectroscopy: a long-term reliable tool for measuring brain activity during verbal fluency." Neuroimage **43**(1): 147-155.
Scheiber, F. A., K. K. Ryckman and E. Demir-Lira Ö (2022). "Maternal depressive symptoms and maternal child-directed speech: A systematic review." J Affect Disord **297**: 194-207.
Schlaug, G., S. Marchina and A. Norton (2009). "Evidence for plasticity in white-matter tracts of patients with chronic Broca's aphasia undergoing intense intonation-based speech therapy." Ann N Y Acad Sci **1169**: 385-394.
Schneider, J. M. and M. J. Maguire (2019). "Developmental differences in the neural correlates supporting semantics and syntax during sentence processing." Developmental Science **22**(4): e12782.

Scholkmann, F., U. Gerber, M. Wolf and U. Wolf (2013). "End-tidal CO2: an important parameter for a correct interpretation in functional brain studies using speech tasks." Neuroimage **66**: 71-79.
Scholkmann, F., S. Kleiser, A. J. Metz, R. Zimmermann, J. Mata Pavia, U. Wolf and M. Wolf (2014). "A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology." Neuroimage **85 Pt 1**: 6-27.
Schroeter, M. L., M. M. Bücheler, K. Müller, K. Uludağ, H. Obrig, G. Lohmann, M. Tittgemeyer, A. Villringer and D. Y. von Cramon (2004). "Towards a standard analysis for functional near-infrared imaging." Neuroimage **21**(1): 283-290.
Schulz, P. (2010). Some notes on semantics and SLI**:** 391-406.
Segaert, K., G. Kempen, K. M. Petersson and P. Hagoort (2013). "Syntactic priming and the lexical boost effect during sentence production and sentence comprehension: an fMRI study." Brain Lang **124**(2): 174-183.
Seghier, M. L. (2013). "The angular gyrus: multiple functions and multiple subdivisions." Neuroscientist **19**(1): 43-61.
Segura-Pujol, H. and C. Briones-Rojas (2021). "Treatment intensity for developmental language disorder: A systematic review." Int J Speech Lang Pathol **23**(5): 465-474.
Shafer, V. L., C. Ponton, H. Datta, M. L. Morr and R. G. Schwartz (2007). "Neurophysiological indices of attention to speech in children with specific language impairment." Clin Neurophysiol **118**(6): 1230-1243.
Shafer, V. L., R. G. Schwartz and B. Martin (2011). "Evidence of deficient central speech processing in children with specific language impairment: the T-complex." Clin Neurophysiol **122**(6): 1137-1155.
Shafer, V. L., R. G. Schwartz, M. L. Morr, K. L. Kessler and D. Kurtzberg (2000). "Deviant neurophysiological asymmetry in children with language impairment." Neuroreport **11**(17): 3715-3718.
Shalom, D. B. and D. Poeppel (2008). "Functional anatomic models of language: assembling the pieces." Neuroscientist **14**(1): 119-127.
Sharda, M., C. Tuerk, R. Chowdhury, K. Jamey, N. Foster, M. Custo-Blanch, M. Tan, A. Nadig and K. Hyde (2018). "Music improves social communication and auditory-motor connectivity in children with autism." Transl Psychiatry **8**(1): 231.
Shaywitz, S. E. and B. A. Shaywitz (2004). "Neurobiologic Basis for Reading and Reading Disability."
Sheng, L. and K. K. McGregor (2010). "Object and action naming in children with specific language impairment." J Speech Lang Hear Res **53**(6): 1704-1719.
Shuster, L. I. and S. K. Lemieux (2005). "An fMRI investigation of covertly and overtly produced mono- and multisyllabic words." Brain Lang **93**(1): 20-31.
Sierpowska, J., A. Gabarrós, A. Fernandez-Coello, À. Camins, S. Castañer, M. Juncadella, J. Morís and A. Rodríguez-Fornells (2017). "Words are not enough: nonword repetition as an indicator of arcuate fasciculus integrity during brain tumor resection." J Neurosurg **126**(2): 435-445.
