Lasting Impact of Loreta Z-Score Neurofeedback Therapy on Phonological Dyslexia

By

Jessica Cipolla
BA(Hons)

Thesis submitted to Flinders University in partial fulfilment of the requirements for the degree of

Doctor of Philosophy (Clinical Psychology)

College of Education, Psychology, and Social Work

May 2021

Contents

Abstract

Developmental dyslexia is a neurological disorder that results in poor language-related learning despite average intelligence: this includes behavioural symptoms such as poor reading, spelling, and decoding abilities. In addition to these behavioural symptoms, electroencephalography (EEG) research and new data analytic techniques make it possible to investigate alterations in neural networks that correlate with such symptoms. In this thesis, these alterations were assessed by examining their impact on the EEG field activity associated with neural function.

In an initial study, the EEG signatures of a sample of children with dyslexia with marked phonological impairment (phonological dyslexia) were obtained from a relatively large cohort of children with dyslexia and were compared to individually matched control participants. Results indicated that, relative to healthy controls, dyslexia was found to be associated with reduced power of delta, theta, alpha1, alpha2, beta2 and gamma frequency bands in frontal and temporal regions. In contrast, the power in these frequency bands was enhanced in the central and parietal-occipital electrodes. The gamma activity was consistently reduced in participants with dyslexia across all brain regions. Finally, all behavioural measures of dyslexia (6 reading tests, 3 phonological and 2 spelling tests) showed a consistent negative correlation with age of participants with dyslexia. This indicated that participants with dyslexia were continuously falling behind the normative age-expected behaviour at a near-constant rate. Consequently, the observed behavioural deficiencies translated into psychophysiological correlates that replicated some previous findings.

Various methods have been developed to improve the symptoms of dyslexia (e.g., phonological therapy, reading therapy). A promising neuroscience-based method is neurofeedback therapy. Neurofeedback has shown a positive effect in the treatment of symptoms of other disorders (e.g., ADHD, autism, epilepsy); however, research on

neurofeedback in dyslexia is both scarce and inconsistent. Neurofeedback was shown to improve reading and phonological skills, but other studies did not observe any significant effects of neurofeedback in this disorder or found symptoms-unspecific effects (e.g., reduced aggression). Therefore, Study 2 was conducted to examine the effect of neurofeedback in participants with dyslexia. Following Study 1, participants with dyslexia from the baseline study were randomly split into therapy and control groups, and a treatment study was then conducted to assess the impact of LORETA z-score neurofeedback therapy on behavioural and neurological markers of dyslexia. Specifically, the therapy group received 20 sessions of neurofeedback therapy, and the waitlist control group of participants with dyslexia did not. The post-therapy assessment revealed that there were therapy-related improvements in phonological task performance and phonological spelling. Finally, EEG power increased across the frequency spectrum when measured over the frontal lobe, possibly reflecting involvement of reading-related frontal lobe structures.

Notably, the behavioural gains from therapy were retained three months post-treatment. An additional assessment of behavioural task performance showed that participant's performance was as improved as immediately following the end of the therapy and had improved even further in reading, phonological and spelling tasks. Further, performance benefits were present even when corrected for chronological age in reading and phonological (but not spelling) tasks. These findings provided novel evidence that the use of neurofeedback is an effective treatment for phonological dyslexia. It was therefore concluded that the positive effects of neurofeedback in dyslexia are lasting. However, future studies should examine whether such improvements could last longer than three months.

Declaration

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Signed: Jessica Cipolla

Date: November 2020

Acknowledgements

I would like to acknowledge Flinders University for their never-ending support through this arduous journey and my illness. I would also like to acknowledge that this research has been conducted with the support of an Australian Government Research Training Program Scholarship.

Thank you to my supervisor, Richard Clark, without whom this research would have never been possible. Thank you for not only your guidance, support, time commitment, and resources but also for our chats and your empathy throughout my candidature. Thank you to Brain Health Clinics and everyone at the clinic that helped along the way.

Thank you to my friends and family that have been a constant source of love and encouragement. I would have never been able to finish without you. To my friend Artyom, your guidance and statistics help was invaluable, as was your ability to help calm some of my PhD related anxiety attacks! Lisa, you're amazing! Your guidance and support have honestly meant the world to me. I wouldn't be here if you hadn't seen potential in me way back in undergrad and encouraged me to achieve my goals. To Jeanette, Lisa (again), Bec, Francesca, and my girls thank you from the bottom of my heart for the check-ins, the sanity breaks, and being a constant cheerleading squad.

To my mom, who never stopped believing in me, thank you for your love and support through the stress, and while I was sick. You never stopped believing I could achieve anything I put my mind to, no matter the hand I was dealt. I wouldn't be the person I am today without your unconditional love. If I become half the woman you are, I can take on the world.

Finally, thank you to the love of my life and the smartest person I know, Odjen. From staying up late at night helping me figure out stats, to giving up entire evenings and weekends to listen to me babble thesis nonsense just so I can bounce ideas off someone, to setting food

in front of me and reminding me self-care is necessary; I need you to know these things didn't go unnoticed (even if I forgot to acknowledge them at the time). I am so happy that I have you by my side. We can grow as we go.

Chapter 1. Introduction

What is Developmental Dyslexia?

Developmental dyslexia is a neurological disorder that leads to impaired reading, writing, and spelling abilities (Fletcher et al., 2018; Gvion & Friedmann, 2010; Sahari & Johari, 2012). Importantly, it is usually found in children and adults who otherwise demonstrate intact or even above-average cognitive abilities and intelligence. Understanding the nature of dyslexia is very important because it constitutes approximately 80% of all specific learning disorders (American Psychiatric Association, 2013) and affects between 5 and 20% of the world population (De Santana et al., 2012; Klein & Shaywitz, 2005).

Dyslexia was first defined as 'word blindness' by Adolf Kussmaul (1877) who described stroke patients' selective loss of reading abilities with intact verbal and non-verbal reasoning skills. Rudolph Berlin (1884) first used the term 'dyslexia' in 1884, which was used until it finally transformed into 'developmental dyslexia' after Pringle Morgan described the case of boy Percy, who had congenital (i.e., inborn) word blindness (Wagner, 1973). Somewhat similar to stroke patients, the boy could not learn to read despite his above-average cognitive (verbal and non-verbal) capabilities.

The initial term 'word blindness' emphasizes an impairment in visual processing - that is, a specific deficit in visual processing, selectively affecting written words (Hinshelwood, 1911; Orton, 1925). This vision-specific view of the disorder was revised in the 1950s with the introduction of the principles of 'generative phonology' (Lees & Chomsky, 1957). The idea of dyslexia was reformulated as a language disorder with an emphasis on the acquisition of phonological skills (Mann & Liberman, 1983). Consequently, dyslexia is a neurological condition that does not relate to a lack of vision (Fletcher et al., 2018).

Current Definition/Diagnosis

Dyslexia is not classified as a separate disorder in the Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM 5; American Psychiatric Association, 2013), but it is a part of a Specific Learning Disorder category. Besides problems with learning to read (dyslexia), this category in DSM 5 includes other major learning difficulties inwriting and mathematics (dyscalculia). According to the DSM 5, four criteria must be fulfilled to diagnose dyslexia:

a) The primary criterion is the difficulty to learn how to read in school-age years. Importantly, these difficulties must have persisted for at least six months without any signs of improvement despite the additional training and provisional interventions. Specifically, participants with dyslexia constantly make errors during reading and writing as well as require more effort to read and understand what was read.

b) The affected academic performance should be significantly lower than what would be expected given the individual's chronological age. The significance of the difficulties is assessed via standardised achievement tests and a comprehensive clinical assessment.

c) Although these difficulties mentioned above may begin in the early years of schooling, it is also possible that the symptoms could be fully manifest only in later years, that is, with increased demand for the affected academic skills (e.g., timed tests, demanding academic tasks).

d) Importantly, it should also be confirmed that the observed difficulties do not stem from problems with basic auditory or visual acuity, intellectual disabilities, and other mental or neurological disorders.

Finally, the DSM 5 requires that dyslexia diagnosis should be based on a clinically assessed history of individual's psycho-educational and physical development, medical and

family factors, and school reports. Dyslexia can co-occur with other types of specific learning disorders (i.e., writing and dyscalculia), which should be considered.

Over the years, various studies postulated different neurocognitive deficits that may be involved in dyslexia (Goswami, 2003; Habib, 2000a; Ramus, 2004). These theories include (but are not limited to) (i) the phonological theory that describes dyslexia in relation to the ability to process and recall phonemes (Carroll et al., 2003); (ii) the magnocellular theory that refers to the malfunction of magnocellular cells in the primary visual area (Gori et al., 2016), and (iii) the cerebellar theory (Gross-Glenn et al., 1991), which proposes that anatomical changes in the cerebellum can lead to automatization deficits. Some of the most prominent of these theories will be discussed below. Note, however, that the understanding of the etiology of dyslexia is still developing and further refinements occur with every generation of dyslexia research. These theories should not be viewed as mutually exclusive but rather as approaching the disorder from different theoretical perspectives and backgrounds (Ramus et al., 2003).

Theories of Developmental Dyslexia

Phonological Theory

One of the theories of the origin of dyslexia is the phonological theory (Vellutino et al., 2004). This theory is based on an assumption that children with dyslexia have difficulties in learning to separate individual sounds of words and then match those sounds with their visual letter representations. The process of sound-letter matching has been referred to as 'phonemic awareness' and can be assessed using a non-word decoding test. In these tests, participants with dyslexia are asked to read pronounceable non-words, such as salder, poot, dar, that require rules of the letter-sound correspondence to be read correctly, but at the same time lack any meaning. Performance on phonological awareness tasks can predict future language development (Carroll et al., 2003; Pfost, 2015). For instance, Landerl et al. (2019)

conducted a longitudinal study and traced the cognitive development of 1120 children in five different languages. The researchers reported that within each language, there was an interaction between children's performance on phonological awareness tests and their reading abilities. Knoop-van Campen and colleagues (2018) found that phonological awareness was associated with word reading efficiency in both the participants with dyslexia and the control group. Notably, only in the participants with dyslexia, there was an indirect link between working memory and word reading efficiency via phonological awareness (Knoop-van Campen et al., 2018). Finally, there is clear evidence from neuroimaging literature that patterns of cerebral connectivity, as well as alterations in cortical structures implicated in language can explain the observed phonological impairments in dyslexia (Hampson et al., 2006; Xia et al., 2016).

Collectively, these findings provide convincing evidence that phonological capabilities must be, directly or indirectly, related to reading performance and therefore phonological task performance should serve as a diagnostic criterion of dyslexia (Peterson et al., 2013; Ziegler & Goswami, 2005). In other words, because phonological task performance is closely linked to reading, one could use phonological awareness as a convenient task to diagnose dyslexia. Therefore, the phonological aspect of dyslexia was an essential component of the current thesis (see below for details).

Rapid Auditory Processing Theory

In addition to the general phonological deficit, the rapid auditory processing theory suggests that a more primitive auditory deficit causes dyslexia; specifically, a difficulty in the processing of quickly changing sounds (Jernigan et al., 1991; Tallal, 1980). In line with the phonological view on dyslexia, proponents of this theory argue that the ability to process rapidly presented auditory stimuli adequately is a vital component of processing phonological tasks, which is crucial when learning to read. In other words, the rapid auditory processing

theory also presumes the presence of deficient phonological abilities. In line with these assumptions, it has been shown that individuals with dyslexia show poor performance in frequency discrimination (Ahissar et al., 2000; McAnally & Stein, 1996), and in temporal order judgment tasks (Nagarajan et al., 1999; Tallal, 1980). Additionally, there is some evidence that dyslexia results in failure to correctly represent short sounds, especially when presented in fast transitions (e.g., /ba/ versus /pa/), which, in turn, results in problems with differentiating between the acoustic events (Gaab et al., 2007; Goswami et al., 2011; Lehongre et al., 2011; Richardson et al., 2004). Related to this is the concept of categorical perception, which occurs when acoustic differences between different exemplars of the same phonemic category are not perceived as different (Liberman et al., 1967). Liberman and colleagues (1957) proposed that this categorical perception is unique to speech and that it lays in the anatomy of speech production (Liberman et al., 1957). Individuals with dyslexia, on the other hand, may have reduced categorical perception of consonant contrasts (i.e., words that are identical except for one consonant (Adlard & Hazan, 1998; Mody et al., 1997; Serniclaes et al., 2004). This reduced categorical perception of consonant contrasts also underlines the phonological component of this theory of dyslexia. Collectively, research suggests that people with dyslexia show reduced performance on phoneme categorisation tasks (e.g., differentiating on a 7-steps continuum between /ʃa/ and /sa/), even for the phonemes that are placed at the different endpoints of a continuum (Brandt & Rosen, 1980; Hakvoort et al., 2016; O'Brien et al., 2018; Serniclaes et al., 2004; Zhang et al., 2012). This disadvantage remains even when participants with dyslexia are given more time to process the stimuli (O'Brien et al., 2019).

Marshall and colleagues (2001) examined 82 typically reading children and found moderate correlations between the measures of rapid auditory and phonological abilities (phoneme deletion, rhyme oddity nonword repetition). In a follow-up experiment, Marshall

and colleagues compared 17 children with dyslexia to an age- and reading-matched sample of control participants on the same tasks. In the rapid auditory processing task, participants with dyslexia performed at the same level as reading-age-matched controls, but their performance was lower than chronological-age-matched controls. In other words, these studies show that the basic auditory deficit may lead to the phonological deficit, and to corresponding reading difficulties. When taken together, these results provide consistent evidence that dyslexia could be related to basic auditory deficits and, based on the phonological theory (Vellutino et al., 2004) it can be concluded that dyslexia has a strong phonological component and provides an explanation for the reasons why learning of phonemes is dysfunctional in participants with dyslexia.

Visual Theory

The visual theory of dyslexia emphasises the role of visual impairments in hindered letter processing which leads to the difficulties seen in dyslexia (Lovegrove et al., 2013; Stein & Walsh, 1997). The theory proposes that dyslexia is caused by visual difficulties such as unstable binocular fixations (having both eyes fixated on the same point; Cornelissen et al., 1992), poor vergence (pupils moving simultaneously; Eden et al., 1994) and increased visual crowding (inability to find the visual target amongst other stimuli; Spinelli et al., 2002). The theory proposes that in some cases, the magnocellular pathway is selectively disrupted, leading to visual deficits in dyslexia (Stein & Walsh, 1997).

The lateral geniculate nucleus of primates contain two types of neurons: magnocellular and parvocellular (Merigan & Maunsell, 1993; Schiller & Lee, 1994). In short, the lateral geniculate nucleus is a structure that has six layers. The magnocellular cells are large neurons that could be found in the 2 ventral layers of the lateral geniculate nucleus (magnus meaning great or large in Latin). The parvocellular cells are, in contrast, small neurons that are located in the 4 dorsal lateral geniculate nucleus layers. The magnocellular

layers are known to be involved in movement detection and in the detection of quick changes in the environment. On the other hand, the parvocellular layers can detect finer shapes and are necessary for colour vision. As mentioned above, there is accumulating evidence that the magnocellular pathway may be specifically affected in dyslexia.

Magnocellular Theory

Specifically, this theory suggests that dyslexia may be linked to the disruption of magnocellular neurons (Stein & Walsh, 1997). Due to their size, magnocellular neurons can be very fast in transmitting information. In the case of visual processing, they are responsible for rapid visual information processing. Specifically, magnocellular neurons in visual brain areas define the speed and quality of the attentional selection of target items (e.g., letters) for further processing (e.g., reading). Importantly, the magnocellular neurons are also found in other sensorimotor systems, such as the motor, tactile, auditory, and visual systems. Therefore, the magnocellular approach to dyslexia attempts to combine and link all other theories by suggesting that dysfunction in these neurons causes the auditory (rapid auditory processing theory) and visual (visual theory) dysfunction which leads to the difficulty with processing phonemes (phonological theory) seen in dyslexia.

Interestingly, there is overwhelming evidence that magnocellular neurons in the visual system are impaired in dyslexia (Gori et al., 2016; Stein, 2018). For instance, previous studies showed a reduction of volume of magnocellular cells in the retina and the lateral geniculate nucleus (Pammer & Wheatley, 2001). Such alterations in magnocellular neurons have been reported in histological examination of postmortem brains in dyslexia (Livingstone et al., 1991) as well as in vivo (Giraldo-Chica et al., 2015; Müller-Axt et al., 2017). For instance, Demb et al. (1998) showed that, relative to healthy controls, participants with dyslexia have overall reduced activity in the primary visual cortex (V1) and in a secondary cortical visual area (V2, MT+) that receives input from the magnocellular pathway (Zhang et al., 2013).

Most importantly, Demb et al. showed convincingly that the strength of activation in these brain areas was predictive of participants' reading performance.

Another way to assess the functioning of magnocellular cells is through a motion detection task. One of the key brain structures responsible for motion detection is the magnocellular–dorsal pathway (Boets et al., 2011; Gori et al., 2014; Menghini et al., 2010). The origin of this pathway is found in the ganglion cells of the retina. The magnocellular–dorsal pathway further projects first to the magnocellular layer of the lateral geniculate nucleus, and then to the occipital and parietal cortices (see Maunsell, 1987). It was proposed that hindered visual motion perception could be associated with developmental dyslexia (Boden & Giaschi, 2007; Laycock & Crewther, 2008; Tallal, 2004; Vidyasagar & Pammer, 2010). In line with these ideas, recent work demonstrated that not only motion perception is impaired in children with dyslexia relative to matched controls, but that visual motion perception in pre-reading age children can reliably predict the success of future reading development (Gori et al., 2016). These researchers also provided evidence that motion detection training improves reading skill in children and adults with dyslexia (Gori et al., 2016), consistent with some magnocellular deficiency in the visual system.

Cerebellar Hypothesis

Another theory of dyslexia is the cerebellar hypothesis, which posits that abnormal cerebellar function may result indirectly in dyslexia symptoms (e.g., motor control, working memory, attention, reading; Eckert et al., 2003; Fawcett & Nicolson, 1999; Koyama et al., 2013; Stoodley, 2016). The cerebellum is located in the posterior cranial fossa, near the brainstem. It is highly interconnected with many other brain areas and receives information from both the sensory systems and the spinal cord. The cerebellum plays a key role in virtually all physical movement; the primary function of the cerebellum is to regulate voluntary motor movements, posture, balance, and speech, and ensure coherent muscular

activity. During brain development, the cerebellum is also responsible for the acquisition of motor skills. Despite its relatively small size (~ 10% of the total brain weight), the cerebellum contains roughly half of the brain's neurons (Jimsheleishvili & Dididze, 2019).

The cerebellum has strong functional and anatomical connections with brain regions involved in phonological processing as well as verbal working memory (e.g., temporoparietal cortex, frontal brain regions; (Stoodley et al., 2012). Carreiras et al. (2007) showed that various cerebellar regions were active when participants performed different reading- and language-related tasks, including lexical decision tasks (right cerebellum), when reading aloud (bilateral), comparison of non-words and consonant strings (right lobules; Joubert et al., 2004). In a study in which participants read words and pseudowords, Mechelli et al. (2003) showed that the right cerebellum was active when participansts had to read words and pseudowords (Hagoort et al., 1999; Tan et al., 2001; Xu, 2001). Therefore, studies show collectively that different subregions of the cerebellum play an active role in reading, lexical decision making, reading of pseudowords and phonological tasks, which is in line with the phonological view of dyslexia.

There is evidence from functional neuroimaging research for this theory. Gross-Glenn et al. (1991) examined children with dyslexia and observed symptoms that were characteristic of cerebellar dysfunction (e.g., dystonia, decreased muscle tone, discoordination). Using positron emission tomography (PET), Gross-Glenn and colleagues found that 80% of participants with dyslexia had decreased activity in the right cerebellum. These researchers proposed an indirect causal chain between cerebellar problems and reading difficulties, in which dysfunction in the cerebellum leads to problems with physical speech ability (i.e., ability to move the tongue, lips, etc. to produce speech sounds) which, in turn, causes poorer phonological awareness (Nicolson, Fawcett & Dean, 2001). Further, they hypothesised that the reduced articulation speed hinders one's working memory abilities as they would not be

able to rehearse the information to keep it in the "phonological loop" (i.e., part of working memory dealing with spoken and written information; Baddeley, 1975). Consequently, this hindered articulatory and working memory representation results in deficits in phonological awareness through impaired sensitivity to the phonemic structure of language (Snowling & Hulme, 1994). This describes the indirect effect through which cerebellar impairment could lead to proper phonological processing and results in hindered reading performance.

The cerebellar hypothesis was not supported by other studies, with no reliable correlation between reading abilities and postural stability test observed (Barth et al., 2010; Hoeft et al., 2011). Given that postural stability was found to be specifically affected in children with dyslexia when compared to children who are slow learners but did not have dyslexia, the postural stability test was frequently used for assessments of cerebellar functions (Nicolson & Fawcett, 2005). Barth and colleagues (2010) found no reliable associations between assessments of cerebellar functions and academic performance of participants with dyslexia; also, these participants did not show specifically poor performance on the cerebellum-related task. On the other hand, phonological awareness and vocabulary were strong predictors of the success of reading intervention and reading performance. In a different study, Hoeft et al. (2011) also found the cerebellum was not one of the areas that could predict reading gains in dyslexia. Combined, these findings do not show any evidence that malfunction of the cerebellum is associated with reading difficulties. They also contribute further evidence of the phonological dysfunction in dyslexia, which is observed even in the absence of clear links with the cerebellum.

In a more recent study, van Oers et al. (2018) conducted an anatomical assessment of the cerebellum in participants with developmental dyslexia (N = 26) and in healthy controls without any neurological dysfunctions (N = 25) using a voxel-based morphometry approach (i.e., a measure of differences in local concentrations of brain tissue). In this study, there was

no correlation between dyslexia and cerebellar structure and van Oers et al. concluded that there were no dyslexia-related anatomical differences of the cerebellum that could support the cerebellar deficit hypothesis. Although cerebellar differences may be specifically pronounced in a subgroup of individuals with dyslexia who show both phonological and fluency deficits (Nicolson, Fawcett, & Dean, 2001), it is safe to say that even if some individuals with dyslexia have dysfunction in the cerebellum, as it appears to not be present in all individuals with dyslexia it may not be the cause of dyslexia. More research is necessary to determine the role of the cerebellum in dyslexia as well as the role it may play in defining subtypes of the disorder. Importantly, it seems that various theories of dyslexia show a consistent association of this disorder and phonological abilities. However, each theory has its unique explanation as to how the phonological deficit is elicited.

Subtypes of Dyslexia

Many studies argued for the existence of a dual-route model of reading (Coltheart, 1978; Coltheart et al., 1993; Marshall & Newcombe, 1973; although see Coltheart, 2006 for a comparison of the dual-route model with an alternative connection model of reading). This model assumes that successful reading is achieved via two processes that extract and represent spoken or written words in memory: the so-called "lexical" and "sublexical" procedures for reading aloud. The lexical procedure is necessary to link or match the written word (i.e., orthographic representation) with an associated phonological representation of this word that is stored in memory (i.e., mental lexicon). Importantly, the lexical procedure can only be used with known words, but not for unfamiliar nonwords. The sublexical procedure generates phonological representations of words. This procedure is achieved by using the knowledge of the correspondence between written words and the corresponding phonological representation of letters/words (i.e., the so-called grapheme-morpheme correspondence rules). Therefore, the lexical procedure is used to process irregular words correctly, and the

sub-lexical procedure is involved in the processing of regular words (3/4 of all English words) and nonwords.

As also briefly mentioned in the previous paragraph, an alternative model of dyslexia is the connectionist model (Plaut, 1999). In short, this model posits that there is no strict dichotomy between the regular and irregular words described above. In contrast, according to the connectionist model, language performance relies on strict rules that are learned gradually. In other words, this model argues that language acquisition is a process of learning the statistical regularities (i.e., connections) between written and spoken words (Plaut, 1999). Nevertheless, the connectionist model offers little explanation about how learning to read is acquired in children. It can also not account for some empirical findings in reading research (e.g., position of irregularity, position-sensitive Stroop effect, etc. see Coltheart, 2006 for more details). Therefore, the current work will mostly concentrate on the dual-rote model of reading as the most commonly used model in dyslexia research.

Using the dual-route model of reading, researchers have attempted to classify dyslexia into either surface or phonological subtypes (Castles & Coltheart, 1993). Patients with surface dyslexia have specific problems with reading exception words that require lexical processing and, at the same time, relatively preserved abilities to read regular words and nonwords, which requires sub-lexical processing (Behrmann & Bub, 1992; Coltheart et al., 1983; Marshall & Newcombe, 1973). The impairment in irregular word reading in surface dyslexia is thought to be a result of a damaged lexical route. Patients with phonological dyslexia, in contrast, have difficulties with the pronunciation of nonwords due to damaged sublexical procedures, while reading of irregular words (e.g., "have", “colonel”) is relatively intact (Patterson, 1995; Warrington & Shallice, 1980). Given that most English words involve sub-lexical processing, identifying phonological dyslexia could be the most straightforward in English-speaking children. Individuals with phonological dyslexia would

also be most likely to show greater dysfunction in their overall reading ability as the sublexical procedure is involved in the processing of the greatest portion of the English language.

Therefore, dyslexia is not a homogeneous disorder, as was shown previously (Ramus et al., 2018). For instance, by recording brain fMRI in both subtypes, van Ermingen-Marbach and colleagues (2013) examined neurofunctional mechanisms in groups of children with dyslexia with and without phonological deficits. Although both groups showed significantly increased activation in the right cerebellum, there were also additional activations that varied across the two types. Specifically, the group with phonological deficits showed increased activity in the left inferior frontal gyrus (BA 44), the left supplementary motor area (BA 6), the left precentral gyrus (BA 4) and the right insula (BA 13). On the other hand, the non-phonological deficit subgroup resulted in a higher level of activity in the left supramarginal gyrus (BA 40) and in the angular gyrus (BA 39). These differential patterns of brain activations suggest that dyslexia with phonological deficits has distinct neurological mechanisms when compared to those without. Consequently, when taken together with the dual route model these physiological results suggest that therapies for dyslexia should take these subtypes into consideration.

As well as the phonological and surface subtypes proposed by Castles & Coltheart (1993) as described above, there have been attempts to classify dyslexia into many other subtypes. For example, (Boder, 1973) proposed the dysphonetic and dyseidetic subtypes in an attempt to group dyslexia via visual or auditory/phonological deficits, subtypes with and without verbal language deficit (Leonard et al., 2002), as well as dyslexia with phonological or visual attention span deficits (Bosse et al., 2007; Ramus et al., 2018). However, research on these further subtype classifications have not been as complete and do not seem to take the theories of dyslexia into account (Bosse et al., 2007; Leonard et al., 2002; Ramus et al.,

2018). As shown, although many researchers agree that dyslexia consists of subtypes, there is still no consensus regarding classification for these subtypes or their definitions. Importantly, none of the mentioned typologies has been sufficiently accepted by the scientific community. One of the easiest approaches to classify dyslexia is to sort participants into groups with or without phonological difficulties. Therefore, the current thesis will be based on this definition. Further, because dysfunction in the ability to process phonemes leads to a large disadvantage in the successful learning of reading and writing, a phonological dysfunction is the most relevant clinically.

Treatments of Dyslexia

Treatments of dyslexia include interventions to enhance phoneme awareness, reading fluency, and reading comprehension, as well as word analysis techniques and simple rote learning methods (Snow et al., 1998). It seems that the effectiveness of dyslexia treatment depends on the time of the intervention: the earlier the onset of intervention, the more effective it becomes (Wanzek & Vaughn, 2007). Therefore, this and some earlier studies (Jenkins & O'Connor, 2002; Santa & Høien, 1999) recommended starting remediation procedures even before an official diagnosis of dyslexia to minimize the negative impact of this disorder (Blachman et al., 1999; O'Connor et al., 2005; Vaughn & Fletcher, 2010; Vellutino et al., 2006). There is some evidence in the literature that it is also possible to predict dyslexia before the onset of reading instruction by testing children's phoneme awareness and letter knowledge (Mathes et al., 2005).

Bowyer-Crane et al. (2008) used a randomised controlled trial design to compare two interventions designed for children who are at risk of poor literacy. The authors directly compared two interventions programs. The phonology-training program was based on reading intervention and was designed to target the development of decoding skills. The oral language program was based on the training of spoken language skills. Both interventions

were conducted every day for 20 weeks. The phonology-based reading program resulted in better outcomes relative to the oral language program when tested on tasks that were specific for phoneme awareness, letter-sound knowledge and that measured reading and spelling skills. On the other hand, the oral language group resulted in improved vocabulary and grammar task performance. Importantly, the authors showed that the observed positive outcomes in both treatment groups were still present five months after the treatment was over. Therefore, this study showed that training interventions could significantly improve reading comprehension in children who are at risk of dyslexia (e.g., who have parents with dyslexia). Additionally, it showed that these training-related improvements could be relatively robust and could be found months after the end of the intervention. These findings are also in line with an earlier work by Scammacca and colleagues (2007), who conducted a meta-analysis of 31 studies examining the effectiveness of reading interventions in students with reading difficulties. These authors found that reading interventions do show a positive effect and improve performance in treatment relative to controls (for more detail, see Shaywitz et al. 2004), although performance was still not on par with non-dyslexic peers. Note also that although successful, behavioural interventions alone are very demanding and time-consuming, involving 20 weeks of daily training as described above. This is a commitment that might not be unattainable for some pupils. Therefore, it makes sense to investigate whether there are more effective and efficient ways to improve performance in children with dyslexia.

Functional Neuroanatomy of Dyslexia

There has been a significant improvement in the last few decades in the understanding of the neural and functional correlates of dyslexia and its underlying brain mechanisms. Different neuroimaging methods were used to examine neurological alterations that are associated with impaired reading skills in dyslexia, such as functional magnetic resonance

imaging (fMRI; Devlin et al., 2006; Odegard et al., 2008; Shaywitz et al., 1998; Temple et al., 2003; Xia et al., 2016), and positron-emission tomography (PET; e.g., Dufor et al., 2007; Gross-Glenn et al., 1991; McCrory et al., 2000; Paulesu et al., 2014).

The next section will discuss the most consistent neuroimaging findings in dyslexia research and their relation to the specific theories of dyslexia (e.g., brain regions that are specifically related to phonological processing). Subsequently, how different brain areas are related to more complex tasks like reading will be discussed. Previous research showed that functional alterations of brain activity in individuals with dyslexia have been observed in the neural circuits that are engaged by typical readers and are implicated in the language network, including left-lateralised temporoparietal, occipitotemporal, and inferior frontal cortices (Paulesu et al., 2014). In more detail, the following section will concentrate on brain regions such as the: angular gyrus, Broca's area, dorsolateral prefrontal cortex, fusiform gyrus, inferior temporal gyrus, left inferior frontal gyrus, primary visual and auditory cortices, Wernicke's area, and others that were the most consistent findings in neuroimaging research in dyslexia. Interestingly, reduced brain activity in these regions was also observed when the performance of participants with dyslexia was compared to that of younger controls who were matched for reading abilities (Hoeft et al., 2007). This shows that dyslexia is not simply a result of delayed maturation. This also provides evidence that these deficits are not linked to simply a lower level of reading ability, but represent a dysfunction specific to dyslexia. Note also that although language-related brain areas are introduced and discussed separately, they are highly functionally and anatomically interconnected (i.e., left-lateralised temporoparietal, occipitotemporal, and inferior frontal cortices) as they all are involved in successful language processing.

The Occipito-Temporal Cortex

The occipito-temporal cortex is an extended area of the brain that is involved exclusively in visual content processing and contains two important regions relevant to dyslexia: the inferior temporal gyrus and the fusiform gyrus.

Inferior Temporal Gyrus (BA 20)

It has been proposed that the left inferior temporal gyrus may function as a quick word form recognition system (Brambati et al., 2004; Brown et al., 2001; Barry et al., 2004). Forexample, Corina et al. (2001) conducted an fMRI study and asked healthy controls and participants with dyslexia to either perform a phonological judgement task (judging whether presented tone pairs were the same) or lexical judgment task (detecting a rhyme between pairs of real and/or pseudo words). As a result, the authors found that during phonological judgment, participants with dyslexia showed higher activity in the right relative to the left inferior temporal gyrus. Additionally, during the lexical judgment task, the group with dyslexia relative to healthy controls showed reduced activity in the left inferior temporal gyrus. These findings showed that the inferior temporal gyrus was consistently under activated in participants with dyslexia when compared to healthy controls as well as to the right hemisphere within participants. Additionally, this brain area seems to be sensitive to basic auditory processing that does not require active reading.

Fusiform Gyrus (BA 37)

The visual word form area is found in the left Fusiform gyrus and is thought to be involved in word and letter identification by processing lower-level shapes before they get associated with corresponding phonology or semantics (Dehaene & Cohen, 2011; McCandliss et al., 2003; however, see Ardila et al. (2015) for a different view on this brain region). Monzalvo et al. (2012) used fMRI to examine neural patterns of brain activations during the processing of visual stimuli (houses, checkerboards, words) in participants with

dyslexia and in healthy controls. In this study, although participants with dyslexia showed intact neural responses when processing houses and checkerboards, they also had significantly reduced activations in the visual word form area during the processing of words. These findings imply that people with dyslexia may have specific difficulties with processing words, which is reflected in reduced visual word form area activity (Monzalvo et al., 2012). Interestingly, although the visual word form area is sensitive to processing of lower-level shapes (Dehaene & Laurent, 2011), dyslexia may affect processing of such shapes when they are parts of words, but not when they are parts of houses and other objects.

It was shown repeatedly that participants with dyslexia show significantly reduced activation across the occipitotemporal cortex, a brain region that is known for its sensitivity to written words and word-like stimuli (Olulade et al., 2014; Richlan et al., 2010). The occipitotemporal cortex (left ventral part) is actively involved in fast and effortless visual word processing and is linked to phonological decoding (Richlan et al., 2010; Wimmer et al., 2010). It secures the link between visual-orthographic information and phonological information in healthy controls (Price & Devlin, 2011).

Dyslexia-related under-activation in the greater occipitotemporal cortex was shown across different age groups (Richlan et al., 2011). Additionally, the occipitotemporal cortex was shown to be equally active during the processing of existing words and pseudowords in both younger and older participants with dyslexia (Pugh et al., 2001; Richlan et al., 2009; Vinckier et al., 2007). Such consistency of results across age groups suggests that people with dyslexia may experience difficulties in recruiting this reading-sensitive brain region early on in the course of development (Richlan et al., 2011). Apart from word identification difficulties, the occipitotemporal cortex has also been linked with the rapid naming deficits reported in dyslexia (Norton & Wolf, 2012), which again emphasizes the contribution of this brain region to dyslexia.

Note also that BA37 most likely is not exclusively the visual word form area. In more detail, this brain region has been repeatedly associated with the processing of faces and facial features with stronger activation for faces relative to words (Hasson et al., 2002), facial emotion processing (Kesler-West et al., 2001), mental rotation (Vingerhoets et al., 2002), and many other visual tasks (Giesbrecht et al., 2003; Vuilleumier et al., 2001). Ardila and colleagues (2015) performed a meta-analysis to study the connectivity of this brain region in relation to language and visual processing. As a result, the authors found evidence in favour of BA37 as a language-specific brain region but with a strong emphasis on visual perception. In other words, the authors reported that BA37 is strongly connected to two distinct neural networks that are related to visual perception as well as semantic language processing.

The Left Temporo-Parietal Cortex

The left temporoparietal cortex is a relatively large brain region that is consistently under-activated during phonological processing across different age groups in dyslexia (Habib, 2000b; Temple et al., 2001). The left temporoparietal cortex includes several important brain areas that play a role in dyslexia (Wernicke's area, Angular gyrus). The next few paragraphs will briefly outline the function of these left temporoparietal cortex brain areas and their role in dyslexia.

Wernicke's Area (BA 22)

Wernicke's area is located in the left temporoparietal cortex and plays an active role in speech perception and in the building of phonological representations (Flowers et al., 1991; Paulesu et al., 1996). The planum temporale is an area located at the heart of Wernicke's area. It is a cortical area that is located posterior to the auditory cortex and is thought to be involved in language processing (Barta et al., 1995; Nakada et al., 2001). Specifically, various functional neuroimaging studies reported that the planum temporale is

activated during phonological decoding and language-related tasks (Blau et al., 2010; Dehaene-Lambertz et al., 2010; Nakada et al., 2001; Shapleske et al., 1999; Simon & Rudell, 1967). For instance, the planum temporale was shown to almost double in the strength of its functional activations in literate compared to illiterate participants (Castro-Caldas et al., 1998). In a different study, Van Atteveldt et al. (2004) showed participants either congruent or incongruent sound-letter combinations in an fMRI study. As a result, the authors found that the planum temporale was one of the unique brain areas that responded to incongruent sound-letter combinations but not to letters presented alone. In other words, the planum temporale of Wernicke's area may be used to integrate speech sounds and visual letters (van Atteveldt et al., 2004).

Angular Gyrus (BA 39)

The angular gyrus is functionally connected to Wernicke's area and is thought to be responsible for a link between visually presented information and its linguistic representations (Horwitz et al., 1998; see also Pugh et al., 2000). Specifically, Horwitz and colleagues used PET to test participants with dyslexia and healthy controls. During single-word reading, control participants were found to have a statistically significant correlation between their cerebral blood flow in the left angular gyrus and regional cerebral blood flow in vision-specific extrastriate occipital and temporal lobe regions. This correlation during the reading task has been seen consistently in normative populations and is thought to be descriptive of functional connectivity between these brain areas (Rumsey et al., 1997). Importantly, participants with dyslexia did not result in functional connectivity between these brain areas. In other words, it seems that dyslexia results in reduced connections between the angular gyrus and visual brain areas, which could explain the difficulties in individuals with dyslexia to link visual information and its linguistic representations (Horwitz et al., 1998; Pugh et al., 2000; Richlan, 2020).

In healthy controls, the left temporoparietal cortex is associated with the processing of printed letters and linking them to individual sounds (Xu et al., 2018); however, participants with dyslexia show reduced activation in the left temporoparietal cortex even when compared with skill-matched children (Rumsey et al., 1994). These results imply that the left temporoparietal cortex is dyslexia-specific and that it is not related to general reading ability (Hoeft et al., 2007). Additionally and unlike healthy controls, people with dyslexia of all ages do not seem to show increased activation in the left temporoparietal cortex with increased efforts in reading tasks (Shaywitz et al., 1998), indicating a lack of the left temporoparietal cortex sensitivity to reading stimuli in dyslexia. Importantly, it was also demonstrated that participants with dyslexia with initial under activation in the left temporoparietal cortex during phonological processing tasks showed an increase in fMRI activity in this same brain area after they were trained to improve both oral language and reading abilities in a remediation program (Temple et al., 2003). Therefore, areas in the left temporoparietal cortex may reflect the lack of appropriate dyslexia-specific skills, which could be acquired through the remediation program.

Dorsolateral Prefrontal Cortex (BA 46)

The dorsolateral prefrontal cortex was shown to be one of the key brain regions that is specifically involved in executive functioning and cognitive control (Vahabzadeh & McDougle, 2014). Additionally, together with the frontopolar cortex (BA10), it has been shown to be actively involved in memory processes (Arnsten & Jin, 2014; Zinchenko et al., 2018), reward processing (Kobayashi et al., 2010) and social interactions (Rilling & Sanfey, 2011). Nathaniel-James and Frith (2002) showed further that the dorsolateral prefrontal cortex evaluates different potential responses in a given task and is involved in response selection. Most importantly, the dorsolateral prefrontal cortex plays a crucial role in phonological awareness in healthy participants and children with dyslexia (Kovelman et al.,

2012). Kovelman and colleagues conducted an fMRI study and asked a group with dyslexia and typical reading children (ages 7-13) to perform an auditory word-rhyming task as a measure of phonological awareness. They observed that explicit phonological judgements in non-dyslexic children resulted in activation of the left dorsolateral prefrontal cortex but not in children with dyslexia. Importantly, the left dorsolateral prefrontal cortex was also active in younger kindergarten-age children (ages 5-6), whose phonological awareness was comparable to the older participants with dyslexia. Therefore, the dorsolateral prefrontal cortex shows impairments specific to dyslexia.

The Left Inferior Frontal Gyrus (BA 45)

The left inferior frontal gyrus (lIFG) is yet another brain region that seems to be affected in dyslexia. However, in contrast to the occipitotemporal cortex and left temporoparietal cortex in which researchers have found an under activation, the majority of lIFG cortex studies traditionally report increased activity in dyslexia (Hoeft et al., 2007; Shaywitz et al., 1998). It was hypothesised that activation of lIFG can be related to compensatory mechanisms that involve subvocal reading or simply enhanced efforts in dyslexia to perform the task (Hoeft et al., 2007; Price, 2012). This compensatory theory is supported by studies that have reported that non-dyslexic, typically developing children have less activation in this brain region during a reading task (Hoeft et al., 2007). Additionally, Temples and colleagues (2003) also found enhanced functional activations in the lIFG of participants with dyslexia during a phonological processing task after a remediation program to improve oral language and reading abilities (discussed above). Interestingly, activation patterns in the lIFG do not differ between dyslexia and healthy controls when matched for reading abilities (Hoeft et al., 2007). Given these results, although the lIFG is important in the role of phonological processing and reading, it may be that the lIFG is sensitive to general

reading ability as well as the level of reading skill and therefore may not be related to dyslexia specifically.

Broca's Area (BA 44)

The inferior frontal gyrus is the location of another well-known brain region that is involved in language production: Broca's area (Kennison, 2017). The primary role of this brain area is related to the motor component of speech production. In other words, Broca's area is responsible for the movements that are necessary for coherent and reliable articulation (D'mello & Gabrieli, 2018). It plays a role in syntactic processing (Bouchard et al., 2013). Finally, Broca's area is closely linked with phonological and semantic processing, verbal working memory, and silent reading (Fiez & Petersen, 1998; Price, 2012; Temple et al., 2001).

Importantly for the current work, Broca's area may also be associated with dyslexia. For instance, Paulesu et al. (1996) used PET to test a group of participants with dyslexia with primarily phonological difficulties and compared them to age-matched healthy controls. Participants were asked to perform a rhyming and a short-term memory task with visually presented letters. As a result, both groups of participants showed comparable activation patterns: Broca's area was activated in a rhyming task and the temporoparietal cortex was active in the short-term memory task. However, the participants with dyslexia had a very low degree of coherence (i.e., connectivity) between this area and other brain areas. These findings support various other studies discussed above that reported reduced functional connectivity between different brain areas in dyslexia.

Primary Visual and Auditory Cortices

In line with the basic auditory and visual deficit explanation of dyslexia discussed above (Geiger & Lettvin, 1987; Slaghuis et al., 1993; Stein, 2001; Tallal, 1980), dyslexia has been shown to result in reduced activation in brain regions associated with visual processing

streams (e.g., visual areas BA 5, 7, 39, BA 19; Horwitz et al., 1998; Stein & Walsh, 1997), reduced left-hemispheric structural connectivity between the visual thalamus (lateral geniculate nucleus) and middle temporal area V5/MT (Müller-Axt et al., 2017), as well as in regions that support processing of nonverbal visual stimuli (Demb et al., 1998; Eden et al., 1996). It was shown, surprisingly, that processing of nonverbal information was tightly linked to reading disability (Boets et al., 2011; Richardson et al., 2004; Tallal, 1980). For instance, training in rapid auditory processing with nonlinguistic acoustic stimuli improved reading performance and processing of non-verbal stimuli in some, but not in all participants with dyslexia (Gaab et al., 2007). Note also that disorder-related differences in functional brain activity in basic visual brain areas often disappear once participants with dyslexia and control participants were matched for reading skills or when participants with dyslexia undergo behavioural training (Alexander & Slinger-Constant, 2004; Eden et al., 2004; Olulade et al., 2013). For instance, Olulade and colleagues (2013) found that reading intervention could increase activity in the visual V5/MT brain area (BA 19). These results showed that the dysfunction of visual magnocellular neurons is not the primary cause of dyslexia but rather results in hindered reading abilities.

Structural Brain Alterations in Dyslexia

In addition to differences in functional brain activations, dyslexia is also associated with structural brain differences across networks that are known to be involved in reading, including regions that have functional alterations in dyslexia (Eckert et al., 2016; Kronbichler et al., 2008; Langer et al., 2017). For instance, a common finding is a dyslexia-related grey matter volume reduction in the left temporoparietal cortex and in the visual word form area (BA 37; Brown et al., 2001; Hoeft et al., 2007; Kronbichler et al., 2008). It was shown that children who are at risk of dyslexia also have grey matter volume reduction in the superior temporal gyrus (BA 22) and sulcus (Eckert et al., 2016; Raschle et al., 2011; Richlan et al.,

2013). Given that these studies were conducted in pre-reading age children, brain volume differences cannot be explained by a lack of reading experience in dyslexia relative to controls.

Furthermore, dyslexia has been associated with weaker reading-related white matter connections between brain regions starting as early as 5 to 17 months old (Hoeft et al., 2011; Langer et al., 2017; Myers et al., 2014; Vandermosten et al., 2012; Wang, 2017). This weaker connectivity pattern was shown to be related to phonological and orthographic difficulties in this disorder (see Hoeft et al., 2011; Langer et al., 2017; Myers et al., 2014; Vandermosten et al., 2012). In contrast, children with dyslexia with improved reading skills show stronger [right-lateralised] white-matter connections (e.g., in superior longitudinal fasciculus; Hoeft et al., 2011). Similarly, non-dyslexic children with a family risk of dyslexia show stronger white matter connections relative to children with a family history of the disorder who indeed turned out to have dyslexia later on (Wang et al., 2017). Wang and colleagues (2017) suggested this increase in right-lateralised white-matter connections may represent compensatory involvement of the right hemisphere to account for hindered left-hemisphere processes in dyslexia which is a strong theory. It appears that children with dyslexia may rely on and therefore build stronger connections in these right hemisphere areas to compensate for dysfunction in the left hemisphere. A similar explanation was proposed for the findings of dyslexia-specific stronger connections in the corpus callosum (Dougherty et al., 2007; Robichon & Habib, 1998). More specifically, this increased connectivity pattern in the corpus callosum was proposed to be a sign of an additional involvement of the right hemisphere in dyslexia (Gabrieli, 2009).

There is consistent evidence that dyslexia is a highly heritable disorder, with almost 60% evaluated dyslexia participants having a family member with dyslexia (Friend et al., 2008; Heath et al., 2014). Therefore, various studies attempted to examine brain regions in

children who are at risk of developing dyslexia to track anatomical characteristics that could help to predict dyslexia before it was formally diagnosed, thus establishing a causal role between certain brain regions and dyslexia (Langer et al., 2017; Leppänen et al., 2002; Molfese, 2000; Raschle et al., 2011; Torppa et al., 2010; van Viersen et al., 2017).

Interestingly, the risk of dyslexia can be identified as early as six months of age (Leppänen et al., 2002). Those infants who are at risk of developing dyslexia have structural brain changes in the left arcuate fasciculus (Langer et al., 2017), an axonal bundle that connects the posterior region of the temporoparietal junction (intersection of the temporal and parietal lobes) with the frontal cortex which is crucial for reading and language processing (Catani & Mesulam, 2008). In line with these findings, infant studies (5-18 months) showed a link between the strength of white matter integrity in the arcuate fasciculus and future reading skills (Langer et al., 2017). In another study, future dyslexia at the age of 8 was predicted based on these same newborns' neural responses to speech and non-speech sounds (Molfese, 2000), which once again supports a strong neurological foundation of dyslexia. Finally, another study reported that infants with a family history of dyslexia showed different activation levels in the left hemisphere when listening to human speech (Leppänen et al., 2002), which may provide an additional method for identifying dyslexia in infancy.

To summarize, there is strong evidence that dyslexia results in both structural (e.g., left temporoparietal cortex, visual word form area, superior temporal gyrus, superior temporal sulcus etc.) and functional abnormalities (e.g., inferior temporal gyrus, fusiform gyrus, left temporoparietal cortex, Wernicke's area, angular gyrus, etc.) in normal brain functioning. However, due to its high cost and relatively limited access, neuroimaging (fMRI, MRI and PET) may not be the most convenient approach to test the symptoms of dyslexia for the purposes of both diagnoses and for the measurement of therapy effectiveness. Therefore, the

next section will concentrate on a popular and relatively accessible neuroscientific method that has a high potential in dyslexia research: Electroencephalography (EEG).

EEG Correlates of Developmental Dyslexia

Another useful and widely used technique for identifying the neural correlates of behavioural performance in dyslexia is electroencephalography (EEG). The current section will concentrate on EEG findings in developmental dyslexia. Specifically, I will outline some of the most consistent neurophysiological correlates of developmental dyslexia as measured by EEG frequency analysis.

When neurons fire, there is a measurable change in electrical activity due to the flow of positively charged ions across the neuronal membrane (Luck & Kappenman, 2011). When millions of neurons are activated simultaneously, this electrical signal becomes strong enough to be detected on the surface of the scalp. EEG records neuronal activity using specialised electrodes that attach to the scalp. Measurable differences in this scalp electrical activity across comparison groups or across time can provide researchers with important information about the functionality of the underlying neural structures.

EEG and its Measurement

When neurons fire in specific brain areas, rhythmic oscillations that are detectable via the scalp electrodes occur and are measured in a wide range of frequencies (i.e., 0.05 Hz - 30 Hz; see Buzsáki & Schomburg, 2015). More specifically, EEG brain oscillations are a result of recurrent loops impacting neuronal activity within specific brain regions. When currents from source regions in the underlying brain are conducted through the volume of the brain, they can be measured at the scalp surface. However, note that what is measured at the scalp is voltage and not the current directly. Specifically, the voltages are measured by referencing the activity at each scalp point to another point that is often a non-cephalic location, such as the ear lobes or at the thickest bones in the skull (left and right mastoids).

Note that the strength of the current reduces in size with the distance from its underlying source. Therefore, in order to detect the signal, it is critical that millions of neurons are active simultaneously. The resulting source currents can be of different frequencies and are linearly summed at each point on the scalp. To identify the different frequency components, a procedure called the fast Fourier transform is used, which identifies the amplitude of each frequency at each point. Brainwaves occur at various frequencies (measured in cycles per second or hertz, i.e., Hz) that are related to different perceptual and cognitive operations (Klimesch, 1999; Palva & Palva, 2007). The classic names of these EEG bands are delta (0.5–4 Hz), theta (4–8 Hz), alpha (8–12 Hz), beta (12–30 Hz), and gamma (30–100 Hz). When speaking about EEG frequency bands, it is important to understand a few concepts that will be used later in the text, such as power and power spectrum density. The power represents the amount (or strength) of activity in different frequency bands and is measured as a squared frequency spectrum. Furthermore, power spectrum density refers to the distribution of signal power over these frequency bands. The following step will provide brief information about the general functional meaning associated with different frequency bands then continue with dyslexia-related alterations in these frequency bands.

Delta

Delta is a slow (0.5–3.5 Hz) thalamocortical rhythm that occurs when a neuron is hyperpolarized, amongst other things. This is called the low fidelity mode of thalamocortical rhythms. Essentially, when in low fidelity mode, the neuron is not processing modulatory inputs. This is why delta is so prominent in sleep (Başar et al., 2000; Buzsáki & Draguhn, 2004). Murphy et al. (2009) described that these slow waves have distinct cortical origins and could be sourced to the medial frontal gyrus and, importantly for the current thesis, the inferior frontal gyrus. Delta band activity is not exclusively sleep-related, but it is also observed when people are at rest and awake (Chen et al., 2008; Demir, 2006). Specifically, of

interest in the current thesis, altered frontal delta activations in dyslexia might be linked to deficient processing of slow-rate speech information (Goswami et al., 2011).

Apart from language-specific processing, delta waves also seem to play a role in motivational and reward processing (Knyazev, 2007). Knyazev et al., (2012) suggested that delta oscillations may be elicited in response to various cognitive processes that are related to attention and emotion (Knyazev et al., 2009; Knyazev, 2007). Delta is also involved in behavioural inhibition (Kamarajan et al., 2005; Knyazev, 2007; Putman, 2011). Finally, there is also recent evidence that the delta frequency can serve as a carrier frequency for higher frequencies via the mechanism of cross-frequency coupling (e.g., see Canolty & Knight, 2010).

Theta

Theta oscillations (4–8Hz) can originate in the hippocampus and in fronto-cortical areas (Vertes, 2005) and represent an 'on-line' state of these brain areas (Buzsáki, 2002). Important for the purpose of the current work, theta oscillatory activity is closely linked to reading difficulties (Arns et al., 2007; Goswami, 2011; Klimesch, 1999; Penolazzi et al., 2008).

Additionally, theta is thought to be involved in working memory processes (Klimesch, 1996, 1999; O'Keefe & Burgess, 1999). Studies showed that increased theta activations are elicited in when participants have to process novel or conflicting information (Cavanagh & Frank, 2014). Cavanagh and Frank hypothesised that the induced changes in the power of theta could be a neural signature of increased top-down cognitive control. Interestingly, theta activations have been linked to cognitive control both when recorded during active task performance and when at rest (Pscherer et al., 2019).

Finally, and related to the topic of the current thesis, theta power is enhanced when participants remember words or other stimuli. Specifically, theta power was larger for those

words that were successfully remembered during a recognition session relative to those that were forgotten (Klimesch, 1999). Therefore, the presence of theta for the purposes of the current work is that it is a necessary element for the proper encoding of stimuli that will be able to be retrieved at a later date (learning).

Alpha

Alpha oscillations (8–13 Hz) have historically been associated with a state of relaxation and are specifically active during non-arousal. Alpha is thought to originate in the thalamus, and thalamocortical structures can up- or down-regulate alpha's involvement in cognitive functions (Bollimunta et al., 2011; Vijayan et al., 2013). The thalamus is a neuroanatomical hub that could link information between the language-related frontal cortex (i.e., IFG and Broca's area) regions with the basal ganglia and the cerebellum (Barbas et al., 2013). Consistently, there is some empirical support for the hindered activity in the auditory thalamus in dyslexia (Díaz et al., 2012). These authors found that the processing of phonemes results in reduced activity in the auditory thalamus in the left hemisphere in dyslexia. Consistently, Duffy et al. (1980) found increased alpha power in the language-related frontal brain region of the left hemisphere in participants with dyslexia. Note, however, that there is also some evidence of generally reduced interhemispheric alpha in the central-parietal cortex (Dhar et al., 2010).