Sikora, K., A. Roelofs, D. Hermans and H. Knoors (2019). "Executive control in language production by children with and without language impairment." Int J Lang Commun Disord **54**(4): 645-655.
Silver, E., R. Korja, E. Mainela-Arnold, E. P. Pulli, E. Saukko, S. Nolvi, E. L. Kataja, L. Karlsson, H. Karlsson and J. J. Tuulari (2021). "A systematic review of MRI studies of language development from birth to 2 years of age." Dev Neurobiol **81**(1): 63-75.
Simos, P. G., R. Rezaie, J. M. Fletcher, J. Juranek and A. C. Papanicolaou (2011). "Neural correlates of sentence reading in children with reading difficulties." Neuroreport **22**(14): 674-678.

Simpkins, S. D., H. B. Weiss, K. McCartney, H. M. Kreider and E. Dearing (2006). "Mother - Child Relationship as a Moderator of the Relation Between Family Educational Involvement and Child Achievement." Parenting **6**(1): 49-57.
Sitaram, R., A. Caria and N. Birbaumer (2009). "Hemodynamic brain-computer interfaces for communication and rehabilitation." Neural Netw **22**(9): 1320-1328.
Skeide, M. A., J. Brauer and A. D. Friederici (2014). "Syntax gradually segregates from semantics in the developing brain." Neuroimage **100**: 106-111.
Skeide, M. A. and A. D. Friederici (2016). "The ontogeny of the cortical language network." Nature Reviews Neuroscience **17**(5): 323-332.
Slobin, D. I. and C. A. Welsh (1967). "Elicited imitation as a research tool in developmental psycholinguistics."
Smith-Lock, K. M., S. Leitao, L. Lambert and L. Nickels (2013). "Effective intervention for expressive grammar in children with specific language impairment." International Journal of Language & Communication Disorders **48**(3): 265-282.
Smith, E. E. and J. Jonides (1999). "Storage and executive processes in the frontal lobes." (0036-8075 (Print)).
Smitha, K. A., K. M. Arun, P. G. Rajesh, B. Thomas and C. Kesavadas (2017). "Resting-State Seed-Based Analysis: An Alternative to Task-Based Language fMRI and Its Laterality Index." AJNR Am J Neuroradiol **38**(6): 1187-1192.
Soares, A. P., F. J. Gutiérrez-Domínguez, H. M. Oliveira, A. Lages, N. Guerra, A. R. Pereira, D. Tomé and M. Lousada (2022). "Explicit Instructions Do Not Enhance Auditory Statistical Learning in Children With Developmental Language Disorder: Evidence From Event-Related Potentials." Front Psychol **13**: 905762.
Solé-Padullés, C., J. Castro-Fornieles, E. de la Serna, R. Calvo, I. Baeza, J. Moya, L. Lázaro, M. Rosa, N. Bargalló and G. Sugranyes (2016). "Intrinsic connectivity networks from childhood to late adolescence: Effects of age and sex." Developmental Cognitive Neuroscience **17**: 35-44.
Soltanlou, M., M. A. Sitnikova, H. C. Nuerk and T. Dresler (2018). "Applications of Functional Near-Infrared Spectroscopy (fNIRS) in Studying Cognitive Development: The Case of Mathematics and Language." Front Psychol **9**: 277.
Soriano-Mas, C., J. Pujol, H. Ortiz, J. Deus, A. López-Sala and A. Sans (2009). "Age-related brain structural alterations in children with specific language impairment." Hum Brain Mapp **30**(5): 1626-1636.
Stephens, G. J., L. J. Silbert and U. Hasson (2010). "Speaker–listener neural coupling underlies successful communication." Proceedings of the National Academy of Sciences **107**(32): 14425-14430.