In line with the language-specific role of alpha oscillations, Drijvers and colleagues (2016) found an increased alpha frequency in response to audio-presented shortened relative to complete forms of words (e.g., yeshay for yesterday). It was theorised that the shortened words create higher auditory cognitive load resulting in increased alpha. Alpha oscillations also seem to be sensitive to and reflect a mechanism for the prediction of upcoming sensory input (Arnal & Giraud, 2012; Lewis et al., 2016), including predictions of upcoming linguistic information (Röhm et al., 2001). In that study, Röhm and colleagues asked

participants to read a number of sentences and recorded their EEG brain activity. It was shown that semantic processing of sentences during reading might load working memory resources, which is reflected in elevated alpha power (but see Terporten et al., 2019). Therefore, the alpha frequency can be an indirect marker of semantic processing during reading.

The power of the alpha frequency band has also been linked to selective attention processes, i.e., selection of objects that will be attended (Sauseng et al., 2005). In more detail, it was suggested that the lower power of alpha frequency reflects enhanced neural excitability that supports selective attention. This conclusion is based on previous reports that alpha power reduced significantly when participants were preparing to pay attention to the target item (de Pesters et al., 2016). Moreover, the magnitude of the reduction in the power of alpha has also been correlated with neural responses to the target (Gould et al., 2011; Wöstmann et al., 2019) and with improved behavioural performance during cognitive tasks (Thut et al., 2006).

There is growing evidence that alpha oscillations may play an active role in complex cognitive functions. For instance, it was shown recently that alpha activity could account for over 60% of inter-subject variability in perceptual learning (Freyer et al., 2013). In more detail, perceptual learning refers to training- and experience-related improvements in perceptual abilities (Fahle, 2005; Seitz & Dinse, 2007). For instance, Freyer et al. (2013) showed that alpha oscillations recorded over parietal electrodes shortly prior to task onset, as well as alpha frequency measured at central electrodes during the two-point discrimination task, were highly predictive of the learning outcome. Specifically, these alpha oscillations could explain approximately 64% of interindividual differences in the task performance improvement (i.e. learning). These findings implied that alpha oscillations could be descriptive of the degree of engagement of neuronal populations during learning processes.

Even more convincingly, in a recent study, Brickwedde et al. (2019) used neurofeedback to either enhance or reduce somatosensory alpha oscillations (i.e., alpha frequency measured over the somatosensory cortex, BA 7) and examined whether participants have different levels of perceptual learning depending on the feedback training goal. Participants who could successfully enhance their alpha power after neurofeedback training had higher perceptual learning. On the other hand, participants who were trained to decrease their alpha power showed no improvements in learning. Taken together, pre-learning alpha over the somatosensory cortex could account for 59% of interindividual variability in perceptual learning. In other words, it seems that a higher level of alpha is necessary for successful perceptual learning, and reduced alpha seems to block the learning process. Importantly, the results showed that other frequency bands (i.e., theta, beta, and gamma) could explain less than 10% of the learning variance. This finding once again emphasises the unique role of alpha oscillations in the learning process. Of note, there is also some evidence that participants with dyslexia show an altered pattern of brain activity over the right somatosensory cortex (Renvall et al., 2005), suggesting that apart from visual and phonological processing, dyslexia can also alter other sensory functions/areas. Therefore, a combination of the alpha frequency and somatosensory brain area could serve as a promising potential target for neurofeedback therapy in dyslexia (see below for details of neurofeedback therapy; Brickwedde et al., 2019).

Individual Alpha Frequencies (IAF)

One of the ways to measure interindividual variability in alpha oscillations is via the use of individual alpha peak frequency (IAF). The IAFs, sometimes referred to as individual alpha peak frequency or just alpha peak frequency, refers to the frequency of maximum power within the extended alpha range (Klimesch, 1999). Therefore, a standard method to detect an IAF in the EEG spectrum consists of finding the frequency at which the power

spectral density is maximal within the frequency range of 8-14 Hz (Klimesch, 1999; Kropotov, 2016). Inter-individual alpha peak variability (IAF) has been related to individual variability in various perceptual task performance (Cecere et al., 2015; Samaha & Postle, 2015) and cognitive task performance (Bornkessel et al., 2004; Klimesch et al., 2006). In other words, it was shown that individual variance in IAF could account for the differences observed in performance across participants in various perceptual and cognitive tasks. For instance, Bornkessel et al. (2004) is a great example of how IAF can be used to evaluate participant's cognitive performance. They asked participants to read ambiguous sentences (sentences that were composed to either deliver the message clearly or were ambiguous regarding "who did what") while their EEG brain activity was recorded. After the recording, the group was median-split into the high-IAF, and low-IAF subgroups and the data was analysed as a function of these subgroups. Particularly, the authors measured the event-related potentials of EEG (ERPs). An ERP represents recorded brain response to a sensory or cognitive event (in this example, the event being the sentences). As a result, the low-IAF group revealed a sustained ERP positivity when processing the ambiguous part of the sentence, and the high-IAF group did not. The sustained positivity in the low-IAF group could be viewed as enhanced neural activity that was necessary for the participants to perform the task. This means that the low-IAF group required more effort and neural resources to process ambiguous sentences. Therefore, it is possible that the low-IAF group had difficulty overcoming the ambiguity during reading, as revealed by the enhanced magnitude of the ambiguity effect in this group. Importantly, the group difference was observed only when the group was split based on IAF, but not when based on reading span, speed of processing, or accuracy of processing. The work by Bornkessel and colleagues, as well as other studies described below, provide solid evidence to support the theory that IAF

may be descriptive of a trait-like characteristic that may be useful to take into consideration in research.

Importantly, the heterogeneity and subtle inter-individual differences in IAFs may complicate the traditional definition of frequency bands (e.g., Klimesch et al., 2007). The alpha frequency was traditionally defined as an oscillatory brain activity observed within a certain relatively strict frequency range (8-14 Hz); however, the observed variances in IAF may suggest that such a strict definition may not be feasible. This becomes especially relevant when studying various patient groups (e.g., dyslexia, Parkinson's disorder, and ADHD) that may show significantly higher IAF variability relative to healthy controls (e.g., Arns et al., 2012).

Previous work used IAF as a baseline or a certain functional reference point to define all frequency bands of interest to account for these inter-individual differences (e.g., Babiloni et al., 2012). For instance, the delta frequency band was defined in a frequency range of IAF - (minus) 8 to IAF-6 Hz, theta as IAF-6 to IAF-4 Hz etc. This way, the authors could define frequency ranges that were specific for each individual participant and could also account for IAF variability.

Moreover, the alpha spectrum itself seems not to represent a unified pattern of activity; instead, it consists of at least three functionally independent segments. In other words, one could use the IAFs to further subdivide the alpha frequency range into three relatively independent components: lower-alpha (alpha 1), medium alpha (alpha 2) and higher alpha (alpha 3). For instance, Klimesch et al. (1998) found that alpha 1 might reflect phasic alertness, alpha 2 reflects expectancy, and alpha 3 reflects task performance. Furthermore, synchronization and desynchronization between these different components of alpha oscillations may lead to differences in cognitive states. For instance, desynchronization in alpha 1 and alpha 2 has been associated with processes of alertness and external attention,

whereas desynchronized alpha 3 is indicative of enhanced cognitive processing (Klimesch et al., 1998; Klimesch et al., 1999). To summarize, interindividual differences in alpha frequencies can be used as a reference point to define the frequency bands of interest, including the distinction within alpha frequency itself.

Beta

Beta oscillations are small and relatively fast oscillations (in the range of 13–30Hz) that are associated with a state of increased mental activity and focus of attention, including increased alertness or relaxed attentiveness (Baumeister et al., 2008). Previous findings suggest that beta oscillations originate in deep cortical layers (Bollimunta et al., 2008; Buffalo et al., 2011) and could involve pyramidal cells and fast-spiking interneurons (Lundqvist et al., 2011; Miller et al., 2018). Ketz and colleagues (2015) suggested that excitatory activity from the mediodorsal thalamus to the deep layers may generate beta-band activity (Miller et al., 2018).

Beta is related to sensorimotor processes (Kilavik et al., 2013), as well as a range of other mental functions including multisensory integration and attentional processes (Arnal & Giraud, 2012; Donner & Siegel, 2011). Important for the current thesis, the beta frequency could reflect the processing of sentences that are related to each other (i.e., semantically coherent) during reading comprehension (Lewis et al., 2016). It was shown that reading tasks reduce beta activity in the right parietal and occipital areas (Ackerman et al., 1995; Flynn et al., 1992). It was also demonstrated that beta oscillations are increased when one is required to withhold speech, which points to the role of this frequency band in the maintenance of motor memory, specifically in the maintenance of planned verbal actions (Engel & Fries, 2010; Piai et al., 2015).

Recently, it has been suggested that beta activity is not a unitary process and can be further subdivided into smaller components. For instance, reward feedback studies identified

two distinct beta components: a high beta component (20–35 Hz; Marco-Pallares et al., 2008) and low beta component (12–20 Hz; Yaple et al., 2018). Specifically, the high beta is observed in response to unexpected events (i.e., an unexpected, low probability gain; HajiHosseini et al., 2012). On the contrary, the low beta frequency was observed in response to the lack of expected gains (Yaple et al., 2018).

Beta oscillations are also good predictors of interindividual differences in learning in general and in motor task learning in particular. It was shown previously that beta oscillations are suppressed during motor tasks, but they reappear once the motor task is over (Pfurtscheller et al., 1998; Pfurtscheller & Lopes Da Silva, 1999; Salmelin & Hari, 1994; Stancak & Pfurtscheller, 1995). In a recent study, Espenhahn et al. (2019) tested whether beta oscillations recorded over the sensorimotor cortex at rest and during motor activities could explain and account for individual differences in the acquisition of a motor task (i.e., wrist flexion/extension tracking task). They found that beta power during movement could explain a significant portion of the variability in learning. Specifically, a smaller magnitude of movement-related beta desynchronization in the ipsilateral sensorimotor cortex that is measured before the onset of training can predict improved subsequent motor performance. To conclude, these results show that beta oscillations can be reliable predictors of learning success (Espenhahn et al., 2019).

Gamma

Gamma oscillations are very fast EEG activity (30–100 Hz). Gamma oscillations are linked to intensely focused attention and to the binding of information across different brain areas (Goddard et al., 2012). Specifically, synchronous gamma activity across widely distributed collections of neurons may integrate information from different brain regions into "a coherent cognitive percept" (Engel & Singer, 2001). Additionally, Engel and Singer proposed that gamma activity might also be descriptive of such states as arousal, sensory

awareness, and synchronization between different populations of neurons (Aoki et al., 1999; Keil et al., 1999; Tallon-Baudry et al., 1998). This is particularly relevant for the current thesis because dyslexia is characterized by difficulties in communication between different brain regions involved in the language networks in general and reading specifically (e.g., integration of speech sounds and visual letters; van Atteveldt et al., 2004).

Cortical gamma was observed in various tasks, including auditory discrimination (Joliot et al., 1994), somatosensory discrimination (Sauvé, 1999), working memory (Tallon-Baudry et al., 1998) and sensory-motor processing (Aoki et al., 1999). Important for the current thesis, gamma power has been shown during working memory tasks (Pesaran et al., 2002) and learning tasks (Bauer et al., 2007). Previous studies recorded intracranial EEG gamma activity over Broca's area of participants with dyslexia and found that the strength of this measured activity is associated with participants' performance on reading of pseudowords (Flinker et al., 2015). Furthermore, participants with dyslexia have lower gamma oscillations in the left hemisphere during phonological processing (Lehongre et al., 2013), suggesting that gamma frequency could be used to assess the success of phonemic encoding in dyslexia (Lehongre et al., 2011). Additionally, Benasich and colleagues (2008) suggested that resting-state frontal gamma power was predictive of language skills. For instance, researchers showed that children with language development difficulties also had significantly lower gamma over frontal regions relative to matched control with no risk of language development difficulties. Therefore, adequate gamma frequency over frontal regions could also be a marker of successful linguistic development.

It should be noted that there is also some controversy in the research community regarding the adequacy of measuring gamma activity from scalp electrodes (i.e., non-invasively). Specifically, some authors argue that gamma frequency measured from scalp electrodes could

be contaminated by muscle-related artifacts (Muthukumaraswamy, 2013). Therefore, the results of gamma frequency analysis should be examined carefully.

Measurements of Oscillatory Activity

In addition to frequency band classification, oscillatory neural activity can also be categorized into event-related activations (as mentioned above) as well as spontaneous (i.e., resting-state; Delorme & Makeig, 2004). In more detail, resting-state recordings are made when participants are in a state of quiet wakefulness, not performing any particular overt task and not receiving any additional external stimulation. Recording of brain activity "at rest", without relation to any specific tasks has attracted much attention over the last several decades and has been shown to provide meaningful information about brain function (Busch et al., 2009; Klimesch et al., 2007). In more detail, it was suggested that the brain does not merely passively respond to incoming information but that it can produce meaningful neuronal outputs even in the absence of external sensory or any other kind of input (Singer, 2013). For instance, it has been shown repeatedly that neuronal response to incoming stimuli is greatly influenced by the brain's condition before the onset of a stimulus. This was shown in various perceptual and motor tasks (Busch et al., 2009; Drewes & VanRullen, 2011).

In contrast to resting-state, event-related responses are elicited in response to the external stimulus, such as stimulus presentation during a visual search or motor task (Luck, 2005). Importantly, event-related recordings can also be made in relation to some internal process that can be marked in terms of a temporal onset, such as purposeful mental imagery. Therefore, it is important to look not only at event-related (or stimulus-driven) activity but also at resting state or baseline oscillatory patterns. There is converging evidence about the involvement of event-related oscillations as well as resting-state activations in different cognitive operations (Busch et al., 2006; Gruber et al., 2008). Important for the current thesis,

there are consistent attempts to link event-related and resting-state neural oscillations to specific disorders.

EEG Activity in Dyslexia

Oscillatory EEG rhythms can inform about many underlying brain pathologies, which has been shown to be the case in dyslexia. For examples, Arns et al. (2007) identified a number of EEG time-frequency anomalies that correlated with poor language task performance in a group of participants with dyslexia. The anomalies included reduction of the power of theta and delta bands over frontal and right temporal regions, as well as increased beta amplitude. As discussed above, the deviant pattern of activity over the frontal regions in dyslexia may reflect poorer cognitive control and suppression of task-irrelevant information in this group, which could translate into inefficient language task performance.

Another measure of interest in the investigation of dyslexia is EEG coherence. Coherence measures the degree of similarity in the EEG activity of different scalp or brain sources. It can signal the degree of functional connectivity between different brain regions and, as such, may correlate with performance on various cognitive tasks (Shaw, 1981). For instance, measures of EEG coherence in different frequency bands (delta, theta, beta and alpha) show a positive correlation with behavioural performance on phoneme deletion, rapid naming letters and spelling tasks (Arns et al., 2007). In other words, better functional connectivity is associated with improved performance on dyslexia-specific behavioural tasks. This line of reasoning is also consistent with previous neuroimaging studies (e.g., PET, discussed above) that found reduced connectivity between various brain regions in dyslexia that was also associated with hindered performance on cognitive tasks (e.g., Horwitz et al., 1998). In other words, different brain regions involved in the language network need to communicate to support reading and other behavioural tasks important for dyslexia (e.g.,

phoneme deletion, spelling tasks). The strength of this communication within the language network seems to be hindered in people with dyslexia.

Fadzal and colleagues (2012) recorded EEG activity in dyslexia and control groups in a relaxed state and also while participants were writing. The authors found enhanced beta activity in dyslexia relative to typically developing children during writing at four electrodes (C3, C4, P3 and P4). It appears that children with dyslexia consume more energy during writing tasks, thus, showing more enhanced activity of beta waves (Fadzal et al., 2012). As also discussed above, beta oscillations were shown to be reduced or disappear during motor tasks (Salmelin & Hari, 1994; Stancák & Pfurtscheller, 1995). As beta oscillations during motor tasks are less reduced in participants with dyslexia, this, once again, may imply problems with cognitive control and inhibition in this disorder.

In a recent study, Papagiannopoulou and Lagopoulos (2016) examined EEG power spectra measured in children with dyslexia and controls. Results indicated disorder-related differences in spontaneous oscillatory activity in different EEG bands (i.e., delta, theta, alpha, and beta). In more detail, participants with dyslexia showed increased theta power in frontal brain regions (Broca's area) and overall increased theta power in the left hemisphere. The increased theta band (especially over the frontal regions) signals an abnormal resting-state function in dyslexia that could be observed before the formal reading instructions. The participants with dyslexia also had significantly increased delta and theta activity in Broca's area relative to Wernicke's area. These results replicated previous findings on the lack of coherence between different reading- and speech-related brain areas in dyslexia. Importantly, healthy controls did not reveal this asymmetry between the two areas.

Consistently reduced and diffused interhemispheric coherence of alpha activity in the central-parietal cortex is reported (Dhar et al., 2010). Furthermore, some researchers reported dyslexia-specific lower gamma oscillations in the left hemisphere during phonological

processing (Lehongre et al., 2013) and reading-related decreased beta in the right parietal and occipital areas (Ackerman et al., 1995; Flynn et al., 1992). Although examination of EEG can provide only limited information about the underlying neuroanatomy of dyslexia, there is still an observable, recurrent pattern of left hemisphere frontal and occipitotemporal deviations in participants with dyslexia. Note, however, that the previous EEG studies were not always consistent in their findings due to differences in methodology, sample sizes and tasks used (Arns et al., 2007; Fadzal et al., 2012; Papagiannopoulou & Lagopoulos, 2016). Therefore, the current dissertation accounts for these limitations when examining the neurophysiological correlates/markers of dyslexia. More specifically, and as will also be discussed exhaustively in the "Current thesis" subsection, given the variability in approaches and findings in the previous literature, the current work intended to identify which, if any, frequency bands and electrode site activity seen in children with dyslexia may deviate from the norm. This baseline measurement was necessary to establish a robust baseline that the subsequent measurements will be compared against (see below for more details).

Neurofeedback and its Efficacy

Electroencephalography (EEG) has a very high temporal resolution with millisecond precision. The EEG information about specific and consistent brain activity in various disorders can also be used for assessment of therapy outcome and as part of the therapy itself. For assessment, researchers have long used EEG brain activity to measure the success of an intervention, therapy, or training program for dyslexia. For example, Gonzalez and colleagues (2016) measured ERPs in response to written words before and after behavioural training to match letters and sound. Results indicated enhanced negativity approximately 200 ms after stimulus onset (i.e., N170) in response to words in participants with dyslexia relative to control. The N170 is an ERP marker that reflects the neural processing of faces, highly familiar objects or words (Rossion et al., 2003). Participants who were successful in the

training showed a reduced N170 post-training relative to before the training. In contrast, those participants who were not successful in the training program showed no such reduction.

Apart from the event-related potentials, there is convincing evidence that dyslexia is also characterized by alterations in different frequencies of brain activity. For instance, Fronceca and colleagues (2006) measured EEG activity in 36 children with reading difficulties and a matched group of healthy controls. As a result, it was shown that the dyslexia group showed higher absolute power values of the delta, theta and alpha 1 bands, and lower relative power values of alpha 2 frequency band at the majority of electrodes. Importantly, the authors could also show that the values of alpha 2 correlated with the students' performance on the Wechsler Intelligence Scale: verbal performance and total IQ score. In other words, this study demonstrated that EEG measurements could be linked to specific, dyslexia-related psychological parameters (Fonseca et al., 2006). Taken together, these findings demonstrate that EEG could be used as an assessment tool for the outcome of behavioural therapy.

EEG information can also be used for neurofeedback therapy. Unlike some other physiological and psychological states (e.g., emotions, anxiety), participants cannot be aware of their brain processes and neuronal activations. However, EEG neurofeedback allows participants to experience proxies of brain electrical activity in real-time via a computer-brain interface, in a manner that allows them to train and gradually improve brain function (Sherlin et al., 2011).

Neurofeedback has a relatively long history of development and evolution (Foster & Drago, 2009). Thorndike (1898) first introduced the idea of operant conditioning by showing that responses that produce desirable relative to undesirable effects become more likely to occur again. This idea was further refined by Skinner (1948), who showed in numerous experiments that one could use reward and punishment to increase or decrease certain

behaviours. A “reward” is the presentation of a positive event that follows the desired behaviour, such as the presentation of food, tones, etc. According to operant conditioning, any event that increases the likelihood that a response will occur is considered a reinforcer.

Durup and Fessard (1935) first demonstrated that brain activity could also be a subject to operant conditioning principles (see also Loomis et al., 1936). Loomis and colleagues (1936) let participants sit in a dark room and listen to an auditory tone that was presented simultaneously with a light stimulus. Since Berger (1929), it was shown that the presentation of a light in a dark room naturally suppresses alpha in the occipital part of the brain. Interestingly, repeated joint presentation of the tone and light resulted in the tone eliciting alpha suppression even when the light was no longer being presented (Loomis et al., 1936). Following the rules of classical conditioning, the authors also reported the extinction effect, i.e., the conditioned response (alpha suppression) disappeared if the auditory signal was no longer paired with the light stimulus.

Jasper and Shagas (1941) continued studying conditioning of brain activity (i.e., alpha suppression) and demonstrated that it took only 10 joint repetitions of the conditioned and unconditioned stimuli in order for the conditioned stimuli to show the same or even greater level of alpha-blocking relative to unconditioned stimuli. Furthermore, Jasper and Shagass hypothesized that other stimuli besides light could also lead to alpha-blocking. To support this, they conducted an experiment where participants had to say subvocally (internally) ‘‘block’’ and press a button, which switched on a light. Subsequently, participants had to subvocally say ‘‘stop’’ and were asked to stop pressing the button. As a result, the subvocal commands (block, stop) became associated with alpha-blocking, and participants could essentially control their brain activity as measured by EEG (Jasper & Shagass, 1941b).

Currently, neurofeedback therapy uses a combination of the principles of operant conditioning and electrophysiology to induce desired brain states and improve participants’

behavioural symptoms (i.e., to facilitate self-regulation of brain function, Sherlin et al., 2011; Thibault et al., 2015). In a typical neurofeedback session, EEG activity of a participant is measured and displayed into psychologically meaningful feedback. In more detail, the feedback is presented as a part of participants' activity (watching a moving, playing a video game, or when a participant receives some other visual, auditory or tactile feedback). For example, the amount of white noise on a monitor while watching a movie, the intensity of tactile feedback, or the speed of a video game could depend on participants' measured EEG. In simplistic terms, when specific brain activity at a certain electrode falls within the desired normative range, participants are given a reward (such as a character moving in a video game or being able to watch a movie of interest without any distortion). Different reward algorithms might be chosen by the therapist, usually based on some computational mix of the range of transformed Fourier time-frequency EEG values obtained during neurofeedback. Positive rewards may be given incrementally as one or more of the computed values moves towards the desired range, such as incremental brightening of a computer screen. Alternatively, a negative reward is delivered as the computed values move away from the desired range, such as incremental darkening of the screen.

In order to know what EEG activity to provide positive or negative rewards for, the clinician must create a protocol (or goal) for the therapy. That is, they must choose a specific EEG marker (or several) and then set a target for that marker. One possibility is to either enhance or reduce power in a specific frequency range and certain brain region based on findings in the literature (e.g., reduce beta at C3, reduce 12-15Hz at Cz; Gunkelman, & Johnstone, 2005). Standardized approaches, such as this, are more rigid because they cannot take into account possible individual differences in brain function of each participant in the therapy. On the other hand, these approaches are quicker, as only a few specific electrodes are required and are much cheaper because no pre-testing or additional software is required.

Another possibility is to train EEG activity in brain regions and frequencies of interest towards “normative functioning”. In this case, the norm is defined via a statistical comparison of the patient’s EEG activity to a normative database of healthy controls. Note that this approach is more demanding and costly, as it requires an additional EEG testing prior to the therapy onset and that the clinician has purchased and is trained to use the specific software. Therefore, the majority of research that tested the efficacy of neurofeedback in dyslexia used the former, more rigid approach.

For example, as mentioned above, Fadzal et al., (2012) found enhanced beta at C3, C4, P3 and P4 electrodes in dyslexia. Therefore, it may be beneficial to use neurofeedback to train participants with dyslexia to reduce beta in those areas. Neurofeedback can also target the sensorimotor rhythm, which is an oscillatory rhythm found over the sensorimotor cortex in the range of 13 to 15 Hz, slow cortical potentials, which represent slow (usually less than 1Hz) negative shift recorded from the cortex, most prominently at the vertex (Cz), as well as beta and theta activities (He et al., 2019).

An increase in the power of the sensorimotor rhythm correlates with the reduction of hyperactivity/impulsivity symptoms in ADHD (Mohammadi et al., 2015). In more detail, these authors developed a neurofeedback training that consisted of two phases, each involving 15 x 45min sessions. In phase 1, participants learned to enhance sensorimotor rhythm (12-15 Hz) and reduce theta activity (4-8 Hz) at the C4 electrode. Subsequently, in phase 2, they were trained to increase beta (15-18 Hz) and reduce theta activity at C3. Participants’ behavioural performance was measured via the attention endurance test while their parents filled out the ADHD rating scale. As a result, there was a substantial improvement in the participants’ attention scores. Additionally, neurofeedback-based sensorimotor rhythm modulation was shown to benefit participants with learning difficulties

(Hashemian & Hashemian, 2015), epilepsy (Sterman & Egner, 2006), and autism (Pineda et al., 2008).

It was shown that 20 sessions of neurofeedback are required to have a noticeable therapeutic effect (Rogala et al., 2016). Indeed, neurofeedback has been shown to be effective in the treatment of various disorders, including traumatic brain injury (Lucas, 2015), depression (Koberda, 2014), anxiety (Koberda, 2014; Lambos & Williams, 2015a), addiction (Cannon et al., 2008), seizures (Frey, 2015; Lucas, 2015), attention-deficit/hyperactivity disorder (Decker et al., 2015; Koberda, 2014), autism (Koberda et al., 2012), cognitive dysfunction (Koberda, 2014; Lambos & Williams, 2015b), and cerebrovascular accident (Koberda, 2014).

Quantitative Electroencephalography (qEEG)

QEEG is normally obtained from the scalp as a signal involving fluctuations in voltage over time and then converted to a digital format and amplified so that a stream of digital values representing the temporal flow (time-domain) of the EEG signal can be processed by a computer and subjected to a numerical analysis of one form or another.