Sterne, J. A. and G. Davey Smith (2001). "Sifting the evidence-what's wrong with significance tests?" Bmj **322**(7280): 226-231.
Stifter, C. A., S. Putnam and L. Jahromi (2008). "Exuberant and inhibited toddlers: Stability of temperament and risk for problem behavior." Development and psychopathology **20**(2): 401-421.
Stokes, S. F., A. M. Wong, P. Fletcher and L. B. Leonard (2006). "Nonword repetition and sentence repetition as clinical markers of specific language impairment: the case of Cantonese." J Speech Lang Hear Res **49**(2): 219-236.
Stothard, S. E., M. J. Snowling, D. V. Bishop, B. B. Chipchase and C. A. Kaplan (1998). "Language-impaired preschoolers: A follow-up into adolescence." Journal of Speech, Language, and Hearing Research **41**(2): 407-418.
Strand, S. and G. Lindsay (2009). "Evidence of ethnic disproportionality in special education in an English population." The Journal of Special Education **43**(3): 174-190.
Su, M., P. Li, W. Zhou and H. Shu (2021). "Effects of socioeconomic status in predicting reading outcomes for children: The mediation of spoken language network." Brain and Cognition **147**: 105655.

Suh, S., H. W. Yoon, S. Lee, J. Y. Chung, Z. H. Cho and H. Park (2007). "Effects of syntactic complexity in L1 and L2; an fMRI study of Korean-English bilinguals." Brain Res **1136**(1): 178-189.
Sun, X., K. Zhang, R. Marks, Z. Karas, R. Eggleston, N. Nickerson, C. L. Yu, N. Wagley, X. Hu, V. Caruso, T. L. Chou, T. Satterfield, T. Tardif and I. Kovelman (2022). "Morphological and phonological processing in English monolingual, Chinese-English bilingual, and Spanish-English bilingual children: An fNIRS neuroimaging dataset." Data Brief **42**: 108048.
Suttora, C., M. Zuccarini, A. Aceti, L. Corvaglia, A. Guarini and A. Sansavini (2021). "The Effects of a Parent-Implemented Language Intervention on Late-Talkers' Expressive Skills: The Mediational Role of Parental Speech Contingency and Dialogic Reading Abilities." Frontiers in Psychology **12**.
Szameitat, A. J., S. Shen and A. Sterr (2009). "The functional magnetic resonance imaging (fMRI) procedure as experienced by healthy participants and stroke patients--a pilot study." BMC Med Imaging **9**: 14.
Szekely, A., T. Jacobsen, S. D'Amico, A. Devescovi, E. Andonova, D. Herron, C. C. Lu, T. Pechmann, C. Pléh, N. Wicha, K. Federmeier, I. Gerdjikova, G. Gutierrez, D. Hung, J. Hsu, G. Iyer, K. Kohnert, T. Mehotcheva, A. Orozco-Figueroa, A. Tzeng, O. Tzeng, A. Arévalo, A. Vargha, A. C. Butler, R. Buffington and E. Bates (2004). "A new on-line resource for psycholinguistic studies." J Mem Lang **51**(2): 247-250.
Tachtsidis, I. and F. Scholkmann (2016). "False positives and false negatives in functional near-infrared spectroscopy: issues, challenges, and the way forward." Neurophotonics **3**(3): 031405.
Taha, J., V. Stojanovik and E. Pagnamenta (2021). "Sentence Repetition as a Clinical Marker of Developmental Language Disorder: Evidence From Arabic." J Speech Lang Hear Res **64**(12): 4876-4899.
Takeuchi, H., Y. Taki, H. Hashizume, K. Asano, M. Asano, Y. Sassa, S. Yokota, Y. Kotozaki, R. Nouchi and R. Kawashima (2015). "The impact of parent-child interaction on brain structures: cross-sectional and longitudinal analyses." J Neurosci **35**(5): 2233-2245.