One of the possible numerical analyses is a fast Fourier transform. The fast Fourier transform is a mathematical process whereby digital EEG is shifted from the time to frequency domain (Akin, 2002). Other numerical analyses of the recorded EEG data include coherence analysis, source localization, calculation of the theta to beta ratio and many more (Luck & Kappenman, 2011). Furthermore, the qEEG processed data can then be z-transformed, which allows an assessment of whether any of the recordings are significantly different from the norm in any of the frequency bands of interest. It allows for comparison of the recorded participant's EEG to this large sample, including coherence as well as power and phase shifts (Schmid et al., 1985).

The development of advanced qEEG technology in combination with the emergence of large normative databases opened the door for the application of qEEG for treatment purposes in patients with psychological disorders. Coburn et al. (2006) highlighted the effectiveness of qEEG as a clinical laboratory test used to aid in diagnosing, especially with learning, mood, and dementing disorders. These authors provided a broad overview of studies that were capable of successfully classify dyslexia and learning disorders by means of patients' EEG recordings (Ahn et al., 1980; Lubar et al., 1985).

The qEEG can also aid the selection of the right therapy-related parameters (Arns et al., 2012). Specifically, comparing the activity of a clinical population against a normative database in various brain regions and across different frequency bands can help identify the brain areas in the clinical group that require therapeutic interventions. Subsequently, rather than relying on standardized training protocols of neurofeedback therapy (such as sensorimotor rhythm training described above), clinicians can use the qEEG to target those areas that are abnormal when compared against a normative database. This allows for the creation of an individualized neurofeedback protocol tailored specifically to the participant's deviant oscillatory patterns.

Given that neurofeedback could be an effective non-pharmacological alternative in various disorders, more precise and individualized selection of brain areas that can be trained during the neurofeedback therapy could be particularly important (Enriquez-Geppert et al., 2019). Previous studies contrasted the outcomes of neurofeedback and pharmacological treatment methods and observed comparable results of the two therapies (Arns et al., 2009). This suggests that neurofeedback can ameliorate symptoms of different disorders with clear neurological markers. The most important question for the purpose of the current work is if neurofeedback can also be helpful for children with dyslexia.

Neurofeedback in Dyslexia

After the detailed introduction to the individual frequency bands and oscillatory frequency abnormalities in dyslexia, as well as the different brain areas implicated in dysfunctions seen in this disorder, it could be potentially possible to modulate the oscillatory brain activity linked to dysfunctional brain areas to alleviate behavioural symptoms of dyslexia by normalizing its neural correlates. Specifically, as the dysfunction in the areas discussed above has been implicated in several of the behavioural symptoms (such as phonological encoding, reading and spelling abilities), or simply implicated in the language network, training oscillatory activity in these brain regions could be a promising treatment in dyslexia.

Neurofeedback had been used to treat dyslexia previously. For instance, Raesi et al. (2016) worked with a small group of four boys with dyslexia (8-12 years old) who received 20, 30-minute neurofeedback sessions (conducted three times a week). As dyslexia was found to show a significant dyslexia-specific increase of delta and theta in the frontal and temporal brain regions (Arns et al., 2007), as well as because there was a reduction of beta power in the temporal region (Norman & Walker, 2006), the goal of the therapy was to "reverse" these abnormalities and train participants to reduce their theta and delta waves at a frontal region (F7) and to increase their beta waves at a temporal (T3) region. The results revealed significant improvements in reading accuracy and spelling (but not reading speed) after 20 neurofeedback sessions. Existing research suggested that dyslexia-related increase of theta is an indicator of attentional dysfunction that hinders reading performance. This was concluded because increased theta wave is linked to reduced attention to and engagement with the task (Ackerman et al., 1995; Rippon & Brunswick, 2000). Therefore, the results by Raesi et al. (2016) demonstrated that neurofeedback-related increase in attentional capabilities as

achieved via trained reduction of the power of theta and delta waves improved reading and writing skills.

Mosanezhad and Nazari (2013) reported similar findings after using neurofeedback to treat six children (8-10 years old) with reading "disorders", which included any difficulties with reading and not necessarily just dyslexia. The children were trained in twenty 30-minutes sessions and were taught to increase beta activity and decrease delta and theta activities. Results indicated improvements in behavioural measures of attention and working memory in all participants but no changes in the targeted frequency bands (delta, theta, and beta) in the EEG.

In a different study, Au et al. (2014) used neurofeedback to treat dyslexia in four Chinese children with dyslexia. These children participated in ten sessions of beta enhancement and theta suppression neurofeedback training in the sensorimotor cortex. Additionally, the authors collected neurophysiological measures, neuropsychological assessments, and parental reports before and after the neurofeedback training. Neurofeedback training reduced the theta-to-beta ratios in all participants and improved auditory vigilance and phonological awareness.

Breteler et al. (2010) randomly split 19 children with dyslexia into a therapy group (10 participants) that received neurofeedback treatment and a control group (9 participants). Prior to the therapy, the therapy group's frequency bands and coherence were measured at several frontal and temporal electrode sites (T3, T4, T6, FC7, FC3). The authors identified those electrodes that showed activity that was 1.5 z-scores above or below gender and age-matched non-dyslexic controls. Subsequently, only if there was an abnormal activation pattern detected at the corresponding site, the authors trained the delta oscillations at electrode T6, coherence in the alpha- and/or beta band at F7–FC3 or F7–C3 and coherence in all frequencies at T3–T4 in the therapy group. As a result, the therapy group showed

improved performance in spelling but no significant improvement in reading. In line with an absent improvement in reading, there were no changes in the EEG power and coherence over frontocentral electrodes, but there was a significant increase of alpha coherence, as a potential correlate of enhanced attentional processes that could be responsible for improved spelling performance.

Fernandez and colleagues (2003) administered neurofeedback to a group of 10 children (split randomly into the therapy and control groups) with a learning disorder that was not specific to but included reading difficulties. In this case, the training site was chosen individually for each participant. Specifically, two to three EEG recordings for each participant before the onset of the therapy were collected to locate the site with the most abnormal z-score value of the theta/alpha ratio. Subsequently, the individualized sites were identified and targeted for the training. After 20 training sessions (30 minutes each over 10-12 weeks), the experimental group showed significant improvements in total IQ and ADHD scores when compared to the control participants. Note that the control group showed no improvements or any changes in general. After two years, the same sample was tested again (see Becerra et al., 2006) and 4 out of 5 participants in the experimental group had "overcome" their disability, and participants in the control group remained unchanged.

Walker and Norman (2006) conducted neurofeedback training with 12 dyslexia case studies (7-15 years old) with varying degrees of reading difficulties (1-3 grades difference). The authors conducted 30 to 40 sessions (10 minutes each). The goal of the treatment was to train the participants with dyslexia to reduce any abnormal activities that were detected during an EEG session before the therapy onset, and the sites and frequency bands were again selected individually. Additionally, the participants were trained to increase 16-18 Hz oscillations at T3 (left mid-temporal area) because this brain area was linked to word-non word discrimination (Binder & Price, 2002; Walker & Norman, 2006). As a result, there was

an improved reading effect shown in all participants. Specifically, the authors reported that each of the 12 participants showed significant improvements after 30 to 35 sessions.

In more recent work, Li and Chen (2017) used neurofeedback on a group of 40 participants with dyslexia (20 in the test and 20 in the control group). There were a total of 20 sessions (30 minutes each, three times per week). Similar to the other studies described above, the therapy was designed to strengthen beta waves (between 15 and 18 Hz) in the left temporal brain region (T3), as well as to also suppress power of the delta waves (between 1 and 4 Hz) and theta waves (between 4 and 8 Hz) in this brain region. The results revealed reduced levels of aggression during reading in the neurofeedback group.

As can be seen from the discussed studies, there are definitely some signs of a positive effect of neurofeedback for the treatment of dyslexia. To summarize briefly, previous research showed that neurofeedback resulted in significant improvements in reading and/ or writing performance in dyslexia (Raesi et al., 2016, Walker & Norman, 2006), improved working memory and attention (Mosanezhad & Nazari, 2013), and improved auditory vigilance and phonological awareness (Au et al., 2014). Similarly, it was shown that neurofeedback facilitated spelling, but not reading task performance (Breteler et al., 2010), improved total IQ and ADHD scores (Fernandez et al., 2003), as well as reduced the level of aggression in dyslexia (Li & Chen, 2017). Nevertheless, this form of treatment is not yet evidence-based. Specifically, previous studies suffer from some serious limitations that preclude the possibility of having any definite conclusions. This could potentially be linked to several factors. As discussed previously in the chapter, there are many discrepancies in the exact location of dysfunction seen in the brain for dyslexia. To make matters even more complicated, some of these dysfunctions are linked to poor reading rather than dyslexia per se (as the same “dysfunction” is found when participants with dyslexia are matched to controls by reading ability rather than age-matched). Also, as mentioned above, dyslexia commonly

presents with subtypes and researchers have not agreed upon the best way to cluster and identify these subtypes. Therefore, a standardized protocol, as many of the studies above have attempted, may work on some subtypes and not have any effect on others, which could be a confounding variable.

One large disadvantage of previous dyslexia studies is related to design, including sample size and sample selection. Relatively few studies tested more than 5-10 participants, which could be too low to draw any firm conclusions. The small sample size reduces the power of the study even further, given that these studies did not take into account potential dyslexia subtypes (Ramus et al., 2018)(Ramus et al., 2018). Additionally, many studies did not even test that participants had a clear dyslexia diagnosis (Becerra et al., 2006; Fernández et al., 2003) and, the test groups often included participants with multiple symptoms and comorbid diagnoses, and with and without concurrent use of medication. Therefore, it can be difficult to generalize the findings to other dyslexia samples.

Testing protocols were also not consistent in previous studies (even within a single study, see Walker & Norman, 2006), including 20 to 50 training sessions, each lasting from 10 to 50 minutes. Additionally, many studies do not include a clear description of the types of tests and criteria when reporting positive outcomes of neurofeedback, that is, it is not clear what tests were conducted to assess the reported "improvements" in reading performance. Therefore, although neurofeedback overall has strong support in other domains such as reducing symptoms of anxiety, ADHD, insomnia, and other dysfunctions, the translation of this to the reduction in dyslexia symptoms has not yet been confirmed. Therefore, future studies should consider previous limitations and study this question further.

Current Thesis (Questions and Hypotheses)

Therefore, the goal of the current thesis was three-fold: The first study (Study 1) was intended to identify potential neural correlates of dyslexia as the research in this area has

resulted in mixed findings. Specifically, previous studies found reduced theta and delta bands over frontal and right temporal regions, (Arns et al., 2007); increased theta power in frontal brain regions, (Papagiannopoulou & Lagopoulos, 2016); and enhanced beta activity at central and parietal regions, (Fadzal et al., 2012). Therefore, in Study 1, I was interested in any potential dyslexia-related alterations in brain activity. The frequency bands of interest, as well as brain regions of interest, were set very broadly: low, medium, and high (correspondingly, alpha1, alpha2, and alpha3), as well as delta, theta, beta1, beta2, and gamma bands across four electrode regions (frontal (Fp1, Fp2, F7, F3, Fz, F4, F8), temporal (T3, T4, T5, T6), parietal-occipital (P3, Pz, P4, O1, O2), and central (C3, Cz, C4)).

Study 1 examined the qEEG brain activity in a relatively large sample of participants with dyslexia and compared their neurophysiological characteristics to a gender- and an age-matched group of healthy controls (N total = 94). Furthermore, I took extra care to only include participants with the pronounced phonological dysfunction of the disorder (Castles & Coltheart, 1993). This was done to assure that all participants belonged to the same subtype, thus reducing the potential dilution of findings due to the sample containing various subtypes of dyslexia (Ramus et al., 2018). The phonological subtype was selected for several important reasons. First, difficulties with phonological processing is the core symptom in the phonological theory of dyslexia, but also, phonological processing plays an important role in many dyslexia theories such as the rapid auditory processing theory, magnocellular theory, and cerebellar hypothesis. Furthermore, it was shown that patients with phonological dyslexia have difficulties with sublexical procedures (Patterson, 1995; Warrington & Shallice, 1980). Given that most English words involve sub-lexical processing and participants in the current work are all native English speakers living in Australia, identifying phonological dyslexia is the most straightforward choice regarding the subtype of interest. To summarize, the

phonological subtype was selected in the current work because it is the most evidence-based and classification-easy subtype of dyslexia.

An important decision in the current work was to measure spectral values relative to individual alpha peak frequency (IAF). In more detail, all individual alpha frequencies were defined with respect to IAFs (e.g., Babiloni et al., 2012; see also the IAF section above). This was done because the heterogeneity in IAFs could also result in inconsistent and skewed individual frequency band definitions. In other words, inflexible frequency ranges may not capture the inter-individual differences across participants (Babiloni et al., 2012). Finally, it was also ensured that the participants were all taking part in the same remedial extra-curricular tutoring to help account for potential socio-economic or teaching differences. Therefore, the current work had a carefully selected, homogeneous sample of participants with dyslexia (both in terms of phonological subtype and in terms of homogeneity in remedial training) and a flexible selection of frequency bands of interest.

This review gives rise to several tenable hypotheses that are tested in Study 1. These are: (1) reduced alpha power in participants with dyslexia at parietal, occipital, and temporal brain areas (Babilone et al., 2012), (2) increased theta and delta activity in the frontal brain region (Arns et al., 2007). One of the frontal regions that is related to the left hemisphere neural language network is Broca's area (Kennison, 2017), which has been shown to be active during phonological tasks (Goucha & Friederici, 2015; Rumsey et al., 1992). Finally, there is also some evidence that gamma oscillations recorded intracranially at Broca's area correlate positively with performance on reading of pseudowords (Flinker et al., 2015). Therefore, it was expected to find reduced activity in dyslexia over frontal electrodes in gamma frequency (Flinker et al., 2015). Additionally, as Broca's area is a left hemisphere structure, I expected to find a dyslexia-specific (increased, decreased) pattern of activity in the left hemisphere electrodes. I also expected to find increased slow theta and delta activity

in the right temporal electrodes, as well as increased beta activity in these electrodes in participants with dyslexia relative to control (as in Arns, Peters, Breteler, & Verhoeven, 2007). Finally, participants with dyslexia were expected to show (3) reduced performance in all reading, phonological and spelling tasks.

Second, Study 2 investigated the role of neurofeedback therapy for the treatment of behavioural symptoms and neural markers of dyslexia. A qEEG guided LORETA z-score neurofeedback training protocol was used (see Methods section for more details; Cannon et al., 2006; Collura et al., 2010) to account for previous inconsistencies in experimental designs and neurofeedback protocols. In short, LORETA refers to an EEG-based source localization technique, which allows directing neurofeedback training to a specific subcortical part of the brain. Additionally, the LORETA approach allows for a real-time approximation of activity (coherence, asymmetry and amplitude) in participants' specific brain regions. In contrast to the standardized and rigid forms of therapy, LORETA turns neurofeedback into a more individualized type of therapy, as it can incorporate information about patient's specific neural deviations from the norm into the neurofeedback training protocol.

Note that the selection of individual brain regions for the purpose of the therapy requires a mechanism that would identify abnormalities in the measured signal. One way to detect these abnormalities is to use statistical comparisons to normative databases. Specifically, measured EEG activity in each participant with dyslexia can be compared against a large sample of age- and gender-matched healthy participants that are grouped into a database. The goal of this comparison is to identify the parameters in the EEG of the participant with dyslexia that are deviant from those of the normative database. A convenient way to identify these deviances is the z-score distance of EEG activity in certain brain regions and/or frequency bands (Thatcher et al., 2015). The introduction of z-scores then makes it easy to select a threshold in a given neurofeedback session, as the goal became to

reinforce the given EEG measure. These changes significantly improved the quality and efficiency of neurofeedback (Simkin et al., 2014). Therefore, qEEG guided LORETA z-score neurofeedback is much more effective and efficient relative to standard neurofeedback protocols due to its individualized and precise approach (Budzynski et al., 2009).

It was hypothesized that (1) the participants with dyslexia that received the neurofeedback therapy would show reduced deviance in reading, spelling, and phonological performance scores after the therapy relative to prior to the therapy. Furthermore, it was expected that (2) those neural markers of dyslexia that were found to be deviant in Study 1, would show a reverse pattern of activity, i.e., would become closer to that of healthy, database controls.

Finally, the aim of Study 3 was to study the lasting effects of neurofeedback on the behavioural symptoms of phonological dyslexia (Marzbani et al., 2016). Specifically, it was tested whether the behavioural improvements of the therapy would be retained 3 months after the end of the treatment. In this study, participants from Studies 1 and 2 were re-invited to the clinic three months after the end of the therapy to track the progress of their behavioural performance on the same reading, spelling and phonological tests that were assessed in Studies 1 and 2. Therefore, it was expected that participants with dyslexia would either (1) preserve their therapy-related improvements (if found in Study 2) or would (2) show even better behavioural performance (Enriquez-Geppert et al., 2019). The idea behind the latter hypothesis is that participants may require time to be able to take advantage of the therapy-related changes in brain activity to acquire new skills at a faster rate after the end of the therapy.

The next chapter introduces the research methods relevant for the present thesis: it focuses on the psychological tests used to measure symptoms of developmental dyslexia, a

review of the databases used in the current thesis, general neurofeedback therapy methods, and a general overview of the procedure followed for this thesis.

Chapter 2. Methodology

Relevant Cognitive Neuroscience Methods

The current chapter introduces the research methods relevant for the present thesis: it focuses on the psychological tests used to measure symptoms of developmental dyslexia, a review of the databases used in the current thesis, general neurofeedback therapy methods, and a general overview of the procedure followed for this thesis.

Psychological Tests

Dyslexia research requires an adequate and standardized assessment of reading, phonological skills, semantic processing, spelling, and other language-related skills (Aaron & Berg, 1994; Floyd et al., 2007). For the studies described in the current thesis, a comprehensive test battery was repeatedly used to assess literacy, phonological skills, and text comprehension skills needed for reading development. Importantly, a provisional psychologist (under the supervision of a registered psychologist) additionally administered the same number of tests after experimental interventions to track the progress. Note also that the participant's group assignment (therapy, waiting list groups) was kept blind from the test administrator. The following tests were included in this battery.

Woodcock-Johnson III Tests of Achievement (WJ III ACH)

The Woodcock-Johnson III achievement subtests (McGrew & Woodcock, 2001) that were used in the current work were selected to assess basic reading skills:

a) Word Attack (test 13) subtest measures the ability to apply phoneme/grapheme knowledge to decode unfamiliar printed text. For instance, participants must pronounce pseudowords that are phonetically regular (e.g., gradly, vorse) aloud. The test ends following six consecutive incorrect responses.

b) Sound Awareness (test 21) measures the ability to understand and utilize the sounds within words (i.e., phonological awareness). For this purpose, with increasing

difficulty, participants are asked to assess different aspects of phonological awareness: rhyming, deletion (i.e., remove part of a word and say remaining part), substitution (change part of a word or word sound to create a new word) and reversal (reverse part of a word or word sounds to create a new word).

c) Letter-Word Identification (test 1) assesses oral word decoding skills. The test starts with easy tasks, and the difficulty gradually increases. Participants first have to identify letters, then name and read isolated words of increasing difficulty aloud from a list. The test ends when participants make six consecutive errors.

d) Reading fluency (test 2) measures participants' speed of semantic processing. Each participant has three minutes to read simple sentences and to agree or disagree with the statement by circling Yes or No to each. Sample item: "A cow is an animal".

e) The Spelling test (test 7) requires participants to spell orally presented words correctly. The difficulty of the task progresses with the span of the test, starting from the measurements of prewriting level abilities (e.g., drawing, tracing, writing single letters).

f) The Passage Comprehension test (test 9) examines participants' ability to read short passages silently as well as filling in a missing word in the passage (i.e., find and write down a fitting, missing word). Among other things, this part concentrates specifically on participants' comprehension and vocabulary skills. In other words, the passage comprehension test measures participants' adequate understanding of the text in the process of reading. Importantly, participants are intentionally limited in the number of times a certain text can be read to reduce the impact of decoding and fluency on task performance and provide all participants with equal conditions.

g) Spelling Sounds task (test 20) measures one's ability to translate spoken parts of non-words into graphemic units. In other words, the test measures how well a participant

can map a spoken non-word to its written form (i.e., phonologically mediated mapping of orthography).

It was shown that the WJ III ACH subtests have good median test-retest reliability when tested in the age group of 5 to 19 years old (> 0.8; see Schrank et al., 2015); strong inter-rater reliability of .93, and moderate internal structure validity (e.g., correlation $r = 0.65$ with the Wechsler Individual Achievement Test; see McGrew & Woodcock, 2001). Importantly for the purpose of the current work, WJ III achievement tests results can also be reliable predictors of reading disorders. For instance, it was shown that the reading task performance in WJ III is closely related to these participants' performance on phonological awareness and rapid automatized naming tasks (Mockler, 2004). Similarly, Abu-Hamour et al. (2012) showed that reading performance in WJ III could be predicted by using such cognitive task performance as phonological awareness, rapid automatized naming, general processing speed and working memory. Note that disturbances in phonological awareness, rapid automatized naming, general processing speed, and working memory are thought to be causal to dyslexia. Their results provide consistent evidence that WJ III achievement tests can explain variability in reading performance in individuals with reading disorders.

York Assessment of Reading for Comprehension Australian

The York Assessment of Reading for Comprehension (YARC) is a diagnostic reading assessment measure to assess pupils' reading and comprehension abilities (Colenbrander et al., 2017; Martin, 2011). Participants must read aloud two different sets of passages (fiction and non-fiction) in order to assess their reading abilities: reading accuracy and reading fluency. Additionally, participants answer a set of eight comprehension questions to examine their literal and inferential comprehension skills. The final score represents a total score for all eight questions.

The summated score of this measure was standardized on a large representative sample of Australian school children in 2011, in which 1100 male and female students (reception to year 7) across 44 schools took part in the study. It has moderate to high internal reliability ($\alpha = 0.63 – 0.86$) for reading comprehension. Additionally, a different sample of UK students was used to validate this measure and to assure that the YARC passage reading test could not be answered by using general knowledge or guessing. Concurrent validity (moderate to high; $r = 0.60 – 0.91$) was assessed via correlating students' (years 3, 5, 7 and 9) YARC results with the National Assessment Program: Literacy and Numeracy tests (NAPLAN; 2011). Finally, performance on YARC is also highly correlated with reading abilities in low-progress readers (Wheldall & Arakelian, 2016). Specifically, the authors found significant positive correlations ($r > 0.8$) of the YARC measures with Neale Analysis of Reading Ability (NARA) and different reading tasks in 78 poor readers. These findings show that the YARC is a reliable measure to assess participants' reading abilities.

Test of Word Reading Efficiency–Second Edition

The Test of Word Reading Efficiency–Second Edition (TOWRE-2; see Torgesen et al., 2011) was developed to examine a participant's phonemic decoding efficiency. In more detail, this task requires participants to pronounce printed phonemically regular words (Sight Word Efficiency) and non-words (e.g., pash, zug, scad; Phonemic Decoding Efficiency) and evaluates participants' accuracy and fluency of task performance. In both tests, participants are presented with a list of vertically printed words and non-words, and the task is to process as many words and non-words as possible within 45 seconds. Thus, these tests evaluate the two most important types of word reading skills. The TOWRE-2 has a reliability coefficient from 0.87 to above 0.90 (based on a sample of 1700 participants; Torgesen et al., 2011). Additionally, TOWRE-2 performance scores can be used to differentiate between healthy controls and individuals with learning disabilities (Tarar et al., 2015). Specifically, it was

shown that individuals with learning disabilities and speech-language disorders perform below the average on TOWRE-2. These results show that the test is sensitive to detect poor reading in participants with learning disabilities.

Normative Databases

Studies in the current thesis rely heavily on normative databases both during the neurofeedback therapy (Neuroguide database; Applied Neuroscience Laboratories) and for the control group comparison in Study 1 (HBI database; www.hbimed.com). Therefore, it is necessary to mention the rationale for using such databases (relative to in study control group comparisons), their validity, and use in other available material. I will also briefly describe the criteria for the measurement of adequacy of the databases used in the current work.

Normative databases are currently used in both research and in clinical applications. These databases are used as a statistical norm that can be used in comparison to various patient and/or therapy groups (Thatcher, 2010). The goal of any normative database is to ensure they are composed of a "healthy" (non-clinical) sample of the population that can be used as a control reference group. A wide range of neuroscience disciplines have specialized normative databases including, but not limited to, MRI, fMRI, and PET normative databases, nerve conduction velocity databases, genetic and motor development normative databases and, most importantly for the current work, EEG normative databases. These databases are often the result of collaborative efforts across many different institutions, which allows for greater cross-validation of the EEG recordings. Normative databases can reduce the cost of studies because no additional resources are necessary to compose a control group. This can also improve the power of the statistical analysis, as many more participants can be tested within the resources available (e.g. time, researchers, financial).

Across the scientific community, there are a set of fixed criteria to evaluate a database (Thatcher et al., 2003). When a database is developed, it is expected that the creators will

produce a thorough public report with information about the database. This report should include information on: (1) the inclusion/exclusion criteria for participants whose data will be included in the database, (2) psychometric evaluation to ensure high statistical validity and reliability, and (3) the cross-validation. The database should have a large enough sample size with an adequate number of cases to allow some analysis of demographic group differences (i.e., age groups, gender, socioeconomic status, geographical and/or ethnic background). Further, the database samples should be screened to ensure they are as normative or healthy as possible (e.g., no neurological or psychiatric disorders, no brain traumas, no pathologies in development etc.). Finally, a database should be used in a number of peer-reviewed publications focused on evaluating the properties of the database. These peer-reviewed publications are considered to be vital for database, as the high standards of the academic peer-review system would serve as a smart filter against the existence of sub-optimal databases that could harm both academic and clinical applications (Thatcher et al., 2003).

Usually, normative databases contain data of healthy individuals whose data will be compared against a test group of interest to the researcher. Additionally, some databases (e.g., Neuroguide) also provide an opportunity to compare an individual participant (e.g., dyslexia patient) against a "normal" population for therapy purposes. In this latter case, the underlying goal is to identify certain parameters in the tested individual that are deviant from those of the control group. This allows for statistical z-score comparison between the clinical data and the normative database and can inform the clinician or researcher about how much the clinical participant deviates from the norm. For example, as described in the qEEG section in the previous chapter, EEG data from a participant can be compared to EEG data from a normative database. It is thus possible to calculate z-scores statistical deviation in the recorded brain activity between the participant and the normative reference group. This can both aid clinical diagnosis and allow selection of abnormal brain activity to target for

neurofeedback therapy. The databases are not able to make diagnoses on their own. Instead, the results of such comparisons could be analyzed by an educated specialist who would use this information in combination with patients' symptomatology and previous clinical history to diagnose certain medical conditions (see also Thatcher, 2010).

Apart from the general requirements for all databases discussed above, EEG databases also have specific EEG-related parameters. For instance, it is advised to match the characteristics of amplifiers when comparing a normative database and patient's EEG (Simkin et al., 2014). Additionally, it is important that the EEG database followed accepted standards during data acquisition, artifact rejection phases, and data analysis phases (Collura, 2014). For the purpose of the current thesis, I used two EEG databases: Neuroguide and Human Brain Index (HBI) database. Both of these databases satisfy the strict criteria outlined above and are widely used in EEG research. In the next step, I will provide some examples of the use of the two databases in previous, peer-reviewed research.

Human Brain Index (HBI) Database

The data of control (i.e., non-dyslexia) participants in Study 1 of the current thesis were selected from the Human Brain Index (HBI; www.hbimed.com) normative database. This is a widely used and validated database that consists of 3000 EEG recordings collected from over 1000 healthy participants aged from 7 to 89 years (Markovska-Simoska & Pop-Jordanova, 2011). Importantly, this database contains recordings of EEG brain activity from healthy participants with confirmed absence of any head injuries, no psychological, neurological or psychiatric dysfunctions, as well as no developmental disorders and/or learning disabilities (i.e., typical mental and physical development). As it is such a large and well-compiled resource, it has been used in multiple studies as a healthy control comparison for research purposes (Markovska-Simoska & Pop-Jordanova, 2011; Markovska-Simoska & Pop-Jordanova, 2011; Ogrim et al., 2012; Pop-Jordanova et al., 2020; Ros et al., 2017;

Shamaeva et al., 2018). Finally, apart from the possibility of finding a well-matching control group, which is not always easy to do when testing a control sample from scratch, the use of the HBI database can additionally be financially prudent as well as save time and equipment resources.

Neuroguide

Neuroguide (Applied Neuroscience Laboratories) has a normative database that contains data and demographic information of 678 participants whose ages range from 2 months to 82 years old. Additionally, Neuroguide is software developed for the analyses of EEG power and connectivity measures. This database and software were used in Study 2 of the current thesis. It is widely used and accepted in both basic and applied EEG research settings and was used for the LORETA current source density analysis. Neuroguide allows for a normative database comparison of an individual patient and age-matched controls using EEG and LORETA current source density (Cannon et al., 2012).

Cannon and colleagues (2012) used Neuroguide to calculate the reliability of the LORETA current source density. The authors collected 4 minutes of EEG activity in eyes-closed and eyes-opened conditions in tested 19 participants two times (i.e., 2 identical recordings per participant) 30 days apart. The raw EEG data were analysed in Neuroguide by computing fast Fourier transform (i.e., computing frequency representation of data), power (the strength of activity in certain frequency bands), coherence (degree of similarity between two signals), and phase (part of an ongoing oscillation/cycle measured in 360 degrees or radians) for four frequency bands (delta, theta, alpha and beta) and LORETA current source density in eight regions of interest. As a result, the findings indicated a very good reproducibility for total absolute power and coherence across the two testing sessions. Additionally, LORETA current source density in Neuroguide had very good reliability with an average of 0.81 in the eyes-closed condition and 0.82 in the eyes-open condition. Finally,

activity measured across the eight regions showed good to very good agreement across time as well (Cannon et al., 2012). To summarise, Neuroguide is a reliable and effective tool to conduct research and to produce high-quality work (for more uses in peer-reviewed publications see also: Aldosari et al., 2018; Bell et al., 2019; Gerez et al., 2018; Groeneveld et al., 2019; Menolascino et al., 2017; Park et al., 2018).

Neurofeedback

In a typical neurofeedback session, participants have several electrodes (e.g., 19 if all electrodes are used, although the therapy can entail the use of a full cap to the use of single electrode placements) placed on the scalp while their brainwave activity is presented to them in the form of feedback (either visually, auditory, or even tactile) via a brain-computer interface. When the participant's oscillatory brain activity moves in the desired direction the clinician has chosen, a "reward" is then provided to the participant. The main purpose of the neurofeedback is to operant re-train brain electrical field patterns related to functions of interest. This training of brain activity is a relatively long-lasting process and can be thought of in terms of operant conditioning and procedural learning. By reacting to positive and negative feedback, participants re-train brain functions associated with the signals obtained, thus, potentially resulting in long-lasting effects after the end of neurofeedback training (Sherlin et al., 2011). The desired oscillatory activity is the "desired behaviour", feeding back this information in a measurable way allows for the subject to know what the desired behaviour is, and a "reward" is presented to allow for reconditioning their oscillatory activity. In line with this idea, it was shown very early after the first uses of EEG that blocking the alpha rhythm of the EEG (i.e., when alpha waves disappear after one concentrates on a stimulus) could be explained in terms of Pavlovian responses (Jasper & Shagass, 1941; Knott & Henry, 1941). Thus, it was shown that classical conditioning principles could also be applicable to such EEG concepts as alpha-blocking (see Chapter 1 for more detail).

LORETA Z-Score Neurofeedback

One drawback of early neurofeedback protocols that became apparent in the late 1990s after initial evaluations of this method in both research and therapeutical settings was the lack of specificity and uniform standards (Simkin et al., 2014; Thatcher et al., 2015). Therefore, the clinical applications of neurofeedback became difficult to research and replicate (Simkin et al., 2014). To overcome this limitation, Thatcher introduced the idea of z-transforming participants' recorded brain activity that would be compared against a normative database to simplify and standardize neurofeedback while also making it possible for the therapy to be individually tailored to the patient's specific dysfunction (Thatcher et al., 2015). A participant's oscillatory activity in an area of interest can be compared in real-time to the normative database and identify the statistically significant areas and frequencies that can be targeted to be "normalized". These changes significantly improved the quality and efficiency of neurofeedback (Simkin et al., 2014).

Another limitation of early neurofeedback methodology was the inability to link a patient's symptoms to a specific area of the patient's brain (Simkin et al., 2014). In more detail, during traditional neurofeedback therapy, clinicians and researchers would apply electrodes to the same scalp areas for all patients regardless of their symptoms. To overcome this limitation, a neurofeedback approach to therapy has become more specific and takes each patient's specific disorder and symptomology into account. This approach was supported by the introduction of z-scores to real-time three-dimensional EEG source localization (i.e., LORETA) that allowed localization of disorder-specific brain regions that could be targeted and subsequently trained via neurofeedback.

LORETA, or is low-resolution brain electromagnetic tomography, can compute and visualize 3D images of brain electrical activity (Pascual-Marqui et al., 2002). LORETA relies on the current source density analysis, which is a method to calculate and estimate the source

of the recorded potentials. In other words, the current source density can estimate the activation of what part of the brain could plausibly explain the currently measured EEG activity. LORETA splits the brain into tiny (~ 7 mm3) voxels (i.e., volumetric pixels) and creates images from the electrical activity at each voxel represented as a squared magnitude of the estimated current source density (Pascual-Marqui et al., 1999). Thus, for example, if there was a language production dysfunction, LORETA could calculate the approximate scalp/electrode location corresponding to a potential hypothesis that there is a dysfunction in Broca's area (BA44). Combined with the z-score method discussed above, the oscillatory activity in the electrode placement corresponding with that area can then be compared to the normative database allowing a z-score to be calculated. If that difference is found to be statistically significant, that oscillatory activity can then be trained for that specific area.

Therefore, a combination of the two methods (LORETA and z-score training) allows the clinician/researcher to apply the most current research findings to their therapy. EEG source localization assists the selection of the individual brain regions and, thus, may significantly improve the success rate of therapy. More specifically, neurofeedback can target and reinforce the functioning of those dysregulated network nodes and connections that are explicitly linked to the patient's symptoms (Simkin et al., 2014). Consequently, this procedure further increased both the specificity and clinician efficiency of neurofeedback therapy (Foster & Thatcher, 2015; Koberda, 2014).

Currently, LORETA z-score neurofeedback is one of the most advanced and frequently used neurofeedback protocols available (Budzynski et al., 2009). To identify an electric "dipole" (i.e., hypothetical source of observed EEG activity), LORETA uses a 19-channel EEG cap and three-dimensional source imaging (see Pascual-Marqui et al., 1994). Therefore, a combination of the two methodologies (i.e., LORETA and z-score neurofeedback) can be used to strategically and precisely target individual brain regions (i.e.,

Brodmann areas; Krigbaum & Wigton, 2014; Thatcher, 2010). Information from each of the Brodmann areas (power, coherence) can then be compared against a normative database (e.g., NeuroGuide) of age- and gender-matched controls (i.e., neurotypically developing individuals; Thatcher et al., 2005; Thatcher et al., 2003). It can then select all metrics within the regions of interest (see Table 2.1 for areas implicated in language dysfunction) that showed abnormal levels of activity, which was defined as ≥2 *SD* from parameters of the normative database.

As mentioned in the previous section, NeuroGuide (Applied Neuroscience Laboratories) has a normative database that includes the EEG data (i.e., quantitative EEG recorded from 19 scalp locations) of 678 healthy individuals (age ranging from two months to 82 years with an average of ~ 50 participants per age group; Thatcher et al., 2003). Thatcher and Lubar (2008) proposed the use of z-score values derived from each of the metrics (i.e., different brain frequencies of interest) and compared them against the corresponding values from the normative database. Importantly, the LORETA z-score neurofeedback training allows computing of the z-scores in areas of interest, based on the participant's symptoms in real-time (Thatcher & Lubar, 2008).

For the current thesis, the therapy group received 20 sessions of LORETA z-score neurofeedback training. Previous studies showed that ~20 sessions are necessary to observe noticeable and maintainable behavioural effects (Fuchs et al., 2003). As discussed above, the majority of Neurofeedback studies in the past did not exceed 20 therapy sessions. Additionally, as the current work used an advanced LORETA Z-score Neurofeedback, the 20 training sessions is an adequate number to achieve significant results. Of note, approximately 20 LORETA z-score neurofeedback sessions were used in the treatment of various disorders, including traumatic brain injury (Koberda, 2015a), depression (Koberda, 2014), anxiety (Koberda, 2014; Lambos & Williams, 2015), addiction (Cannon et al., 2008), seizures (Frey,

2015; Koberda, 2015), attention-deficit/hyperactivity disorder (Decker et al., 2015; Koberda, 2014), autism (Koberda, 2012), cognitive dysfunction (Koberda, 2014; Lambos & Williams, 2015a), and cerebrovascular accident (Koberda, 2014a). Additionally, LORETA z-score neurofeedback therapy was shown to be not only effective but also efficient as noticeable improvements were observed in some research in as little as 10 to 20 sessions, relative to 30 to 40 sessions often recommended for traditional, non-individualized neurofeedback protocols (Brickwedde et al., 2019; Rogala et al., 2016). Various neurofeedback studies in clinical settings relied on 20 therapy sessions (e.g., Albrecht et al., 2017). In the current thesis, I decided to select a standard number of sessions (N = 20) to assure the robustness of findings.

General Procedure

In this section, I will briefly outline the general procedure of the studies in the current thesis (see individual studies for more details) and then outline the general procedure for pre-processing of the physiological data.

Pre-assessment Phase

First, participants with dyslexia were contacted and recruited through information sessions that were held at the Specific Learning Difficulties Association of South Australia (SPELD SA, see Appendix A for the recruitment email sent to inform parents of the sessions). This provided the investigator with a large selection pool of potential participants for recruitment. This was also an important factor in the study design in that all participants were currently part of the literacy clinic, which consisted of once a week one on one tutoring. It also ensured the stability and consistency of the participant's extra tutoring concurrent to the study to reduce the chances of confounding variables.

Participants were first given a screening questionnaire (see Appendix B) to determine the demographic profile, brief medical history, and to eliminate those with comorbid

disorders immediately. Many of the children already had a formal diagnosis given by an independent psychologist, which was verified via the psychological report provided to the investigator. Assessments must have been conducted no more than 18 months prior to admittance. If the child did not yet have a formal diagnosis or if their assessment was > 18 months from the time of admittance into the study, they were given the opportunity to be assessed/diagnosed by a psychologist at a private clinic who was blind to the study. The diagnosis was given by the psychologist if there was a significant discrepancy in the child's performance on the DAS-II IQ test and the YARC.

The children were admitted to the study if they met certain fixed inclusion/exclusion criteria. First, all participants were diagnosed with dyslexia by a qualified psychologist. Next, it was a requirement that all participants with dyslexia had hindered phonological processing, which was assessed via the sound awareness test (WJ III achievement test # 21, see above). Participants were admitted to the study if:

a) Their intellectual abilities were at least average with an IQ score above 80 measured either via DAS-II (Elliot, 2007) and/or via Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV; Wechsler, 2004).

b) Participants' verbal IQ was also > 80 as measured either via the Verbal Composite scale of the DAS-II or on the Verbal IQ scale of the WISC-IV.

c) Participants performed one standard deviation (*SD*) worse on Phonemic tasks (subtest of Test of Word Reading Efficiency, second edition; TOWRE – 2; Torgeson, Wagner, & Rashotte, 2012) relative to what was predicted based on their performance on reading tasks (Word Identification and Word Attack subtests from the WJ III Woodcock, McGrew, & Mather, 2001).

d) If all criteria were met, the parent and child were both given a consent form (see Appendix C) to sign, and the child was admitted to the study. All participants could

withdraw from the study at any time, and they were informed that withdrawal would not have any effect on their ability to access remedial help from SPELD SA in the future. The study was approved by the Flinders Clinical Research Ethics Committee (FCREC number 238/09).

Experimental Phase

The children attended a private psychology clinic in Adelaide (Brain Health Clinics 81/83 South Tce, Adelaide SA), where they were administered the behavioural test battery (described above)[1]. This battery provided their baseline (pre-treatment) test scores which were used in Study 1 as the dyslexia group scores, as well as the child's pre-treatment test scores for Study 2. This procedure took between two and three hours to complete depending on breaks required by the child.

Next, the children were required to perform their baseline resting-state quantitative EEG (qEEG), which was used in Study 1 as the clinical group measurement compared to the database. This qEEG was also used as the pre-treatment EEG baseline measurement for Study 2. That is, in Study 1, the dyslexia group was compared to the database, and this EEG recording was later used as their own baseline in Study 2. Prior to the EEG session, all participants received necessary information about the testing session (included in Appendix D) risks involved in the EEG procedure in general and also received instructions for a successful collection of EEG data (see Appendix D, e.g., clean hair with no hair product etc.).

EEG recording of the Hbimed database control group for Study 1 was performed using a Mitsar 21-channel EEG system (Mitsar Ltd., Russia). Participants wore an electrode cap (Electro-Cap International Inc.) with attached tin electrodes. The EEG was recorded continuously from 19 electrodes (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3,

[1] Note that there was no conflict of interest, since there were no financial benefits obtained from this work.

Pz, P4, T6, O1 and O2) that were located in accordance with the International 10–20 System (Jasper, 1958). The recorded signal was referenced to linked earlobes, it was amplified (bandpass 0.3–70 Hz) and sampled at the rate of 250 Hz. The EEG was recorded during 'eyes open' (EO) and 'eyes closed' (EC) conditions. The EEG data were recorded for 6 minutes during 3 minutes of EO, followed by 3 minutes of EC.

EEG recording of the dyslexia groups (including dyslexia control group for study 2) was accomplished using a Mitsar-EEG-201, a portable and battery-powered (4 x AA rechargeable batteries) 25 channels EEG amplifier. EEG data were recorded from 19 sites (same as above) at 500 Hz using a 16-bit analogue-to-digital converter. Impedances of all electrodes were kept below 5.0 kOhms. The EEG data were recorded for 5 minutes during 2.5 minutes of EO, and 2.5 minutes of EC. In one control participant, the EO condition was recorded five months after the EC condition.

After the baseline EEG recordings, participants were randomly allocated either to the waitlist control group or LORETA z-score therapy group. This was accomplished using a random number generator by administrative staff, and investigators were blind to the process. If the child was selected for the waitlist control, they went home and were scheduled to come back 10 weeks later to complete the same test battery again. If they were selected to receive therapy, they received 20 sessions of 40 minute LORETA z-score therapy training. Participants in the therapy group were asked to come to the lab and receive two neurofeedback sessions per week for ten weeks. Note, however, that such a schedule was not always possible to follow strictly due to participants' personal situations. Importantly, the dyslexia participants who were allocated to the waitlist control group also received therapy, but not until after the end of the study. That is, all dyslexia participants eventually received therapy in the current work.

Before therapy, the child's qEEG was loaded in Neuroguide to create their individualized therapy protocol. The neurofeedback therapy protocol was created by a registered psychologist using Neuroguide's normative database as a reference. Based on previous findings in the literature, certain Brodmann areas were selected as regions of interest (see Table 2.1 and see the previous chapter for the detailed discussion of dyslexia related functional and structural alterations in the brain areas that were used as regions of interest). Then, the recorded qEEG was matched to the Neuroguide database to select those Brodmann areas (from regions of the brain reported as involved in language dysfunction) that had a z-score ≥ 2.0. This then created the participant's individualized training protocol. Subsequent training procedure included real-time measurement of brain activity in areas of interest. Please note that Neuroguide was set such that participants received the desired reward feedback only when the mean z-score across all selected areas met the corresponding criteria (i.e., all-or-nothing approach). Note also that "Z-tunes" is the default and most preferred option as it can be automatically adapted based on participant's performance (i.e., uses Gaussian Adaptive filter) to avoid reinforcement of non-representative (extreme) scores (see Neuroguide manual, Applied Neuroscience). The feedback was given via manipulation of the screen brightness on a multimedia display. The screen went dark when z-scores failed to meet criteria (negative feedback) and became bright (was visible/normal brightness) when z-scores met the feedback criteria (positive feedback).

Table 2.1

Regions of the brain reported as being involved in language dysfunction

Brodmann Area (left and right)	Acquired from (Rationale)	Cortex (Electrodes)	Corresponding brain area
6 *L*	Nicolson & Fawcett, 2010	Central	Premotor cortex and Supplementary Motor Cortex
7 *L, R*	Kassubek et al., 2001	Parietal	Somatosensory Association Cortex
9 *L, R*	Kovelman et al., 2012	Frontal	Dorsolateral and medial prefrontal cortex
10 *L, R*	Zinchenko et al., 2018	Frontal	Anterior prefrontal
17 *L, R*	Sprenger-Charolles et al., 2013	Occipital	Primary visual cortex (V1)
18 *L, R*	Sprenger-Charolles et al., 2013	Occipital	Secondary visual cortex (V2)
19 *L*	Horwitz et al., 1998	Occipital	Associative visual cortex (V3, V4, V5)
21 *L, R*	Krafnick et al., 2014	Temporal	Middle Temporal Gyrus
22 *L, R*	Coltheart, 2000	Temporal	Superior temporal gyrus
37 *L*	Centanni et al., 2019	Temporal	Fusiform gyrus
39 *L*	Hampson et al., 2006	Parietal	Angular gyrus
40 *L*	Conway et al., 2008	Parietal	Supramarginal gyrus
41 *L*	Dole et al., 2013	Temporal	Auditory cortex
42 *L, R*	Dole et al., 2013	Temporal	Auditory cortex
44 *L, R*	Saralegui et al., 2014	Frontal	Inferior Frontal Gyrus (IFG) - Pars opercularis - part of Broca's area

45 *L, R*	Saralegui et al., 2014	Frontal	Inferior Frontal Gyrus (IFG) - Pars triangularis - part of Broca's area
46 *R*	Shaywitz et al., 1998	Frontal	Dorsolateral prefrontal cortex
47 *L, R*	Shaywitz et al., 1998	Frontal	Pars orbitalis

For therapy, the participant again attended Brain Health Clinics. When in the lab, the child first picked a movie that interested them (they were also informed they were allowed to bring in movies from home). They were told to come with clean hair and scalp. They were then sat in a chair in front of a monitor. The electro-cap was applied, impedance was kept under 5 kohms, and the child wore headphones that they found comfortable. The movie was then started, and the lights were dimmed in the room as the movie they selected was put on the screen. When the reward was not being met, the screen would go dark. The volume was kept constant to aid with attention. The therapy itself was provided by a provisional psychologist or certified neuro therapist who was always in the room.

Each forty-minute session was divided into eight, five-minute rounds with a five-second inter-round delay. On every five-minute round, the clinician's goal was to have an average level of reward between 45-55%. This range means that the reward goal was to be reached 45-55% of the time during each round. The z-threshold was reduced by 0.1 *SD* when the average per cent reward in a single round exceeded 55%, and it was increased by 0.05 *SD* when the average per cent reward fell below 45%. To illustrate, if the starting threshold level was $z = 2.7$, then the goal for the round would be to train the brain activity down to 2.6 for 55% of the time. Once the percentage reward reached 55% with the reduced z-score of 2.6, it would then be further reduced from 2.6 to 2.5. If this reduction caused the reward threshold to fall below 45%, the desired z-threshold would then be increased by 0.05 *SD* to $z = 2.55$. The goal of the neurofeedback session was to have eight consecutive rounds with a z-

threshold < 0.5 *SD* (see Kropotov, 2009). Note again that this z-score training was performed for specific brain regions that were selected based on individualized statistically significant deviations from the norm in areas of known neural markers of dyslexia (see Table 2.1). This approach allowed for training towards normalization of neural activity, specifically in the targeted brain networks.

The behavioural test battery was administered again after the end of the therapy in the therapy group or after the waiting time was over in the wait-list group. Participants on the waitlist received therapy following their ten-week wait time as mandated by the Flinders Clinical Research Ethics Committee (FCREC). Additionally, a subgroup of children that received LORETA z-score neurofeedback therapy were then asked to come back three months following therapy to complete just the psychological test battery an additional time which is the analysis used for Study 3. This was done as it was hypothesized that skills acquisition might take longer than therapy to see measurable results. Specifically, therapy-related alterations in EEG power in several targeted brain regions (see Study 2) could facilitate these children's learning processes, thus allowing them to start catching up with healthy controls and show an increase in performance on the psychological test battery. However, it was expected that therapy-related behavioural improvements in dyslexia might take longer to be measured relative to physiological changes, which could be measured immediately. It was hypothesized that neurofeedback therapy would facilitate an increase in the ability of children with dyslexia to acquire the skills that they are taught over the following months. If this were the case, it would be expected that there would be an improvement in performance on the psychological test session that was held three months post-therapy, even if an immediate improvement was not found (see Study 3 for more details). Further methodological details specific to each study can be found in the study chapters ahead.

Data Cleaning and Pre-processing of EEG Data

Data pre-processing were based on previous literature and recommendations (Luck & Kappenman, 2011). Specifically, after the recording, the EEG data was re-referenced offline to linked earlobes in EEGLAB (Delorme & Makeig, 2004). The data were first bandpass filtered at 2 - 40Hz and further submitted to independent component analysis (ICA) using the Infomax ICA (runica) algorithm as implemented in EEGLAB (Delorme et al., 2007). The ICA is a mathematical and statistical approach to decompose an EEG signal into its underlying hidden factors/constituents. In more detail, the EEG data represent a linear mixture of unknown variables (brain activity as well as muscle artifacts, eye-blinks, etc.) with an unknown rule of how these variables are mixed. These variables (sources of the data) are also called independent components and can be found via the ICA procedure so that components that are not of interest (such as eye-blinks) can be removed from the data before statistical comparisons. During the ICA step, the stopping weight was reduced from 10-6 to 10-7 in order to lengthen the ICA training and improve the decomposition (Delorme & Makeig, 2004). This allowed the artifacts with known patterns for eye blink and muscle activity to be identified by strong variation of an ICA component in time and removed by EEGLAB zeroing the activation curves of the individual ICA components. Finally, the data was processed using the continuous rejection function in EEGLAB using the default parameters. Note that the data pre-processing followed a standard approach recommended by the EEGLAB developers (Delorme & Makeig, 2004).

The pre-processed data was further analysed in Matlab (MathWorks, 2012) using Welch's power spectral density estimate (pwelch) analysis over the whole time of EEG recording (available via the "pop_spectopo" function in EEGLAB) to determine the mean log spectrum of EEG activity (power) within various frequency bands. In other words, Welch's method is used to estimate the power of the signal at different frequencies. This method was

shown to be favourable over other comparable procedures (i.e., Bartlett's method) due to its ability to reduce noise in the estimated power spectra (Welch, 1967). The output of the pop_spectopo function was used to calculate individual alpha frequencies (IAFs) per participant and condition (eyes open, closed). As discussed in the previous chapter, in line with Babiloni et al. (2012), individual IAF peaks were used as a reference to define participants' delta (IAF-8 to IAF-6 Hz), theta (IAF-6 to IAF-4 Hz), alpha 1 (IAF-4 to IAF-2 Hz), alpha 2 (IAF-2 to IAF Hz), and alpha 3 (IAF to IAF+2 Hz) frequency bands. Three fixed bands have been additionally selected for the higher frequencies to keep the results directly comparable to their findings: beta 1 (13–20 Hz), beta 2 (20–30 Hz), and gamma (30–40 Hz; see Babiloni et al., 2012 for a similar approach). The data was then subjected to statistical analysis specific to the hypothesis of the study, which will be covered in the experimental chapters ahead.

The information presented so far described the relevant theoretical and methodological assumptions and requirements that are relevant for the current work. The next chapter will now introduce the first empirical study of the dissertation. It will start with a brief overview of the relevant previous literature and continue with the first set of findings.

Chapter 3. Study 1

Neural Correlates of Developmental Dyslexia: Evidence from Psychophysiology

Abstract

Developmental dyslexia is characterized by psychophysiological abnormalities, including the reduction of power of alpha EEG frequency over frontal and temporal brain regions. In the current study, a resting-state (eyes open, eyes closed) EEG technique was used to compare the neural functioning of a group of participants with dyslexia with a group of age- and gender-matched controls from the HBImed EEG database. Additionally, the participants with dyslexia completed eleven behavioural tests to assess their reading, phonological and spelling abilities. When measured at frontal (Fp1, Fp2, F7, F3, Fz, F4, F8) and temporal (T3, T4, T5, T6) electrodes, dyslexia relative to control participants showed reduced power of delta, theta, low-, medium- and high- alpha bands, low- and high- beta, and gamma frequencies. In contrast, these frequency bands resulted in an enhanced pattern of activations in the central (C3, Cz, C4) and parietal-occipital (P3, Pz, P4, O1, O2) electrodes. Additionally, alpha and beta frequencies in the frontal cortex correlated positively with reading tasks (fluency, comprehension). Finally, the correlation analyses in the dyslexia sample also revealed that these participants' reading, spelling and phonological test performance continuously declined with increase in age. These correlational findings show that dyslexia is associated with a continuous deterioration of phonological and reading performance, that is additionally associated with abnormal patterns of oscillatory brain activations, pronounced mostly in frontal brain regions.

Keywords: Dyslexia, Alpha, EEG, time-frequency, IAF

Introduction

Dyslexia is a neurological disorder that results in difficulties in reading, writing, and spelling (Fletcher et al., 2011; Gvion & Friedmann, 2010; Sahari & Johari, 2012). Interestingly, people with dyslexia show otherwise either intact or better cognitive abilities and intelligence. Studies have shown that dyslexia may affect over 10% of the world population and that it accounts for ~ 80% of all specific learning disorders (American Psychiatric Association, 2013; De Santana et al., 2012; Klein & Shaywitz, 2005). Therefore, due to its prevalence and possible socio-economic impact, it is essential to understand the potential causes and neural correlates of dyslexia.