Tallal, P. (1980). "Auditory temporal perception, phonics, and reading disabilities in children." Brain and language **9**(2): 182-198.
Tambyraja, S. R., K. Farquharson, J. A. Logan and L. M. Justice (2015). "Decoding skills in children with language impairment: Contributions of phonological processing and classroom experiences." American Journal of Speech-Language Pathology **24**(2): 177-188.
Tanaka, N. and S. M. Stufflebeam (2016). "Presurgical Mapping of the Language Network Using Resting-state Functional Connectivity." Top Magn Reson Imaging **25**(1): 19-24.
Tassi, E., A. Boscutti, G. M. Mandolini, C. Moltrasio, G. Delvecchio and P. Brambilla (2022). "A scoping review of near infrared spectroscopy studies employing a verbal fluency task in bipolar disorder." J Affect Disord **298**(Pt A): 604-617.
Taylor, J. S., K. Rastle and M. H. Davis (2013). "Can cognitive models explain brain activation during word and pseudoword reading? A meta-analysis of 36 neuroimaging studies." Psychol Bull **139**(4): 766-791.
Theodorou, E., M. Kambanaros and K. K. Grohmann (2017). "Sentence Repetition as a Tool for Screening Morphosyntactic Abilities of Bilectal Children with SLI." Front Psychol **8**: 2104.
Thomas, R., B. Abell, H. J. Webb, E. Avdagic and M. J. Zimmer-Gembeck (2017). "Parent-Child Interaction Therapy: A Meta-analysis." Pediatrics **140**(3).
Thordardottir, E. T. and S. E. Weismer (2002). "Content mazes and filled pauses in narrative language samples of children with specific language impairment." Brain Cogn **48**(2-3): 587-592.

Tomasi, D. and N. D. Volkow (2012). "Resting functional connectivity of language networks: characterization and reproducibility." (1476-5578 (Electronic)).
Tomblin, J. B., M. Harrison, S. E. Ambrose, E. A. Walker, J. J. Oleson and M. P. Moeller (2015). "Language Outcomes in Young Children with Mild to Severe Hearing Loss." Ear Hear **36 Suppl 1**(0 1): 76s-91s.
Tomblin, J. B., N. L. Records, P. Buckwalter, X. Zhang, E. Smith and M. O'Brien (1997). "Prevalence of specific language impairment in kindergarten children." J Speech Lang Hear Res **40**(6): 1245-1260.
Tops, M. and M. Boksem (2011). "A Potential Role of the Inferior Frontal Gyrus and Anterior Insula in Cognitive Control, Brain Rhythms, and Event-Related Potentials." Frontiers in Psychology **2**.
Torricelli, A., D. Contini, A. Pifferi, M. Caffini, R. Re, L. Zucchelli and L. Spinelli (2014). "Time domain functional NIRS imaging for human brain mapping." Neuroimage **85 Pt 1**: 28-50.
Tosh, R., W. Arnott and N. Scarinci (2017). "Parent-implemented home therapy programmes for speech and language: a systematic review." Int J Lang Commun Disord **52**(3): 253-269.
Tremblay, P. and S. L. Small (2011). "From language comprehension to action understanding and back again." Cereb Cortex **21**(5): 1166-1177.
Tremblay, P. and S. L. Small (2011). "Motor response selection in overt sentence production: a functional MRI study." Front Psychol **2**: 253.
Tsow, F., A. Kumar, S. H. Hosseini and A. Bowden (2021). "A low-cost, wearable, do-it-yourself functional near-infrared spectroscopy (DIY-fNIRS) headband." HardwareX **10**.
Tuller, L., C. Henry, E. V. A. Sizaret and M.-A. Barthez (2012). "Specific language impairment at adolescence: Avoiding complexity." Applied Psycholinguistics **33**(1): 161-184.
Turkeltaub, P. E., L. Gareau, D. L. Flowers, T. A. Zeffiro and G. F. Eden (2003). "Development of neural mechanisms for reading." Nat Neurosci **6**(7): 767-773.