Spontaneous (resting state) electroencephalographic (EEG) oscillatory activity is an important method to study neural brain functioning at rest (i.e., at baseline; Berkes et al., 2011). Resting-state oscillations describe brain EEG activity in the absence of any explicit tasks or instructions (Bai et al., 2017), and it can help to make inferences about fundamental brain states (Giacino et al., 2014; Stam et al., 2005). Although resting-state EEG is measured in the absence of any explicit cognitive tasks, correlational analyses can successfully link resting-state activity in certain frequency bands and brain regions to various cognitive processes, including encoding, storage, regulation, and recall of sensory information (Bartos et al., 2007; Sejnowski & Paulsen, 2006). Therefore, in the context of dyslexia, examining the resting state may be descriptive of the internal or baseline state in this disorder (Sadaghiani et al., 2010) and enhance the understanding of fundamental neurophysiological correlates of dyslexia-specific deficits (Papagiannopoulou & Lagopoulos, 2016).

Previous studies reported that participants with dyslexia have increased delta and theta oscillatory activity in frontal and right temporal regions (Ahn et al., 1980; Arns et al., 2007; Colon et al., 1979; Fonseca et al., 2006; Harmony et al., 1990; Sklar et al., 1972). As also discussed in Chapter 1, theta-band activity is a marker of top-down (i.e., conscious) cognitive

control that is observed both during active task performance and when at rest (Pscherer et al., 2019). Cognitive (also executive) control refers to the ability to select and prioritize specific tasks or goals while inhibiting distracting information (Kanske & Kotz, 2010). These mechanisms of cognitive control play an essential role in language production and speech perception (Ye & Zhou, 2009). Apart from the obvious role of cognitive control in language-related tasks (i.e., ability to read a sentence without being distracted by irrelevant sounds or irrelevant text), it was also suggested that the development of language skills is tightly linked to maturation of control-related brain regions and executive functions in children (Mazuka et al., 2009). Studies on cognitive control that used an event-related design consistently found increased theta activity in frontal and central brain regions (anterior mid-cingulate cortex and medial prefrontal cortex; Cavanagh & Frank, 2014). Frontal brain regions, specifically the inferior frontal gyrus (IFG; BA 44/45), were also shown to support reading and visual word recognition abilities (Salmelin et al., 2000; but see also Du et al., 2020 for the evidence that IFG BA 12/47 are involved in such function). Finally, Kim and colleagues (2019) showed that theta activity in the frontal cortex (F7, F3, AF7, AF3, F5, Fz, F1, F2, F4, F8, AF4, AF8, F6) was predictive of both cognitive control and language regulation. Therefore, reduced resting-state theta activity in frontal and central brain regions may imply difficulties with cognitive control and inhibition processes, as well as language-related difficulties (van de Vijver et al., 2014), and could serve as a neural signature of these cognitive processes (Cavanagh & Frank, 2014).

Delta oscillations are involved in a range of cognitive functions, including synchronization of brain activity, activation of attentional resources (Knyazev et al., 2009; Knyazev, 2007) and response inhibition (Kamarajan et al., 2005; Knyazev, 2007; Putman, 2011). The delta rhythm may also reflect speech comprehension. For instance, delta frequency measured in healthy participants was sensitive to differences between concrete and

abstract nouns (Weiss & Rappelsberger 1998). Delta could also be sensitive to recognition abilities and awareness of speech units in participants with dyslexia. For instance, Molinaro and colleagues (2016) showed that participants with dyslexia had difficulties with entrainment (i.e., neural synchronization) to human speech in delta (0.5–1 Hz) when compared to healthy controls. These authors also reported reduced delta synchronization in the left IFG in participants with dyslexia (Molinaro et al., 2016). To conclude, delta oscillatory activity in frontal regions could be descriptive of language-related abilities in dyslexia.

In a different study, Arns and colleagues (2007) measured resting state (eyes open) EEG activity in a group of participants with dyslexia and control participants. They found increased beta activity at the F7 electrode in participants with dyslexia (Arns et al., 2007). In line with these findings, Fadzal and colleagues (2012) also found enhanced beta activity in children with dyslexia relative to typically developing children, but this time during a writing task. Beta oscillations are normally shown to be inhibited during motor tasks (Salmelin & Hari, 1994; Stancák & Pfurtscheller, 1995). The enhanced beta activity during a motor [writing] task in participants with dyslexia suggests that they require additional neural resources during writing, which results in elevated beta oscillations. Therefore, the findings of enhanced beta during writing (a motor task) may also reflect dyslexia-related difficulties with motor control.

Previous studies also examined whether dyslexia results in altered gamma frequencies. Normally, gamma-band oscillations were shown to play a pivotal role in the integration of sensory information that could be further maintained in short-term memory (Brovelli et al., 2005; Jensen et al., 2007; Sokolov et al., 2004; Treisman & Gelade, 1980). They are also present when a task involves the integration of information from different brain areas. Furthermore, Flinker et al. (2015) measured gamma frequency intracranially over

Broca's area (electrodes based on individual MRI anatomy scans) in participants with dyslexia and found that individual gamma frequencies positively correlated with performance on reading of pseudowords. In a different study, Lehongre et al. (2013) recorded brain activity in the gamma frequency by means of simultaneous EEG and fMRI. As a result, they found gamma oscillations were the dominant brain activity in the left hemisphere of healthy controls, but not in participants with dyslexia. Therefore, participants with dyslexia seem to lack hemispheric specialization for gamma oscillations (i.e., participants with dyslexia showed no gamma dominance in the left hemisphere), which might disrupt their reading performance (Flinker et al., 2015).

Research has found that the alpha frequency band (8-12 Hz) is sensitive to the processing of linguistic information. For instance, increased alpha frequency was observed in response to shortened relative to complete forms of words (e.g., yeshay for yesterday; Drijvers et al., 2016). Additionally, alpha oscillations have been consistently related to attention control (Foxe & Snyder, 2011; Keitel et al., 2019; Thut et al., 2006; Worden et al., 2000) and memory-related tasks (Klimesch, 2012; Mahé et al., 2012), which would play an undeniable role in reading as well as learning abilities. Specifically, the high and low magnitudes of alpha correspondingly reflect excitatory and inhibitory processes during cognitive events (Klimesch et al., 2007). Dyslexia has also been consistently associated functionally with altered cortical oscillations in the alpha band. For instance, Klimesch and colleagues (2001) asked participants with dyslexia to read words and pseudowords while recording their electroencephalogram (EEG). As a result, participants with dyslexia showed a reduction in alpha power over frontal and central regions. Based on previous findings in alpha frequency research, these findings make sense and may represent attentional difficulties during encoding of words in dyslexia (Klimesch et al., 2001).

Recently, alpha power was also shown to be phase desynchronized in the auditory cortex of participants with dyslexia relative to control participants (De Vos et al., 2017). In more detail, these researchers found that readers with dyslexia showed significantly reduced neural alpha synchronization in response to the rate of syllabic and phonemic stimulus delivery. These neural findings were correlated positively with reading and phonological task performance in normal readers but not in readers with dyslexia. These results show that the neural synchronization of alpha is impaired in participants during auditory processing. As alpha synchronization is necessary for the inhibition of task-irrelevant cortical areas, this could point to an inability to inhibit parts of the brain that are not necessary for the task the child is attempting to perform – In this case, processing syllabic and phonemic stimuli which have obvious links to reading. Additionally, Dhar and colleagues (2010) found reduced interhemispheric coherence of alpha activity in the central-parietal cortex (between electrode CP3 and CP4, as well as surrounding electrodes CP2, CP4, CP6, C2, C4, C6, P2, P4, P6) during a visuospatial attention task (Dhar et al., 2010). This abnormal pattern of functional connectivity in participants with dyslexia could imply slower development of connectivity and interhemispheric communication in dyslexia. Finally, participants with dyslexia also have altered cross-frequency coupling, which is thought to hinder attentional processing and integration of audio and visual information (Klimesch, 2012).

Papagiannopoulou and Lagopoulos (2016) examined oscillatory brain activity in children with dyslexia and healthy controls during resting state (eyes closed). The authors found that the group with dyslexia showed decreased alpha (10.6–12.4 Hz) EEG power in the left hemisphere. These results are consistent with earlier findings by Fein et al. (1986), who found reductions of alpha at central and mid-temporal areas (C3, C4, P3, P4) in dyslexia participants, but in both hemispheres. To summarize, previous literature provides inconsistent evidence on dyslexia-related changes in alpha frequency. Resting-state cortical alpha rhythms

were found to be similar (Rumsey et al., 1989), higher (Duffy et al., 1980) and also lower (Babiloni et al., 2012) in children with dyslexia. As discussed in the first chapter, many of these studies had critical limitations such as uneven comparison groups, low sample numbers, and even included children that have not been formally diagnosed with dyslexia by a psychologist, which may account for the discrepancies in the findings.

As previously mentioned, alpha is one of the major rhythms in human EEG (Berger, 1937; Zakharov et al., 2020). It plays a vital role in regulating the level of involvement and disengagement of different brain areas during sensory processing (Foxe & Snyder, 2011; Mathewson et al., 2011), working memory and cognitive control (Jensen & Mazaheri, 2010; Klimesch et al., 2007). Interestingly, individual alpha frequencies (IAF; Klimesch, 1999) have been consistently associated with a variety of perceptual and cognitive tasks (Bornkessel et al., 2004; Cecere et al., 2015; Samaha & Postle, 2015). In more detail, it was shown that there is a negative correlation between participants' IAF and the speed of information processing (Klimesch et al., 1996; Surwillo, 1961), memory performance (Klimesch, 1999) and general intelligence (Grandy et al., 2013). Therefore, the alpha frequency may represent a reliable inter-individual characteristic of the participants' EEG (Gasser et al., 1985; Grandy et al., 2013; Kondacs & Szabó, 1999). Consequently, it is reasonable to account for such individual characteristics when selecting the frequency bands of interest (Babiloni et al., 2012).

Thalamo-cortical structures regulate the involvement of normal alpha rhythm in various cognitive functions (Bollimunta et al., 2011; Vijayan et al., 2013). Alterations in normal alpha oscillations in dyslexia may thus indicate hindered performance in the thalamocortical structures in individuals with this disorder. Indeed, there is consistent evidence of the dysfunction of the auditory thalamus in dyslexia (Díaz et al., 2012). For instance, Diaz and colleagues used functional MRI methodology to test whether dyslexia-

specific phonological difficulties are related to a dysfunction of the auditory sensory thalamus (i.e., the medial geniculate body). The authors reported abnormal responses in the auditory thalamus in the group of dyslexia participants, but not healthy controls specifically when both groups were attending to phonemes, but not other speech features. Therefore, the previously observed alterations in alpha frequency in dyslexia could represent deficient auditory thalamic functioning in dyslexia.

Finally, there is some evidence that the alpha oscillation may not be a coherent frequency band, but, instead, that alpha consists of several functionally distinct sub-components. Klimesch (1999) offered some theoretical speculations about the physiological meaning of low- (~8–10 Hz) and high- alpha frequency (~10–12 Hz; see also Pfurtscheller & Lopes da Silva, 1999). For instance, it was suggested that high-frequency alpha is a marker of cortical processes involved in phonological, semantic, and lexical processes, while low-frequency alpha is sensitive to the modulation of cortical arousal and vigilance (Klimesch, 1999). Additionally, the amplitude of alpha-band may be descriptive of the retrieving of semantic long-term memory information (Klimesch, 1996). Previous studies also attempted to differentiate between different alpha sub-components in dyslexia. Babiloni and colleagues (2012) examined resting-state EEG brain activity in participants with dyslexia vs. healthy controls and found that alpha rhythm amplitudes were generally lower in dyslexia. Furthermore, the authors subdivided alpha into its constituent subcomponents (low: 6-8 Hz, medium: 8-10 Hz, and high: 10-12 Hz) and showed reduced activity in both higher and lower alpha bands in the group with dyslexia. Such disorder-related reduction in the three alpha ranges reflects, correspondingly, disorder-related disruption in phonological, semantic, and lexical performance (Babiloni et al., 2012). As such, this study will use the same approach as Babiloni and colleagues to more precisely differentiate between different kinds of alpha oscillations, as well as to correctly identify individualized other frequency bands with

reference to individual alpha frequencies (see methods section). This will not only allow for a more effective comparison of results in the current and previous works but would also enable a more fine-grained description of neural alterations in dyslexia.

As discussed in Chapter 1, dyslexia is a heterogeneous disorder. Although most researchers are in agreement that subtypes of the disorder may exist, there is a lack of general consensus of theories on how to define and differentiate between these subtypes (see Chapter 1 for a thorough discussion of dyslexia subtypes). To my knowledge, no previous study on resting-state EEG correlates of dyslexia accounted for the potential heterogeneity in their dyslexia sample. Van Ermingen-Marbach et al. (2013) performed an fMRI on participants with dyslexia that showed marked phonological impairments and those that did not and found several functional differences (see Chapter 1 for more detail). These results imply that people with dyslexia may exhibit subtype-specific patterns of brain activity, which should be considered. To ensure certain homogeneity in the sample of participants with dyslexia and to further reduce the risk that subtypes may interfere with identifying neural correlates of dyslexia, only participants with dyslexia with marked phonological impairments were included in the current study.

To summarize, there is converging evidence that participants with dyslexia show altered patterns of brain activity relative to that of matched healthy controls. However, the exact details of dyslexia-related alterations seem to differ across studies. Generally, it was reported that participants with dyslexia have lower alpha over central and mid-temporal brain areas functionally as well as at rest, as well as reduced interhemispheric coherence of alpha oscillations in the central-parietal cortex when measured functionally. Additionally, beta oscillations are enhanced in participants with dyslexia both during resting state and during writing, while also having increased delta and theta oscillations over frontal and right temporal regions. However, previous studies could have been confounded by the lack of

control for subtype-related heterogeneity in the dyslexia sample, although there is some evidence for differential subtype-specific patterns of brain activity in dyslexia (van Ermingen-Marbach et al., 2013). Similarly, previous studies have also mostly ignored the individual alpha frequencies (IAFs) when defining the frequency bands of interest, although there are also accumulating evidence for individual differences in IAF across participants and especially in patient groups (dyslexia, ADHD etc., see below). Finally, previous studies measured EEG brain activity in dyslexia either with their eyes closed or eyes opened. It is not clear whether this factor could further contribute to the diversity of findings of the neural correlates of developmental dyslexia.

Therefore, the aim of the current work was to examine potential differences in the EEG frequency and power between children with dyslexia with marked phonological impairment and typically developing children. To my knowledge, this is the first study that has examined phonological dyslexia resting-state oscillatory brain activity in a large group of participants (N total = 94) using both eyes closed (EC) and eyes opened (EO) conditions and analysed this data using individualized alpha peak frequencies (as discussed above and in chapter 2) to individualize all the frequency bands (see the methods section below). Specifically, potential dyslexia-related changes were investigated in the three alpha bands: low, medium, and high (correspondingly termed alpha1, alpha2, and alpha3), as well as in delta, theta, beta, and gamma bands. Additionally, the purpose of the work was to examine further whether dyslexia may alter the power spectral density in a specific frequency band and whether this difference can vary as a function of resting-state condition (eyes opened, closed) and EEG activations in different brain regions (i.e., frontal, central, parietal, occipital, temporal).

In line with the discussed literature, it was expected that there would be reduced alpha power (alpha2, alpha3) in participants with dyslexia at parietal, occipital, and temporal brain

areas (see Babilone et al., 2012). It was also expected that there would be increased theta and delta activity in the frontal and right temporal brain areas since previous studies also observed dyslexia-related increase in these frequency bands over frontal and right temporal regions (e.g., Arns et al., 2007; Fonseca et al., 2006). It was hypothesized that the beta activity would be increased in participants with dyslexia at frontal and central-parietal electrodes, as it was shown in previous studies both in resting state (Arns et al., 2007) and during a motor writing task (Fadzal et al., 2012). It was expected to see reduced gamma power in predominantly frontal brain areas in the left hemisphere (i.e., Broca's area) of participants with dyslexia as a neural marker of reading performance (Flinker et al., 2015; Lehongre et al., 2013; note also that Flinker et al., 2015 recorded brain activity intracranially). It was additionally investigated whether the power of different frequency bands would vary as a function of the resting-state condition (i.e., eyes open, eyes closed). Although this question had not been tested before in dyslexia samples, there is consistent evidence in the literature that the two resting-state conditions may result in different connectivity patterns in various brain networks (Agcaoglu et al., 2019), as well as have a different influence on various frequency bands (Boytsova & Danko, 2010). Finally, and in line with previous literature (e.g., Flinker et al., 2015), gamma frequency at frontal electrodes of participants with dyslexia were expected to correlate positively with behavioural performance (reading, phonological and spelling).

Materials and Methods

Study Design

This study aimed to analyse electrophysiological differences between children who were diagnosed with phonological dyslexia and a group of healthy children at a resting (eyes closed, eyes open) state. The study included forty-seven participants with phonological dyslexia and a control group of forty-seven qEEG data sets of age- and gender-matched healthy children from the HBImed normative reference database (see Methods chapter for a

detailed discussion of the database). All but four of these participants also completed behavioural testing to assess their reading, phonological, and spelling skills (see below for details).

Participants

A total of 47 participants (male = 28, female = 19, mean age = 10.6, *SD* = 2.1, range = 7.0 - 15.1 years old) were included in the group with dyslexia. In addition, a group of 47 control participants were selected from the Human Brain Index (HBI) database normative reference database as [age- and gender-] matched controls (male = 28, female = 19, mean age = 10.7, *SD* = 2.1, range = 7.7 - 15.4 years old). The HBImed database (www.hbimed.com) consists of 3000 EEG recordings of 1000 healthy participants (7 to 89 years old). The database contains brain recordings from healthy participants with no neurological or psychiatric disorders (see the previous chapter for more information).

Based on effect size measures provided in previous studies (e.g., Babiloni et al., 2012), the sample size was appropriate to detect a critical t size of 1.66 with 85% power (Cohen's *d* = 0.6, allocation ratio = 1, one-tailed), given an alpha level of .05. All participants had normal or corrected-to-normal vision. Both the participant and the parent/guardian signed a written informed consent (see Appendix C) before the experiment and were informed that they were free to withdraw from the study at any time. As mentioned in the general procedure, all participants were in receipt of extracurricular tutoring.

It was ensured that all participants were diagnosed with dyslexia by a provisional psychologist under the supervision of a registered psychologist at a private psychology clinic in Adelaide (Brain Health Clinics 81/83 South Tce, Adelaide SA). Additionally, all participants with dyslexia had significant difficulties in phonological processing as measured via the sound awareness test (WJ III achievement test # 21). Phonological dyslexia was diagnosed if:

a) Participants had at least average intellectual abilities measured by DAS-II (i.e., an IQ score of > 80, Elliot, 2007; or a Full-Scale IQ score of > 80 from the Wechsler Intelligence Scale for Children – Fourth Edition, WISC-IV, Wechsler, 2004)

b) Participants' verbal IQ was at least average as measured either via the Verbal Composite scale of the DAS-II or on the Verbal IQ scale of the WISC-IV (a score of > 80).

c) There was a discrepancy between participants' observed chronological age-adjusted scores on the Reading tasks (measured via the Word Identification and Word Attack subtests from the Woodcock-Johnson Tests of Achievement 3; WJ III Woodcock, McGrew, & Mather, 2001) and Phonemic tasks (subtest of Test of Word Reading Efficiency, second edition; TOWRE – 2; Torgeson, Wagner, & Rashotte, 2012) and the corresponding scores that were predicted by the performance on Verbal Composite or Verbal IQ scales. The discrepancy between the observed and predicted scores was required to be at least 1 *SD* (i.e., observed is smaller than predicted) to be considered significant.

To further assess the disorder-specific behavioural performance in the group with dyslexia and to correlate this performance with the neural markers of dyslexia, several additional tests were conducted. The York Assessment of Reading for Comprehension (YARC; Colenbrander et al., 2017; Wheldall & Arakelian, 2016) was an additional measure of reading and comprehension. Specifically, in this test, participants are asked to read aloud fiction and non-fiction sets of passages to evaluate their reading abilities. This test also requires that participants answer eight comprehension questions to assess their literal and inferential comprehension skills.

Furthermore, participants also completed a series of test batteries from the Woodcock-Johnson III Tests of Achievement (i.e., WJ III ACH). The Woodcock-Johnson measurements

included a) “word attack” task (# 13) that measures the ability to apply phoneme/grapheme knowledge to decode unfamiliar printed text, b) sound awareness (# 21) to measure the ability to understand and utilize the sounds within words (i.e., phonological awareness), c) letter-word identification test (# 1) to examine oral word decoding skills, d) reading fluency (# 2) to measure the speed of semantic processing, e) the spelling sounds test (# 7) to examine spelling of orally presented words and f) the passage comprehension test (# 9) that examines participants’ ability to find a write down a missing fitting word in a passage. Participants performance on several of the WJ III ACH tests were also used as inclusion criteria to ensure that the sample with dyslexia showed specific dysfunction in phonological processing.

Finally, participants’ phonological decoding abilities were assessed via the Test of Word Reading Efficiency–Second Edition (TOWRE-2; see Torgesen et al., 2011). This test was designed to evaluate participants’ reading fluency and phonetic decoding skills. Generally, behavioural performance was measured to confirm that participants with dyslexia have difficulties with disorder-specific tasks and to correlate these results with the electrophysiological recordings.

Note that some participants could bypass administration of the DAS-II if they already had a verifiable diagnosis of developmental dyslexia as confirmed by a psychological report within the previous 18 months. Additionally, the final inclusion criteria for the study were: a) English as a first language, b) they were aged between 7.00 and 15.12 months (Grade 1 to 10), c) they received remedial reading instruction to account for the homogeneity of sample in terms of additional reading, writing and phonological training received.

Note also that participants with more general disorders of language involving comprehension difficulties were not included in the study. Further exclusion criteria were: a) deficits in hearing or visual acuity, b) oral language impairment, c) IQ < 80 to avoid participants whose reading skills are low due to low IQ, d) motor impairment, e) personal or

family history of neurological, psychiatric or psychological impairments (e.g. epilepsy, traumatic brain injury, chronic ill health) and f) participants currently taking psychoactive medication.

EEG Registration

EEG recording of the database group was accomplished using a Mitsar 21-channel EEG system (Mitsar Ltd., Russia). An electrode cap (Electro-Cap International Inc.) with tin electrodes was used to record continuous EEG from 19 sites (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1 and O2) that were placed according to the International 10–20 System (Jasper, 1958) at 250 Hz using a 16-bit analogue-to-digital converter. The input signals were referenced to linked earlobes. All electrophysiological signals were amplified by a factor of 20,000 (Luck, 2014) with a 0.3–70 Hz bandpass filter and sampled at the rate of 250 Hz. EEG recordings were obtained during 'eyes open' (EO) and 'eyes closed' (EC) resting states. The EEG data were recorded for 6 minutes during 3 minutes of EO, followed by 3 minutes of EC. It was made sure that all participants did not have any sore spots on their scalp that would make the recording uncomfortable.

EEG recording of the group with dyslexia was undertaken using a Mitsar-EEG-201, a portable and battery-powered (4 x AA rechargeable batteries) 25 channels EEG amplifier. EEG data were recorded from 19 sites (Fp1, Fp2, F7, F3, F4, F8, T3, C3, C4, T4, T5, P3, P4, T6, O1, O2, Fz, Cz, and Pz) of the International 10–20 System at 500 Hz using a 16-bit analogue-to-digital converter. Subsequently, the data were down-sampled to 250 Hz to be comparable with the data of the HBI database and to ensure all EEG parameters were identical across groups. Impedances of all electrodes were kept below 5.0 kOhms. In one subject of the control group, the EO condition was recorded five months after the EC condition (note, however, that this participants' performance was within 1 SD of the group's mean, i.e., not deviant from the rest of the group).

EEG Data Analysis

All EEG data were corrected offline for artifacts using EEGLAB (Delorme & Makeig, 2004). They were first low- then high-pass filtered at 2 Hz and 40Hz, respectively, followed by an independent component analysis (ICA) using the runica function in EEGLAB. The ICA was performed to remove brain-unrelated sources of activity (eye blinks, muscular activations) from the recorded data. Following the suggestion of EEGLAB developers (Delorme & Makeig, 2004), the stopping weight was reduced from 10-6 to 10-7 in order to lengthen the ICA training and improve the decomposition. Afterwards, artifacts with known patterns for eye blink and muscle activity were identified by substantial variation of an ICA component in time and removed by zeroing the activation curves of the individual ICA components. In addition, ICA components that showed high noise levels greater than -5 dB amplitude at frequencies above 15 Hz and no clear alpha peak above 0 dB were also excluded. Finally, the data were processed using the continuous rejection function in EEGLAB using the default parameters.

The preprocessed data was further analysed in Matlab (MathWorks, 2012) using Welch's power spectral density estimate (pwelch) analysis over the whole time of EEG recording (available via the "pop_spectopo" function in EEGLAB) to calculate the mean log spectrum of EEG activity (power) at various frequency bands. The output of the pop_spectopo function was evaluated in order to calculate the individual alpha frequency (IAF) peaks, that is, the frequency of the highest alpha power (Klimesch, 1999). As mentioned in Chapter 1, the peak frequency of the EEG power spectrum can vary slightly from subject to subject, and, therefore, use of the standardised frequency range for alpha (8 to 12 Hz) could be insensitive to subtle differences between subjects. Moreover, segregation of alpha frequency into lower, middle, and upper alpha bands may have distinct properties, which makes the distinction even more necessary (see for example several studies by

Klimesch et al., 2007). This is particularly relevant when working with patients (e.g., dyslexia, PD, ADHD) whose average IAF may be different from healthy controls (e.g., Arns et al., 2012). To account for this inter- and intra-individual difference, with reference to the IAF, the frequency bands of interest were defined in the following way: delta (IAF-8 to IAF-6 Hz), theta (IAF-6 to IAF-4 Hz), alpha 1 (IAF-4 to IAF-2 Hz), alpha 2 (IAF-2 to IAF Hz), and alpha 3 (IAF to IAF+2 Hz; see Babiloni et al., 2012 for a similar approach). For instance, with an IAF of 10 Hz in the range of 8-15 Hz, the frequency bands of interest were as follows: 2–4 Hz (delta), 4–6 Hz (theta), 6–8 Hz (alpha 1), 8–10 Hz (alpha 2), 10–12 Hz (alpha 3). Note also that the alpha frequency was split into three sub-groups in accordance with the work by Babiloni et al. (2012) to compare the current results to those authors' findings. Alpha has also been split into three subcomponents by other researchers (e.g., see Klimesch et al., 2000). Three fixed bands for higher frequencies were additionally selected and defined as beta 1 (13–20 Hz), beta 2 (20–30 Hz), and gamma (30–40 Hz[2]; see Babiloni et al., 2012 for a similar approach). Also, note that in line with Babiloni et al. (2012), the mean IAF peak was 9.67 Hz (*SD* = 1.33) in the group with dyslexia and 9.51 Hz (*SD* = 1.28) in the control subjects. No statistically significant ANOVA difference was found between the groups ($p > 0.4$), as well as there was no evidence of clustering of IAF values in the group with dyslexia (i.e., the IAF values were homogeneous in the groups).