Uchida-Ota, M., T. Arimitsu, D. Tsuzuki, I. Dan, K. Ikeda, T. Takahashi and Y. Minagawa (2019). "Maternal speech shapes the cerebral frontotemporal network in neonates: A hemodynamic functional connectivity study." Dev Cogn Neurosci **39**: 100701.
UKHSA (2022). Stay at home: guidance for households with possible or confirmed coronavirus (COVID-19) infection. U. H. S. Agency.
Ullman, M. T. and E. I. Pierpont (2005). "Specific language impairment is not specific to language: the procedural deficit hypothesis." Cortex **41**(3): 399-433.
Ungerleider, L. G., S. M. Courtney and J. V. Haxby (1998). "A neural system for human visual working memory." Proceedings of the National Academy of Sciences **95**(3): 883-890.
Ursino, M., G. Ricci and E. Magosso (2020). "Transfer Entropy as a Measure of Brain Connectivity: A Critical Analysis With the Help of Neural Mass Models." Frontiers in Computational Neuroscience **14**.
Valdesolo, P. and D. DeSteno (2011). "Synchrony and the social tuning of compassion." Emotion **11**(2): 262.
Vallar, G., E. Bisiach, M. Cerizza and M. L. Rusconi (1988). "The role of the left hemisphere in decision-making." Cortex **24**(3): 399-410.
van Heuven, W. J., H. Schriefers, T. Dijkstra and P. Hagoort (2008). "Language conflict in the bilingual brain." Cereb Cortex **18**(11): 2706-2716.
van Noorden, L. E., J. Sigafoos and H. L. Waddington (2022). "Evaluating a Two-Tiered Parent Coaching Intervention for Young Autistic Children Using the Early Start Denver Model." Adv Neurodev Disord: 1-21.
Vanderwert, R. E. and C. A. Nelson (2014). "The use of near-infrared spectroscopy in the study of typical and atypical development." Neuroimage **85 Pt 1**(0 1): 264-271.

Vandewalle, E., B. Boets, P. Ghesquière and I. Zink (2012). "Development of phonological processing skills in children with specific language impairment with and without literacy delay: a 3-year longitudinal study." J Speech Lang Hear Res **55**(4): 1053-1067.
Vang Christensen, R. (2019). "Sentence Repetition: A Clinical Marker for Developmental Language Disorder in Danish." J Speech Lang Hear Res **62**(12): 4450-4463.
Vansteensel, M. J., I. S. Selten, L. Charbonnier, J. Berezutskaya, M. A. H. Raemaekers, N. F. Ramsey and F. Wijnen (2021). "Reduced brain activation during spoken language processing in children with developmental language disorder and children with 22q11.2 deletion syndrome." Neuropsychologia **158**: 107907.
Verly, M., R. Gerrits, C. Sleurs, L. Lagae, S. Sunaert, I. Zink and N. Rommel (2019). "The mis-wired language network in children with developmental language disorder: insights from DTI tractography." Brain Imaging Behav **13**(4): 973-984.
Vigliocco, G., M. Ponari and C. Norbury (2018). "Learning and Processing Abstract Words and Concepts: Insights From Typical and Atypical Development." Top Cogn Sci **10**(3): 533-549.
Vissers, C. and S. Koolen (2016). "Theory of mind deficits and social emotional functioning in preschoolers with specific language impairment." Frontiers in psychology **7**: 1734.
Vissers, C., S. Koolen, D. Hermans, A. Scheper and H. Knoors (2015). "Executive functioning in preschoolers with specific language impairment." Front Psychol **6**: 1574.
Vugs, B., M. Hendriks, J. Cuperus and L. Verhoeven (2014). "Working memory performance and executive function behaviors in young children with SLI." Research in developmental disabilities **35**(1): 62-74.