Extracted data were submitted into a 2 x 2 x 4 x 8 repeated measures ANCOVA with between-subjects factor: group (dyslexia, control), and three within-subjects factors: condition (eyes closed, eyes open), region (frontal, temporal, central, parietal-occipital) and frequency bands (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma), while age and gender of participants were entered as covariates. In a separate analysis, a 2 x 2 x 3 x 8

[2] Note also that some previous studies defined gamma frequency at =/> 40 Hz (McDermott, Porter, Hughes, McGinley, Lang, O'Halloran, & Jones, 2018), while the current study followed the procedure of Babiloni et al., (2012) and defined gamma at 30 Hz.

repeated measures ANCOVA was conducted with a between-subjects factor: group (dyslexia, control), and within-subjects factors: condition (eyes closed, eyes open), hemisphere (left, midline, right) and frequency bands (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma), while age and gender of participants were again used as covariates. Note that in cases when the sphericity assumption was violated (Mauchly's test of sphericity), Greenhouse-Geisser correction was applied. Significant effect involving critical factors group and condition are discussed in the results section. Please note that for the purpose of analyses, 19 electrodes were grouped into frontal (Fp1, Fp2, F7, F3, F4, F8, Fz), central (Cz, C3, C4), parietal-occipital (Pz, P3, P4, O1, O2) and temporal (T3, T4, T5, T6), total left-hemispheric (Fp1, F3, F7, C3, T7, P3, P7, O1), right-hemispheric (Fp2, F4, F8, C4, T8, P4, P8, O2) and midline (Fz, Cz, Pz) scalp regions. Finally, in a posthoc analysis, I also contrasted alpha activations between the right and left hemisphere in the frontal and occipital regions (i.e., in regions that showed opposite patterns of alpha activations). Note that the multiple comparisons were adjusted via the Bonferroni correction.

Behavioural Data and Analysis

Eleven behavioural tests were performed to assess participants' reading, spelling and phonological abilities (see supplementary material for the list of tests, which have already been discussed in the previous chapter). The test scores are given in an aged-matched-to-performance score. For example, a 10 years 2 months old pupil gets a score = 10 years 2 months if their reading performance is adequate to their age or < 10 years 2 months if their reading performance is hindered. Therefore, the results inform about the relative age of the subject with respect to the given task tested. The age score is called relative since it corresponds to the age equivalent at which the participant with dyslexia is actually reading and not chronological age. The scores of the behavioural tests were recorded for each subject as well as the age of the subject and can be compared directly. In addition, the gains, and

deficiencies in years of age were calculated for each subject and each test as chronological age-corrected test scores or TSCA. They express how a subject's test score (TS, i.e., the relative age of task performance) compared with their chronological age (CA) and were calculated as TSCA=TS-CA. Using the example above, if that participant's test score revealed a reading age of 8 years 2 months, the child's TSCA would be -2.

Results

Analysis of the Behavioural Data

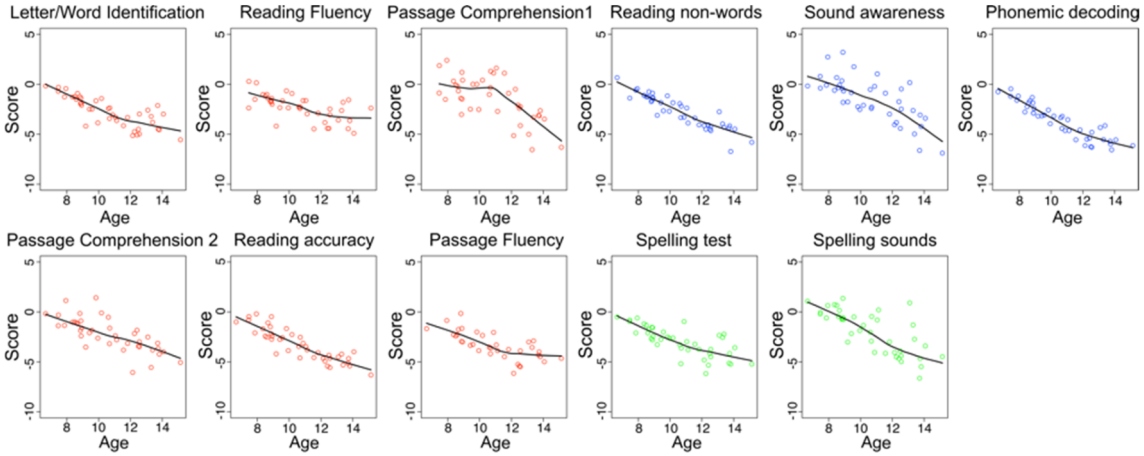
The results of the behavioural tests in the group with dyslexia are shown in Figure 3.1. Here, the gains and deficiencies, defined as the difference between the test score and the chronological age of the subject, TSCA, are plotted against the chronological age of the subjects. As the ages of the subjects increase, the TSCA scores decrease in all tests in close to a linear fashion. Note that correlations were chosen to also present the readers with individual participants' data to spot any potential outliers or subtype-specific clustering of responses.

In more detail, there was a statistically significant negative Pearson correlation between age of participants and their performance on their age-corrected scores in the letter/word identification task (i.e., reading task), $r = -0.79$, $p < 0.0001$ (see Figure 1), passage comprehension (reading task), $r = -0.74$, $p < 0.0001$, reading fluency (reading task), $r = -0.63$, $p < 0.001$, reading accuracy (reading task), $r = -0.88$, $p < 0.001$, passage comprehension (reading task), $r = -0.65$, $p < 0.001$, and passage fluency (reading task), $r = -0.71$, $p < 0.001$. Similarly, I also found a negative correlation between participants' age and performance on reading of non-words task (i.e., phonological task), $r = -0.91$, $p < 0.001$, sound awareness (phonological task), $r = -0.72$, $p < 0.001$, and phonemic decoding efficiency (phonological task), $r = -0.91$, $p < 0.001$, as well as spelling test (spelling task), $r = -0.74$, $p < 0.001$ and spelling sounds test (spelling task), $r = -0.74$, $p < 0.001$. Note that all significant correlations reported survived the conservative Bonferroni correction. These results indicate that

participants with dyslexia are continuously falling behind their normal peers at a near constant rate.

Figure 3.1

Correlation plots



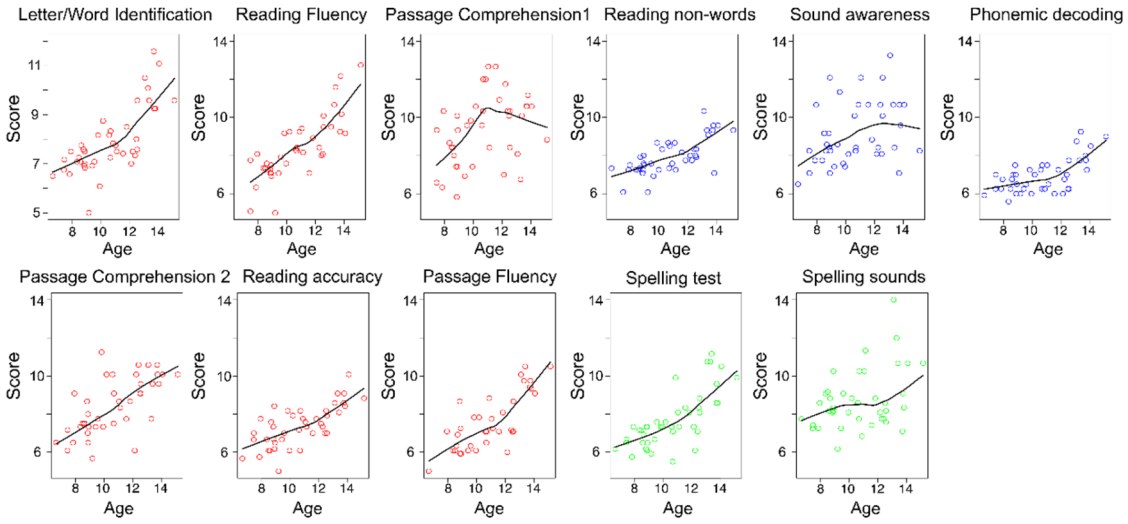
Note. The figure represents negative correlations between participants' age and TSCA scores for the letter/word identification task, passage comprehension 1 (Woodcock and Johnson reading task), reading fluency, reading accuracy, passage comprehension (YARC reading task), passage fluency, non-words reading task (phonological task), sound awareness (phonological task), phonemic decoding efficiency, as well as spelling test and spelling sounds test. Black lines represent locally weighted scatterplot smoothing fits. The colour of individual scores represents three different tasks: red = reading tasks, blue = phonological tasks, green = spelling tasks.

There were also a number of a significant positive correlations between age of participants and their raw performance scores on letter/word identification task (i.e., reading task), $r = 0.74$, $p < 0.001$ (see Figure 2), passage comprehension (reading task), $r = 0.65$, $p < 0.001$, reading fluency (reading task), $r = 0.8$, $p < 0.001$, reading accuracy (reading task), $r = 0.71$, $p < 0.001$, passage comprehension (YARC reading task), $r = 0.37$, $p < 0.02$, and

passage fluency (reading task) $r = 0.77$, $p < 0.001$. Similarly, there was a positive correlation between participants' age and performance on reading of non-words task (i.e., phonological task), $r = 0.7$, $p < 0.001$, sound awareness (phonological task), $r = 0.35$, $p < 0.03$, and phonemic decoding efficiency, $r = 0.63$, $p < 0.001$, as well as spelling test, $r = 0.75$, $p < 0.001$ and spelling sounds test, $r = 0.39$, $p < 0.02$. These results show that, in contrast to the age-corrected data, participants with dyslexia in the sample that are currently receiving extra tutoring show an increase in absolute test performance as a function of age (see Figure 3.2).

Figure 3.2

Correlation plots



Note. The figure represents positive correlations between participants' age and raw test scores for the letter/word identification task, passage comprehension 1 (Woodcock and Johnson reading task), reading fluency, reading accuracy, passage comprehension (YARC reading task), passage fluency, non-words reading task (phonological task), sound awareness (phonological task), phonemic decoding efficiency, as well as spelling test and spelling sounds test. Black lines represent locally weighted scatterplot smoothing fits. The colour of

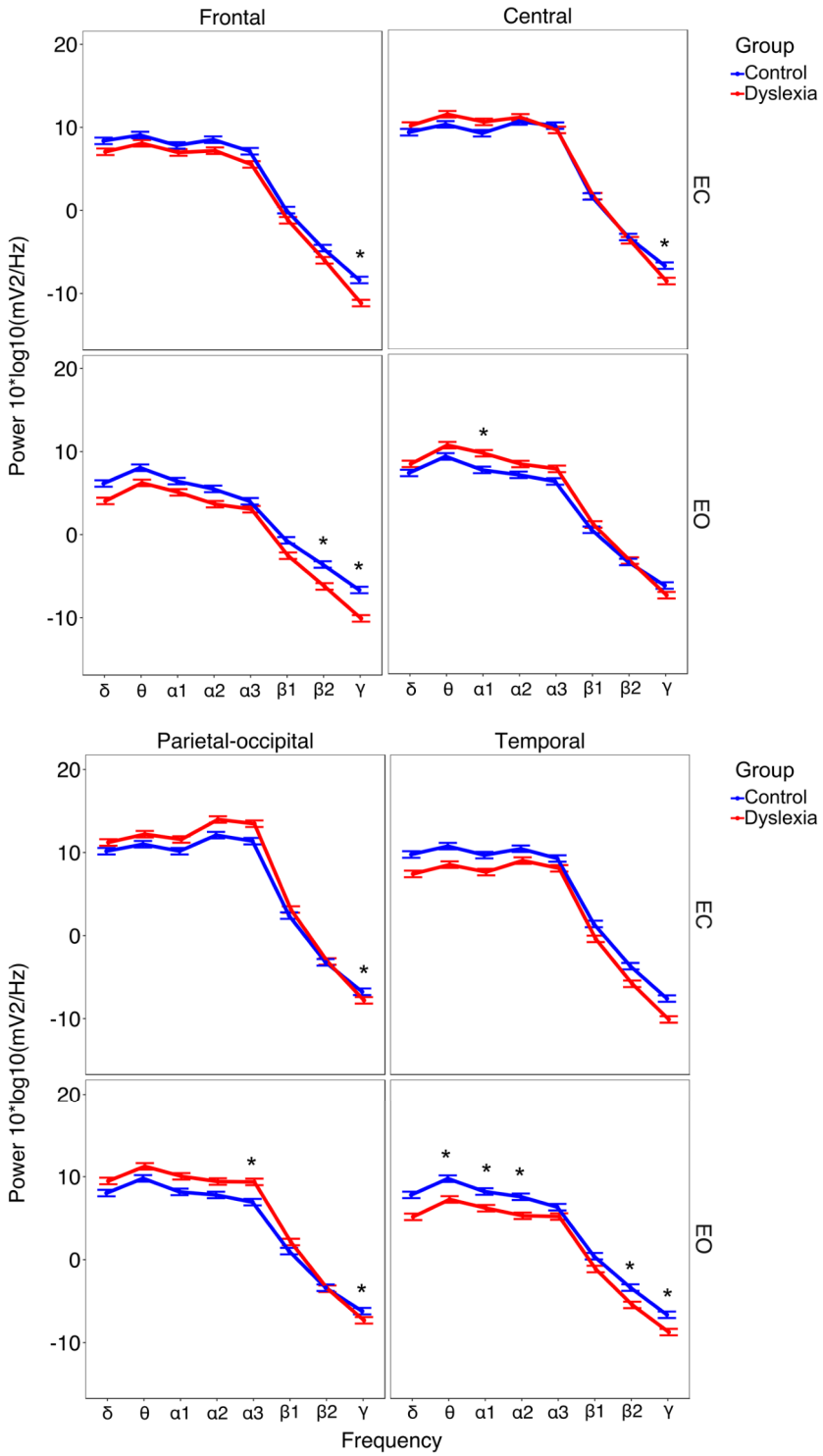
individual scores represents three different tasks: red = reading tasks, blue = phonological tasks, green = spelling tasks.

Analysis of EEG Spectral Patterns

There was a significant interaction of group and frequency, $F(7, 84) = 2.72$, $p < 0.001$, $\eta_p^2 = 0.32$ as well as an interaction of group, frequency and region, $F(21, 70) = 26.57$, $p < 0.001$, $\eta_p^2 = 0.88$ and, finally, a four-way interaction of condition, group, frequency and region, $F(21, 70) = 6.12$, $p < 0.001$, $\eta_p^2 = 0.65$ (see Figure 3.3). In subsequent steps, the three-way interaction of group x frequency x region was examined separately for each of the conditions. The three-way interaction was statistically significant in the eyes-closed condition, $F(21, 70) = 26.56$, $p < 0.001$, $\eta_p^2 = 0.89$, and eyes-open condition, $F(21, 70) = 20.44$, $p < 0.001$, $\eta_p^2 = 0.86$. Post hoc tests revealed that in the eyes closed condition, the frequency x group interaction was significant in the central region, $F(7, 84) = 9.04$, $p <0.001$, $\eta_p^2 = 0.43$, as well as frontal, $F(7, 84) = 6.09$, $p < 0.001$, $\eta_p^2 = 0.34$, and parietal-occipital, $F(7, 84) = 4.62$, $p < 0.001$, $\eta_p^2 = 0.28$, regions, but not in the temporal region, $F(7, 84) = 1.13$, $p = 0.354$, $\eta_p^2 = 0.09$.

Figure 3.3

Power plots as a function of conditions, regions and test groups.



Note. Spectral decomposition of EEG activity (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma) plotted as a function of electrodes region (frontal, temporal, central, parietal-occipital) separately for dyslexia and control groups. Asterisks indicate Bonferroni-corrected significant differences between dyslexia and control participants. The error bars represent standard errors of the mean.

In the eyes open condition, the frequency x group interaction was significant in the central region of interest, $F(7, 84) = 10.17$, $p < 0.001$, $\eta_p^2 = 0.46$, as well as frontal, $F(7, 84) = 6.09$, $p < 0.001$, $\eta_p^2 = 0.34$, parietal-occipital, $F(7, 84) = 8.64$, $p < 0.001$, $\eta_p^2 = 0.42$, and in the temporal region, $F(7, 84) = 6.25$, $p < 0.001$, $\eta_p^2 = 0.34$. The two groups have been subsequently compared across all frequencies in the corresponding conditions (see Figure 3.3 and Table 3.1 for the results of pairwise comparisons). In short, these results indicate that there were frequency differences between dyslexia and control groups that varied as a function of the region of interest and experimental condition. Relative to healthy controls, participants with dyslexia had overall reduced power in frontal and temporal regions (significant for delta, theta, alpha1, alpha2 and gamma frequencies), and they had overall increased power in Central and Parietal-Occipital regions (significant for alpha1, alpha3 and gamma frequencies).

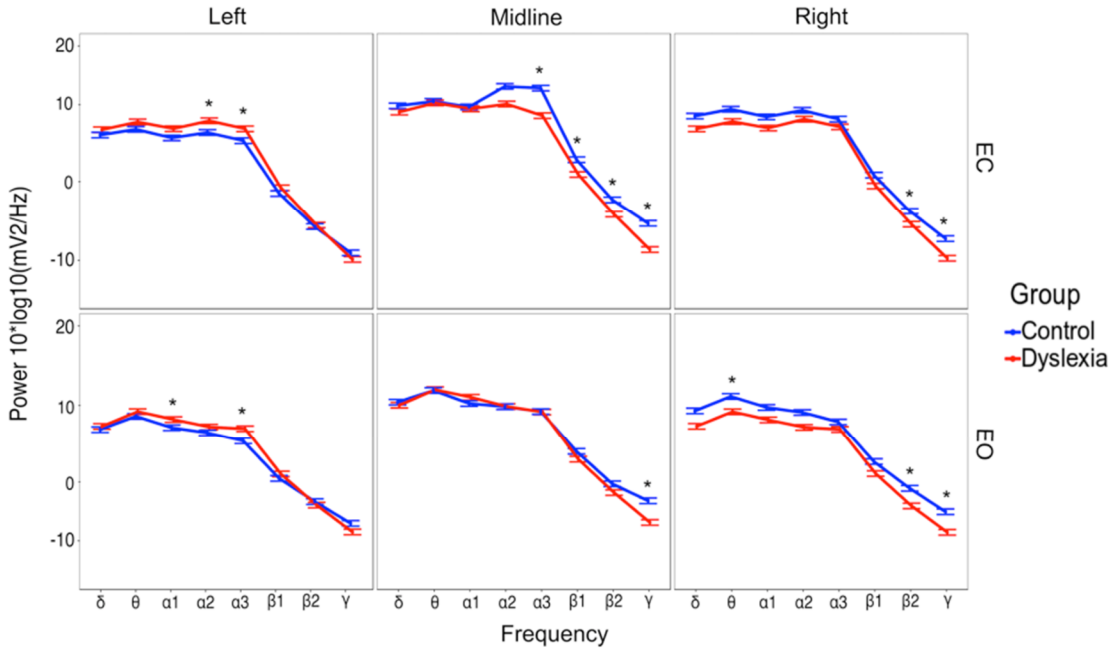
In a separate analysis, I examined whether the observed findings vary as a function of hemisphere. For this purpose, an additional 2 x 2 x 2 x 8 repeated measures ANCOVA was conducted with between-subjects factor: group (dyslexia, control), and within-subjects factors: condition (eyes closed, eyes open), hemisphere (left, right, midline) and frequency bands (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma), with age and gender of participants entered as covariates. Most critically for the current work, there was a four-way interaction of condition x group x frequency x hemisphere, $F(14, 77) = 8.72$, $p < 0.001$, $\eta_p^2 = 0.61$ (see Figure 4). Follow-up analyses separately across the two conditions showed

that the three-way interaction of hemisphere x frequency x group was significant in the eyes closed condition, $F(14, 77) = 33.65$, $p < 0.001$, $\eta_p^2 = 0.86$, and eyes open condition, $F(14, 77) = 33.72$, $p < 0.001$, $\eta_p^2 = 0.86$.

In the eyes closed condition, there was a frequency x group interaction in the left hemisphere, $F(7, 84) = 4.78$, $p < 0.001$, $\eta_p^2 = 0.29$, midline group of electrodes, $F(7, 84) = 17.78$, $p < 0.001$, $\eta_p^2 = 0.59$, and marginally significant in the right hemisphere, $F(7, 84) = 2.08$, $p = 0.054$, $\eta_p^2 = 0.14$. In the eyes open condition, there was a significant frequency x group interaction in the left hemisphere, $F(7, 84) = 9.103$, $p < 0.001$, $\eta_p^2 = 0.43$, midline, $F(7, 84) = 18.07$, $p < 0.001$, $\eta_p^2 = 0.60$, and right hemisphere, $F(7, 84) = 5.28$, $p < 0.001$, $\eta_p^2 = 0.31$. See Figure 3.4 and Table 3.2 for the results of pairwise comparisons (asterisks mark significant differences).

Figure 3.4

Power plots as a function of condition, hemisphere, and test group.



Note. Spectral decomposition of EEG activity (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma) plotted as a function of hemisphere (left, right, midline) separately for dyslexia and control groups. Asterisks indicate Bonferroni-corrected significant differences between dyslexia and control participants. The error bars represent standard errors of the mean.

Finally, I also contrasted participants' alpha oscillations across the two hemispheres (left, right) in the frontal and parietal-occipital brain regions. The data were analysed using a 2 (region: frontal, parietal-occipital brain) x 2 (hemisphere: left, right) x 3 (frequency: alpha1, alpha2, alpha3) x 2 (group: dyslexia, control) repeated measures ANOVA. I found a significant four-way interaction, $F(2, 184) = 18.02$, $p < .001$, $\eta_p^2 = 0.16$. In the next step, the four-way interaction was resolved by region. In the Frontal brain region, the interaction of group x frequency x hemisphere was significant: $F(2, 184) = 14.44$, $p < .001$, $\eta_p^2 = 0.14$. This three-way interaction was further split by group and it was found that the interaction of hemisphere x frequency was significant in the control group, $F(2, 92) = 33.94$, $p < .001$, $\eta_p^2 = 0.42$, but not in the dyslexia group, $F(2, 92) = 1.26$, $p = .288$, $\eta_p^2 = 0.03$. In the control group, the main effect of hemisphere was significant in the alpha 1, $F(1, 46) = 203.73$, $p < .001$, $\eta_p^2 = 0.82$, in the alpha 2, $F(1, 46) = 184.6$, $p < .001$, $\eta_p^2 = 0.8$ and in the alpha 3, $F(1, 46) = 135.43$, $p < .001$, $\eta_p^2 = 0.75$.

In the Parietal-Occipital brain region, the interaction of group x frequency x hemisphere was again significant: $F(2, 184) = 8.2$, $p < .001$, $\eta_p^2 = 0.08$. Consistently, this three-way interaction was also split by group and it was found that the interaction of hemisphere x frequency was significant in the control group, $F(2, 92) = 16.48$, $p < .001$, $\eta_p^2 = 0.26$, but not in the dyslexia group, $F(2, 92) = 0.32$, $p = .729$, $\eta_p^2 = 0.01$. In the control group, the main effect of hemisphere was significant in the alpha 1, $F(1, 46) = 156.83$, $p < .001$, $\eta_p^2 = 0.77$, in the alpha 2, $F(1, 46) = 201.63$, $p < .001$, $\eta_p^2 = 0.81$ and in the alpha 3, $F(1, 46) =$

181.34, $p < .001$, $\eta_p^2 = 0.8$. To summarise, it wasfound that control but not participants with dyslexia had consistently reduced alpha in the left relative to right hemisphere across all frequency bands and brain regions (all p's < 0.01; on average there was 30% increased activity in the right relative to the left hemisphere). In contrast, participants with dyslexia showed no hemisphere-specific differences across all frequency bands and brain regions (all p's > 0.5; the strength of activity was almost identical between the two hemispheres).

To summarize, analysis of physiological data revealed that, relative to control participants, participants with dyslexia showed reduced power of delta, theta, low-, medium- and high- alpha bands, as well as reduced power in low- and high- beta and gamma frequencies when measured at frontal and temporal electrodes. On the other hand, these frequency bands resulted in an enhanced pattern of activations in the central and parietal-occipital electrodes. Further, although control participants resulted in consistently larger power in the left relative to right hemisphere across all frequency bands, there was no hemisphere asymmetry in participants with dyslexia within any frequency band.

Correlation Analysis

Further, I tested if there was a Pearson correlation between participants' spectral power scores at frontal electrodes and their performance in reading, phonological, and spelling tasks. Results indicated a significant positive correlation between the results of the letter/word identification test and alpha 2, $r = 0.32$, $t(40) = 2.2$, $p < 0.05$, alpha 3, $r = 0.4$, $t(40) = 2.8$, $p < 0.01$, and beta 2, $r = 0.31$, $t(40) = 2.11$, $p < 0.05$ (see Table 3.3). There were also significant correlations between the performance on the passage comprehension test and alpha 2, $r = 0.31$, $t(40) = 2.13$, $p < 0.05$, alpha 3, $r = 0.4$, $t(40) = 2.77$, $p < 0.01$, and beta 1, $r = 0.39$, $t(40) = 2.71$, $p < 0.01$. The results of the reading fluency test as well showed a significant positive correlations with alpha 2, $r = 0.34$, $t(40) = 2.28$, $p < 0.05$, alpha 3, $r = 0.37$, $t(40) = 2.52$, $p < 0.05$, and beta 1, $r = 0.32$, $t(40) = 2.19$, $p < 0.05$. Similarly, the York

assessment of reading comprehension results showed a comparable positive correlations with alpha 2, $r = 0.33$, $t(40) = 2.26$, $p < 0.05$, alpha 3, $r = 0.47$, $t(40) = 3.74$, $p < 0.01$, and beta 1, $r = 0.46$, $t(40) = 3.36$, $p < 0.01$. Finally, there was also a significant positive correlations between performance on the word attack test and alpha 3, $r = 0.33$, $t(40) = 2.27$, $p < 0.05$, as well as between the results of the sound awareness test and alpha 2, $r = 0.32$, $t(40) = 2.15$, $p < 0.05$, and alpha 3, $r = 0.37$, $t(40) = 2.56$, $p < 0.05$.

Discussion

The current study examined physiological differences in resting-state spontaneous oscillatory brain activity in children who tested positive for phonological dyslexia relative to a group of healthy children. Specifically of interest were: a) the distribution of the spectral EEG amplitudes at individual frequencies (i.e., delta, theta, alpha, beta and gamma) in the group with dyslexia relative to control, b) behavioural test-scores in the group with dyslexia and dependence of test scores on participant's chronological age and, c) a possible correlation between the behavioural test-scores and the frequency power data of the group with dyslexia.

As a result, there was reduced delta, theta, alpha1, alpha2, beta2, and gamma frequencies in frontal and temporal (eyes-closed and -open conditions) regions in dyslexia relative to control participants. In contrast, enhanced alpha 1 and alpha 3 frequencies in participants with dyslexia were found over central and parietal-occipital electrodes. The gamma activity was always reduced in participants with dyslexia, regardless of the brain region.