Vydrova, R., V. Komarek, J. Sanda, K. Sterbova, A. Jahodova, A. Maulisova, J. Zackova, J. Reissigova, P. Krsek and M. Kyncl (2015). "Structural alterations of the language connectome in children with specific language impairment." Brain Lang **151**: 35-41.
Wadman, R., K. Durkin and G. Conti-Ramsden (2008). "Self-esteem, shyness, and sociability in adolescents with specific language impairment (SLI)."
Walsh, B., F. Tian, J. A. Tourville, M. A. Yücel, T. Kuczek and A. J. Bostian (2017). "Hemodynamics of speech production: An fNIRS investigation of children who stutter." Scientific Reports **7**(1): 4034.
Wang, D., L. Zheng, Y. Lin, Y. Zhang and L. Sheng (2022). "Sentence Repetition as a Clinical Marker for Mandarin-Speaking Preschoolers With Developmental Language Disorder." J Speech Lang Hear Res **65**(4): 1543-1560.
Wang, J., B. L. Yamasaki, Y. Weiss and J. R. Booth (2021). "Both frontal and temporal cortex exhibit phonological and semantic specialization during spoken language processing in 7- to 8-year-old children." Hum Brain Mapp **42**(11): 3534-3546.
Wang, L., O. Jensen, D. Van den Brink, N. Weder, J. M. Schoffelen, L. Magyari, P. Hagoort and M. Bastiaansen (2012). "Beta oscillations relate to the N400m during language comprehension." Human brain mapping **33**(12): 2898-2912.
Wang, Q., Z. Han, X. Hu, S. Feng, H. Wang, T. Liu and L. Yi (2020). "Autism Symptoms Modulate Interpersonal Neural Synchronization in Children with Autism Spectrum Disorder in Cooperative Interactions." Brain Topogr **33**(1): 112-122.
Wang, Y. and W. Chen (2020). "Effective brain connectivity for fNIRS data analysis based on multi-delays symbolic phase transfer entropy." J Neural Eng **17**(5): 056024.
Weiss-Croft, L. J. and T. Baldeweg (2015). "Maturation of language networks in children: A systematic review of 22years of functional MRI." NeuroImage **123**: 269-281.

Weiss, Y., H. G. Cweigenberg and J. R. Booth (2018). "Neural specialization of phonological and semantic processing in young children." Human Brain Mapping **39**(11): 4334-4348.
Wen, H., Y. Liu, I. Rekik, S. Wang, Z. Chen, J. Zhang, Y. Zhang, Y. Peng and H. He (2018). "Combining Disrupted and Discriminative Topological Properties of Functional Connectivity Networks as Neuroimaging Biomarkers for Accurate Diagnosis of Early Tourette Syndrome Children." Mol Neurobiol **55**(4): 3251-3269.
West, G., M. A. Vadillo, D. R. Shanks and C. Hulme (2018). "The procedural learning deficit hypothesis of language learning disorders: we see some problems." Dev Sci **21**(2).
Westerlund, M., L. Bergkvist, D. Lagerberg and C. Sundelin (2002). "Comorbidity in children with severe developmental language disability." Acta Paediatr **91**(5): 529-534.
Wexler, K. (2003). "Lenneberg's dream: Learning, normal language development, and specific language impairment." Language Competence Across Populations: Towards a Definition of Specific Language Impairment: 11-61.
Whedon, M., N. B. Perry and M. A. Bell (2020). "Relations between frontal EEG maturation and inhibitory control in preschool in the prediction of children's early academic skills." Brain and Cognition **146**: 105636.
Wheelock, M. D., J. P. Culver and A. T. Eggebrecht (2019). "High-density diffuse optical tomography for imaging human brain function." The Review of scientific instruments **90**(5): 051101-051101.
Whitehouse, A. J., J. G. Barry and D. V. Bishop (2008). "Further defining the language impairment of autism: is there a specific language impairment subtype?" J Commun Disord **41**(4): 319-336.
Whiteman, A. C., H. Santosa, D. F. Chen, S. Perlman and T. Huppert (2018). "Investigation of the sensitivity of functional near-infrared spectroscopy brain imaging to anatomical variations in 5- to 11-year-old children." Neurophotonics **5**(1): 011009-011009.
Wiggins, I. M., C. A. Anderson, P. T. Kitterick and D. E. Hartley (2016). "Speech-evoked activation in adult temporal cortex measured using functional near-infrared spectroscopy (fNIRS): Are the measurements reliable?" Hear Res **339**: 142-154.
Wiggins, I. M. and D. E. Hartley (2015). "A synchrony-dependent influence of sounds on activity in visual cortex measured using functional near-infrared spectroscopy (fNIRS)." PloS one **10**(3): e0122862.
Wiig, E. H., W. A. Secord and E. Semel (2003). "Clinical evaluation of language fundamentals." San Antonio, TX: The Psychological Corporation.
Wiig, E. H., W. A. Secord and E. Semel (2013). Clinical evaluation of language fundamentals: CELF-5, Pearson.
Wijayasiri, P., D. E. H. Hartley and I. M. Wiggins (2017). "Brain activity underlying the recovery of meaning from degraded speech: A functional near-infrared spectroscopy (fNIRS) study." Hear Res **351**: 55-67.
Wilke, M., K. Lidzba and I. Krägeloh-Mann (2009). "Combined functional and causal connectivity analyses of language networks in children: a feasibility study." Brain Lang **108**(1): 22-29.
Wilson, A. C. and D. V. M. Bishop (2018). "Resounding failure to replicate links between developmental language disorder and cerebral lateralisation." PeerJ **6**: e4217.
Wilson, M. and T. P. Wilson (2005). "An oscillator model of the timing of turn-taking." Psychon Bull Rev **12**(6): 957-968.
Wintgens, A. (2013). Children with communication problems and additional emotional/behavioural problems. Speech and Language Therapy, Routledge**:** 149-158.

Wire. (2020). "Royal College urges county council to reconsider 'significant' cuts to services." from https://westbridgfordwire.com/royal-college-urges-county-council-to-reconsider-significant-cuts-to-services/.
Wolf, M., M. Ferrari and V. Quaresima (2007). "Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications." J Biomed Opt **12**(6): 062104.
Wu, X., F. Lin, T. Zhang, H. Sun and J. Li (2022). "Acquisition time for functional near-infrared spectroscopy resting-state functional connectivity in assessing autism." Neurophotonics **9**(4): 045007.
Xiao, Y., A. D. Friederici, D. S. Margulies and J. Brauer (2016). "Development of a selective left-hemispheric fronto-temporal network for processing syntactic complexity in language comprehension." Neuropsychologia **83**: 274-282.
Xiao, Y., A. D. Friederici, D. S. Margulies and J. Brauer (2016). "Longitudinal changes in resting-state fMRI from age 5 to age 6 years covary with language development." Neuroimage **128**: 116-124.
Yamada, T., S. Umeyama and K. Matsuda (2012). "Separation of fNIRS signals into functional and systemic components based on differences in hemodynamic modalities." PloS one **7**(11): e50271.
Yamada, T., S. Umeyama and K. Matsuda (2012). "Separation of fNIRS signals into functional and systemic components based on differences in hemodynamic modalities." PloS one **7**(11).
Yamada, Y., C. Stevens, M. Dow, B. Harn, D. Chard and H. Neville (2010). "Emergence of the neural network for reading in five-year-old beginning readers of different levels of pre-literacy abilities: An fMRI study." NeuroImage **57**: 704-713.
Yamasaki, T., K. Ogata, T. Maekawa, I. Ijichi, M. Katagiri, T. Mitsudo, Y. Kamio and S. Tobimatsu (2013). "Rapid maturation of voice and linguistic processing systems in preschool children: A near-infrared spectroscopic study." Experimental Neurology **250**: 313-320.
Yaple, Z. and M. Arsalidou (2018). "N-back Working Memory Task: Meta-analysis of Normative fMRI Studies With Children." Child Dev **89**(6): 2010-2022.
Yaple, Z. and M. Arsalidou (2018). "N-back Working Memory Task: Meta-analysis of Normative fMRI Studies With Children." Child Development **89**(6): 2010-2022.
Yeatman, J. D., M. Ben-Shachar, G. H. Glover and H. M. Feldman (2010). "Individual differences in auditory sentence comprehension in children: An exploratory event-related functional magnetic resonance imaging investigation." Brain and Language **114**(2): 72-79.
Yin, W., M.-H. Chen, S.-C. Hung, K. R. Baluyot, T. Li and W. Lin (2019). "Brain functional development separates into three distinct time periods in the first two years of life." NeuroImage **189**: 715-726.
Younger, J. W., K. W. Lee, O. E. Demir-Lira and J. R. Booth (2019). "Brain lateralization of phonological awareness varies by maternal education." Dev Sci **22**(6): e12807.
Youssofzadeh, V., B. J. Williamson and D. S. Kadis (2017). "Mapping Critical Language Sites in Children Performing Verb Generation: Whole-Brain Connectivity and Graph Theoretical Analysis in MEG." Front Hum Neurosci **11**: 173.
Yu, X., S. L. Ferradal, D. D. Sliva, J. Dunstan, C. Carruthers, J. Sanfilippo, J. Zuk, L. Zöllei, E. Boyd, B. Gagoski, Y. Ou, P. E. Grant and N. Gaab (2021). "Functional Connectivity in Infancy and Toddlerhood Predicts Long-Term Language and Preliteracy Outcomes." Cerebral Cortex: bhab230.
Zhang, C., N. D. Cahill, M. R. Arbabshirani, T. White, S. A. Baum and A. M. Michael (2016). "Sex and Age Effects of Functional Connectivity in Early Adulthood." Brain Connect **6**(9): 700-713.

Zhang, H., Y. J. Zhang, L. Duan, S. Y. Ma, C. M. Lu and C. Z. Zhu (2011). "Is resting-state functional connectivity revealed by functional near-infrared spectroscopy test-retest reliable?" J Biomed Opt **16**(6): 067008.
Zhang, J. X., H.-C. Leung and M. K. Johnson (2003). "Frontal activations associated with accessing and evaluating information in working memory: an fMRI study." NeuroImage **20**(3): 1531-1539.
Zhang, X., J. A. Noah, S. Dravida and J. Hirsch (2017). "Signal processing of functional NIRS data acquired during overt speaking." Neurophotonics **4**(4): 041409.
Zhang, Y., X. Jin, X. Shen, J. Zhang and E. Hoff (2008). "Correlates of early language development in Chinese children." International Journal of Behavioral Development **32**(2): 145-151.
Zhao, H., T. Cheng, Y. Zhai, Y. Long, Z. Wang and C. Lu (2021). "How Mother–Child Interactions are Associated with a Child's Compliance." Cerebral Cortex **31**(9): 4398-4410.
Zhou, S., Y. Zhang, Y. Fu, L. Wu, X. Li, N. Zhu, D. Li and M. Zhang (2022). "The Effect of Task Performance and Partnership on Interpersonal Brain Synchrony during Cooperation." Brain Sci **12**(5).
Zhu, L., X. Xiong, X. Dong, Y. Zhao, A. Kawczyński, A. Chen and W. Wang (2021). "Working memory network plasticity after exercise intervention detected by task and resting-state functional MRI." J Sports Sci **39**(14): 1621-1632.
Zwart, F. S., C. Vissers, R. P. C. Kessels and J. H. R. Maes (2019). "Procedural learning across the lifespan: A systematic review with implications for atypical development." J Neuropsychol **13**(2): 149-182.