The observed reduction in oscillatory activity in frontal brain regions is descriptive of several dyslexia-related changes in brain functioning. Cavanagh and Frank (2014) showed that cognitive control is normally expressed as theta activity in frontal brain areas (note though that these authors measured task-related theta activity and not resting state). Cognitive, or executive, control refers to the ability to control, integrate, and regulate several

functions and behaviours and to suppress task-irrelevant information (see also Welsh et al., 1991). Theta activity in the frontal cortex has normally been linked to both cognitive control and language regulation processes in the brain (Kim et al., 2019; Nardone et al., 2011). For instance, Nardone and colleagues (2011) used Transcranial Magnetic Stimulation and theta-burst stimulation protocol over frontal brain regions (dorsolateral prefrontal cortex) in a bilingual patient showing pathologic language switching. They found that excitatory left dorsolateral prefrontal cortex stimulation resulted in the reduction of pathological language switching (i.e., resulted in improved performance). Based on these previous studies, the observed reduction in the theta band frequency in the current study could reflect dysfunction in these frontal areas, which could lead to a reduction in cognitive control and consequently be reflected in difficulties with language processing in dyslexia participants.

This theory is supported by previous literature. For instance, Dhar and colleagues (2010) used a Go-Nogo cognitive control task to show that participants with dyslexia show no control-related P3 ERP component during the processing of Nogo trials (i.e., trials that required activation of executive control to inhibit a prepotent response). The P3 in Nogo trials of healthy controls is a marker of cognitive control and response suppression. The absence of the P3 during a Nogo task in dyslexia, on the other hand, can, therefore, be interpreted as hindered cognitive control. As successful executive functioning is necessary for the combination of information from different networked areas, such as the language network (Ye & Zhou, 2009), it stands to reason that dysfunction in theta in frontal areas could be a neural marker of disruptive processes in language production or comprehension (see Nardone et al., 2011). Varvara and colleagues (2014) found that participants with dyslexia have substantially reduced performance on several executive control task (such as verbal and phonological fluency, auditory attention, visual and verbal working memory). Therefore, the current conclusion about the functional relationship between reduced theta activity in frontal

regions and cognitive control in dyslexia supports the previous literature on diminished cognitive control in this disorder. More specifically, despite relatively poor spatial resolution of the EEG, it can be hypothesized that the abnormal pattern of activity over the frontal regions in dyslexia is indicative of deficient cognitive control (for example, the suppression of task-irrelevant information), which spills over to other cognitive tasks, including inefficient language performance. However, more empirical evidence would be necessary to support this hypothesis.

Another pronounced dyslexia-specific difference in brain activity was found in the alpha frequency band. Alpha is the dominant oscillatory activity and is normally descriptive of many cognitive functions including perception (Benwell et al., 2019; Samaha et al., 2017; Samaha & Postle, 2015), attention (Foxe & Snyder, 2011; Keitel et al., 2019) and memory (Jokisch & Jensen, 2007; Klimesch, 2012; Mahé et al., 2012). As discussed earlier, alpha can selectively inhibit processing of task-irrelevant information in event-related designs (Jensen & Mazaheri, 2010; Klimesch et al., 2007) by regulating cortical excitability (Haegens et al., 2011; Lange et al., 2013). It was also suggested previously that the alpha oscillatory activity could also be split into several functionally distinct sub-components. For example, Klimesch (1999) suggested that the low- (~8–10 Hz) alpha frequency is normally sensitive to the modulation of cortical arousal and vigilance, while high- alpha frequency (~10–12 Hz) is involved in phonological, semantic, and lexical processes. Furthermore, higher alpha band is characteristic of cognitive processes that involve semantic long-term memory (Klimesch, 1996). Therefore, the observed reduction in alpha3 frequency in frontal brain regions is in line with the observed hindered phonological, semantic, and lexical behavioural task performance in phonological dyslexia.

One of the highly relevant frontal lobe regions is Broca's area, which, as previously discussed, is consistently associated with speech production (Kennison, 2017) and is an

integral part of the language network. Previous studies showed that Broca's area is highly active during phonological tasks (Goucha & Friederici, 2015; Rumsey et al., 1992). Flinker et al. (2015) used intracranial EEG recordings and showed that gamma activity measured at Broca's area correlated with performance on reading of pseudowords in participants with dyslexia. Therefore, reduced gamma power in the frontal brain region in the current study may, at least partially, come from the hindered performance of Broca's area and reflect difficulties in phonemic encoding in dyslexia (Lehongre et al., 2011).

Similarly, altered frontal delta activations in dyslexia might be linked to deficient processing of slow-rate speech information (Goswami et al., 2011), and abnormalities in theta oscillations were consistently shown to be associated with reading difficulties (Arns et al., 2007; Goswami, 2011; Klimesch, 1999; Penolazzi et al., 2008). It is reasonable to suggest that the observed reduced oscillatory activity in frontal regions in the current study could partly result from hindered functioning of Broca's area in dyslexia and could reflect dyslexia-specific flaws in the core neurophysiological correlates of linguistic processing (understanding of phonological information), as well as semantic, and syntactic processing. However, more empirical evidence is necessary to establish a causal relationship.

Additionally, it was hypothesized that the thalamus is the origin of alpha oscillations and thalamocortical structures further up- or down-regulate alpha's involvement in cognitive functions (Bollimunta et al., 2011; Vijayan et al., 2013). The thalamus connects sensory organs to areas of primary sensory processing. Furthermore, thalamic nuclei are known to form a hub and bidirectional connections with language-specific brain structures, including the frontal cortex (including the Broca's region), the basal ganglia, and the cerebellum (Barbas et al., 2013). Therefore, the observed reduction in alpha frequency in frontal brain regions in dyslexia could be symptomatic of the disrupted link between language-related frontal brain region(s) and the thalamocortical network. This idea is in line with the findings

of hindered activity in the auditory thalamus in developmental dyslexia (Díaz et al., 2012). Specifically, Diaz and colleagues (2012) showed that participants with dyslexia had reduced activity in the auditory thalamus in response to phonemes.

Interestingly, and in contrast to the pattern of results observed frontally, there was also an increased alpha power at central and parietal-occipital brain regions. This increased alpha power is consistent with the work of Haegens and colleagues (Haegens et al., 2014) who showed that an increase in alpha in parietal and occipital brain regions is associated with enhanced cognitive demands in healthy controls. In more detail, these authors tested alpha oscillations in a large group of healthy participants who participated in the following conditions: resting state, passive viewing of visual stimuli, and a working memory task (Haegens et al., 2014). As a result, they found an increase in alpha peak frequency over parietal and occipital brain regions in all three experimental conditions. This further supports that an increase in alpha at central and parietal-occipital brain regions may indeed be a marker of increased cognitive demand (Haegens et al., 2014). This increase in cognitive demand at rest comes from hindered inhibitory and cognitive control in dyslexia as also discussed above. Consequently, the findings of increased alpha power in dyslexia in parietal and occipital brain regions may be suggestive of increased cognitive efforts in dyslexia to inhibit irrelevant information and maintain brain homeostasis during rest.

Our results also point to hemisphere-specific differences in various frequency bands in dyslexia and control participants. For instance, relative to control, participants with dyslexia had larger alpha over the left hemisphere and reduced alpha over the right hemisphere (i.e., the group with dyslexia resulted in reduced alpha in the right hemisphere). These results are in line with previous findings by Duffy et al. (1980) who found increased alpha in the left hemisphere (temporal, parietal, central and frontal areas) in dyslexia. Similarly, González et al. (2018) also found reduced alpha in the right relative to the left

hemisphere of the group with dyslexia, while this effect was reversed for control participants. Previous studies showed that language production and syntax processing are primarily localized in the left hemisphere or show marked left hemisphere lateralization (Toga & Thompson, 2003). For instance, Schurz et al. (2015) found a reduced connectivity pattern in the left hemisphere of dyslexia participants. Therefore, I interpreted the increased alpha power in the left hemisphere as a compensatory mechanism of reduced connectivity in the language network in dyslexia (Schurz et al., 2015), as well as hindered links between thalamocortical structures and frontal brain areas (see above).

Additional hemisphere analysis in frontal and parietal-occipital brain regions between the two groups showed that healthy controls had higher alpha activity in the right relative to the left hemisphere, while no such asymmetry was found for the group with dyslexia. The findings in the control group are consistent with previous observations of higher alpha amplitudes over the right than left posterior regions (Louis et al., 2016). On the other hand, it is possible that the group with dyslexia did not show such a hemisphere-specific dissociation due to an overall increased level of alpha in this group. In other words, the participants with dyslexia could have reached a ceiling level of alpha in both hemispheres and therefore showed no cross-hemispheric dissociation.

One of the possible explanations for the inconsistencies observed in previous EEG literature in developmental dyslexia could be related to differences in sample size. Specifically, previous studies used sample sizes that were either relatively small or modest (e.g., three participants with dyslexia and three controls, Karim et al., 2013; 6 participants with dyslexia and no controls, Nazari et al., 2012; 21 participants with dyslexia and 19 controls in Papagiannopoulou & Lagopoulos, 2016) or did not match the number of participants with dyslexia and healthy controls (e.g., 23 participants with dyslexia that were compared against only 11 controls, Babiloni et al., 2012). Also, as mentioned, previous

studies have found functional differences in brain activity via fMRI when dyslexia samples were divided into subcategories based on the presentation of marked phonological deficits or their absence (van Ermingen-Marbach et al., 2013). I argued that the neural markers identified above may reflect the inclusion criteria and, thus, be a reflection of neural markers of dyslexia with marked phonological dysfunction. In contrast to previous studies, the current study tested both relatively large and precisely matched samples of dyslexia and healthy controls (N = 47 in each group) and controlled for several potential limitations of previous studies. Therefore, future studies should aim to replicate the methods of the current work to ensure to test appropriate sample sizes, match the number of dyslexia and control participants, and potentially take steps to ensure a more homogenous sample in the group with dyslexia.

The analysis of the behavioural test scores revealed a strong negative dependency of all age-corrected test scores on the chronological age of participants in the group with dyslexia with older subjects showing significantly lower test scores when controlled to their age-matched peers than younger subjects. The observed effect indicates that the children with dyslexia, when compared to their healthy peers, are continuously falling behind at a near-constant rate throughout the ages of 7 to 15 years tested in this study. This observation could come about via two possible scenarios. On the one hand, it is possible that reading, phonological processing, and spelling development stops at a certain age in participants with dyslexia and does not develop any further. Alternatively, it is also possible that participants with dyslexia do improve their skills, but at a much slower rate than healthy controls. The correlation of chronological age and raw performance scores provide evidence in favour of the latter option. Specifically, these analyses showed that participants with dyslexia do improve their performance as a function of age, but such improvement does not occur fast enough. In other words, these results are a clear demonstration that children with

developmental dyslexia with marked phonological impairments that are in receipt of the best current treatment (remedial instruction) can continue to gain skills but at a largely reduced rate when compared to their peers.

Additional correlation analyses revealed several positive correlations between alpha2, alpha3 and beta1 power values and reading tasks, as well as phonological tasks. Increased power in these frequency bands was positively correlated with improved reading and phonological test performance. These findings imply that the strength of power scores is related to successful performance on perceptual and cognitive tasks (i.e., letter/word identification test, passage comprehension test, reading fluency test, York reading comprehension test, word attack test, and sound awareness test; Bornkessel et al., 2004; Cecere et al., 2015). These findings are consistent with previous research. In more detail, participants with higher alpha power and/or peak alpha frequency scores have also previously been shown to perform better on memory tests (see also Klimesch, 1999) and general intelligence tests (Grandy et al., 2013; Grandy et al., 2013). Increased alpha frequency has also been linked to more demanding word processing tasks (Drijvers et al., 2016). Therefore, the observed correlation between behavioural performance and alpha frequency reflects the involvement of this frequency band in dyslexia-related linguistic processing. Additionally, future studies could use the above-mentioned reading and phonological tests to track neuronal markers of language-related impairments in dyslexia.

The current results also indicated that participants showed enhanced alpha oscillations in the eyes-closed relative to –open condition. Alpha is dominant in humans, and its activity is significantly reduced during the eyes-open condition (Adrian & Matthews, 1934; Berger, 1929). Alpha is suppressed by visual stimulation during the eyes-open state, which is to be expected. Previous studies have not accounted for this factor, and it was not clear whether the relatively inconsistent findings regarding dyslexia-related changes in brain activity could at

least partially be accounted for by this factor. Therefore, in the current work, it is shown for the first time that dyslexia-related brain activations were comparable in the two conditions (eyes-open, closed). In other words, the observed behavioural alterations in participants with dyslexia may not be related to the overall state of alertness (Schwabedal et al., 2016).

Summary

To summarize, these findings confirm that the resting state EEG of children with phonological dyslexia differ when compared to healthy controls in frontal, central and temporal brain regions. These alterations in brain activity reflect hindered cognitive control and inhibitory processes in dyslexia, which, in turn, influence many other cognitive functions, including reading, phonological processing, language, and working memory. These neurophysiological correlates of dyslexia could be used as an effective tool to both guide therapy of dyslexia and measure the success of its outcome. Specifically, as mentioned in Chapter 1, a clinician could develop a neurofeedback therapy protocol that would explicitly target the brain areas that show deviant hypo- or hyper-activation in children with dyslexia relative to healthy controls. Subsequently, the effectiveness of such therapy could be examined by the corresponding alterations in brain activity and by an association of the therapy-induced changes in neurophysiology and its association with behavioural task performance in children with dyslexia. These questions, therefore, will be further addressed in Study 2 in the next chapter of the current thesis.

Table 3.1

Pairwise comparisons of dyslexia and control groups across different regions and conditions

Condition	Regon	Frequency	t-value	Sig.	Difference
EC	Central	alpha1	-2.33	0.02	-1.43
EC	Central	alpha2	-0.85	0.40	-0.55
EC	Central	alpha3	0.69	0.50	0.46
EC	Central	beta1	-0.16	0.87	-0.09
EC	Central	beta2	0.73	0.47	0.34
EC	Central	delta	-1.26	0.21	-0.85
EC	Central	gamma	3.78	0.00	1.80
EC	Central	theta	-2.31	0.02	-1.27
EC	Frontal	alpha1	0.88	0.38	0.55
EC	Frontal	alpha2	2.28	0.03	1.45
EC	Frontal	alpha3	3.08	0.00	1.90
EC	Frontal	beta1	2.12	0.04	1.13
EC	Frontal	beta2	2.75	0.01	1.26
EC	Frontal	delta	1.37	0.17	0.94
EC	Frontal	gamma	6.21	0.00	2.72
EC	Frontal	theta	0.98	0.33	0.60
EC	Parietal-Occipital	alpha1	-1.78	0.08	-1.13
EC	Parietal-Occipital	alpha2	-1.86	0.07	-1.29
EC	Parietal-Occipital	alpha3	-1.87	0.07	-1.27
EC	Parietal-Occipital	beta1	-0.49	0.63	-0.26
EC	Parietal-Occipital	beta2	0.96	0.34	0.37
EC	Parietal-Occipital	delta	-1.04	0.30	-0.70
EC	Parietal-Occipital	gamma	4.14	0.00	1.54
EC	Parietal-Occipital	theta	-1.60	0.11	-0.94
EC	Temporal	alpha1	3.27	0.00	1.99
EC	Temporal	alpha2	2.18	0.03	1.37
EC	Temporal	alpha3	1.74	0.09	1.13
EC	Temporal	beta1	3.19	0.00	1.74
EC	Temporal	beta2	4.83	0.00	2.07
EC	Temporal	delta	3.52	0.00	2.29
EC	Temporal	gamma	5.93	0.00	2.46
EC	Temporal	theta	3.91	0.00	2.17
EO	Central	alpha1	-3.89	0.00	-2.06
EO	Central	alpha2	-2.56	0.01	-1.36
EO	Central	alpha3	-2.68	0.01	-1.57
EO	Central	beta1	-1.32	0.19	-0.70
EO	Central	beta2	-0.50	0.62	-0.22
EO	Central	delta	-1.51	0.14	-1.15
EO	Central	gamma	2.66	0.01	1.11
EO	Central	theta	-2.91	0.01	-1.41
EO	Frontal	alpha1	1.25	0.22	0.71

EO	Frontal	alpha2	2.51	0.01	1.38
EO	Frontal	alpha3	1.25	0.22	0.72
EO	Frontal	beta1	2.60	0.01	1.45
EO	Frontal	beta2	4.18	0.00	2.03
EO	Frontal	delta	1.97	0.05	1.51
EO	Frontal	gamma	6.08	0.00	3.02
EO	Frontal	theta	2.22	0.03	1.19
EO	Parietal-Occipital	alpha1	-2.99	0.00	-1.68
EO	Parietal-Occipital	alpha2	-2.56	0.01	-1.42
EO	Parietal-Occipital	alpha3	-3.75	0.00	-2.12
EO	Parietal-Occipital	beta1	-1.49	0.14	-0.72
EO	Parietal-Occipital	beta2	1.20	0.23	0.42
EO	Parietal-Occipital	delta	-1.59	0.12	-1.14
EO	Parietal-Occipital	gamma	3.99	0.00	1.51
EO	Parietal-Occipital	theta	-2.20	0.03	-1.19
EO	Temporal	alpha1	3.46	0.00	1.95
EO	Temporal	alpha2	4.00	0.00	2.23
EO	Temporal	alpha3	1.88	0.06	1.07
EO	Temporal	beta1	2.86	0.01	1.49
EO	Temporal	beta2	4.49	0.00	2.03
EO	Temporal	delta	3.47	0.00	2.59
EO	Temporal	gamma	4.26	0.00	2.03
EO	Temporal	theta	4.77	0.00	2.45

Note. The data for each region include both hemispheres of each subject. Note that the table contains original (non-corrected) p-values.

Table 3.2

Pairwise comparisons of dyslexia and control groups across hemispheres and conditions

Condition	Hemisphere	Frequency	t-value	Sig.	Difference
EC	Left	alpha1	-3.26	0.00	-1.98
EC	Left	alpha2	-3.86	0.00	-2.34
EC	Left	alpha3	-3.82	0.00	-2.33
EC	Left	beta1	-2.52	0.01	-1.36
EC	Left	beta2	-1.53	0.13	-0.69
EC	Left	delta	-2.16	0.03	-1.44
EC	Left	gamma	1.14	0.26	0.52
EC	Left	theta	-3.02	0.00	-1.72
EC	Midline	alpha1	0.32	0.75	0.21
EC	Midline	alpha2	3.17	0.00	2.40
EC	Midline	alpha3	5.28	0.00	3.79

EC	Midline	beta1	4.02	0.00	2.02
EC	Midline	beta2	4.92	0.00	2.02
EC	Midline	delta	1.15	0.25	0.81
EC	Midline	gamma	8.06	0.00	3.61
EC	Midline	theta	0.25	0.81	0.15
EC	Right	alpha1	2.23	0.03	1.31
EC	Right	alpha2	1.55	0.12	0.94
EC	Right	alpha3	1.38	0.17	0.87
EC	Right	beta1	2.44	0.02	1.30
EC	Right	beta2	4.18	0.00	1.68
EC	Right	delta	2.39	0.02	1.51
EC	Right	gamma	7.02	0.00	2.55
EC	Right	theta	2.78	0.01	1.48
EO	Left	alpha1	-3.61	0.00	-1.95
EO	Left	alpha2	-3.00	0.00	-1.59
EO	Left	alpha3	-4.53	0.00	-2.47
EO	Left	beta1	-2.49	0.02	-1.29
EO	Left	beta2	-0.49	0.62	-0.22
EO	Left	delta	-1.77	0.08	-1.29
EO	Left	gamma	1.30	0.20	0.58
EO	Left	theta	-2.94	0.00	-1.45
EO	Midline	alpha1	-1.61	0.11	-0.93
EO	Midline	alpha2	-0.14	0.89	-0.08
EO	Midline	alpha3	0.00	1.00	0.00
EO	Midline	beta1	2.12	0.04	1.04
EO	Midline	beta2	2.84	0.01	1.17
EO	Midline	delta	0.48	0.63	0.36
EO	Midline	gamma	6.32	0.00	2.95
EO	Midline	theta	-0.30	0.77	-0.17
EO	Right	alpha1	2.51	0.01	1.35
EO	Right	alpha2	3.25	0.00	1.73
EO	Right	alpha3	1.39	0.17	0.77
EO	Right	beta1	2.43	0.02	1.28
EO	Right	beta2	5.06	0.00	2.04
EO	Right	delta	2.30	0.02	1.72
EO	Right	gamma	6.20	0.00	2.46
EO	Right	theta	3.51	0.00	1.74

Note. The data for each hemisphere include all regions of each subject. Note that the table contains original (non-corrected) p-values.

Table 3.3

Correlation table

	Alpha 1	Alpha 2	Alpha 3	Beta 1	Beta 2	Gamma	Delta	Theta	Age
Letter/Word Identification	0.21	0.32 *	0.41 **	0.27	0.32 *	0.20	-0.08	0.14	0.74 **
Passage comprehension	0.22	0.32 *	0.40 **	0.39 **	0.24	0.06	-0.05	0.18	0.65 **
Reading Fluency	0.19	0.34 *	0.37 *	0.33 *	0.26	0.22	0.08	0.16	0.78 **
YARC Reading accuracy	0.08	0.17	0.22	0.11	0.16	0.05	-0.16	0.04	0.63 **
YARC Passage Comprehension	0.25	0.34 *	0.47 **	0.46 **	0.22	0.018	-0.03	0.18	0.41 **
YARC Passage Fluency	0.05	0.14	0.15	0.09	0.19	0.10	-0.15	0.001	0.74 **
WJ Word Attack	0.15	0.28	0.33 *	0.11	0.11	0.08	-0.18	0.07	0.71 **
WJ Sound awareness	0.22	0.32 *	0.37 *	0.16	0.13	0.17	-0.17	0.17	0.33 *
Phonemic decoding efficiency	0.13	0.17	0.15	0.13	0.30 *	0.21	-0.04	0.07	0.53 **
WJ Spelling	0.04	0.20	0.16	0.01	0.10	0.19	-0.09	-0.06	0.70 **
WJ Spelling sounds	0.03	0.09	0.05	-0.24	-0.21	-0.03	-0.31	-0.08	0.34

Note * - $p < 0.05$; ** - $p < 0.01$

Supplementary Material

Reading:

a) Woodcock-Johnson – Letter/Word Identification (Test 1)

b) Woodcock-Johnson – Passage comprehension (Test 9)

c) Woodcock-Johnson – Reading Fluency (Test 2)

d) York Assessment of Reading for Comprehension – Reading accuracy

e) York Assessment of Reading for Comprehension – Passage Comprehension

f) York Assessment of Reading for Comprehension – Passage Fluency

Phonological skills:

a) Woodcock-Johnson – Word Attack (reading of non-words Test 13)

b) Woodcock-Johnson – Sound awareness (identification and manipulation of sounds Test 21)

c) Test of Word Reading Efficiency–Second Edition (TOWRE 2) – Phonemic decoding efficiency

Spelling:

a) Woodcock-Johnson – Spelling (test 7)

b) Woodcock-Johnson – Spelling Sounds (Test 18)

Chapter 4. Study 2

LORETA Z-Score Neurofeedback Training as a Treatment for Dyslexia: A Randomized Control Trial

Abstract

Previous studies showed that developmental dyslexia leads to alterations in behavioural performance (e.g., reading, spelling, phonological tasks) and electrical neural brain functioning (e.g., increase in the alpha frequency band in frontal electrodes). The current study examined whether twenty sessions of LORETA z-score neurofeedback therapy can reduce the behavioural and neural markers of phonological dyslexia. For this purpose, 29 participants with dyslexia were split into therapy (N = 15) and control (N = 14) groups with a waitlist control design. The therapy group received 20 LORETA z-score neurofeedback training sessions. Analysis of behavioural performance revealed that the therapy group had improved phonological and spelling task performance at T2 relative to T1 (Time x group interaction). Additionally, a comparison of correlation strength between participants' age-adjusted test scores and their chronological age showed that, relative to the control group, the correlation between T1 and T2 was weaker in the therapy group. These results indicate that performance in the therapy group improved after neurofeedback training; that is, there was a reduction in dyslexia-related deficits as measured by behavioural tasks. Additionally, it was also found that the therapy resulted in an increase in power at frontal regions across all frequency bands (alpha, beta, theta, gamma, delta). These findings imply that LORETA z-score neurofeedback training may be an effective method to improve behavioural (phonological, spelling) markers of dyslexia.

Keywords: Dyslexia, Alpha, EEG, time-frequency

Introduction

Individuals with dyslexia experience difficulties with reading, writing, and spelling while simultaneously having average or better cognitive abilities and intelligence (Sahari & Johari, 2012). Dyslexia is thought to have neurological rather than psychological origins (Fletcher et al., 2011; Gvion & Friedmann, 2010) and is estimated to affect over 10% of the world population (American Psychiatric Association, 2013; De Santana et al., 2012; Klein & Shaywitz, 2005). Due to the high prevalence of dyslexia and the importance of language for successful daily functioning, various studies have attempted to study the neural underpinnings of this disorder.

For instance, Arns and colleagues (2007) used electroencephalographic measurements (EEG) to study resting state (eyes open) brain activity in a group of participants with dyslexia and control participants. They reported increased slow theta and delta activity in the frontal and right temporal brain areas, as well as increased beta activity in the frontal brain areas in the group with dyslexia relative to a control group. Resting-state theta oscillations could be related to working memory performance and to aspects of the regulation of cortical excitability (Arnal et al., 2011; Arnal & Giraud, 2012; Klimesch, 1999; O'Keefe & Burgess, 1999). Studies on cognitive conflict processing usually report enhanced theta activation over frontal and central brain regions (mid-cingulate cortex, medial prefrontal cortex) during the processing of incongruent information (Cavanagh & Frank, 2014). Therefore, enhanced activity (measured at resting state) in this brain region may imply difficulties with cognitive control. Furthermore, delta oscillations in frontal brain areas that could potentially be linked to the anterior cingulate cortex have been associated with attentional regulation (Knyazev et al., 2009; Knyazev, 2007) and response inhibition (Kamarajan et al., 2005; Knyazev, 2007; Putman, 2011). Finally, Arns and colleagues (2007) proposed that the observed dyslexia-

related activation differences in theta, beta, and delta frequency bands could reflect compensatory processing used to overcome disorder-related impacts on reading and writing.

This interpretation of findings, as it relates to the beta frequency, was supported in a subsequent study by Fadzal and colleagues (2012) who found enhanced beta activity in children with dyslexia relative to typically developing children at central and parietal electrodes; however, in this study brain activity was observed during writing performance in children with dyslexia. Beta oscillations are normally suppressed during motor tasks in healthy controls (R. Salmelin & Hari, 1994; Stancák & Pfurtscheller, 1995). Consequently, the fact that participants with dyslexia demonstrated enhanced beta during writing (i.e., in Fadzal et al., 2012) suggests that they may have difficulties with motor control. It may be that people with dyslexia may require additional neural resources to coordinate a motor task.

A more recent work by Papagiannopoulou and Lagopoulos (2016) compared the EEG power spectrum between pre-adolescents with dyslexia and typically developing controls during an eyes closed, resting state. The results partially replicated Babiloni et al. (2012) and indicated decreased EEG power in the left hemisphere for both the alpha range (8-10 Hz) and beta (12.5-30 Hz) oscillations in the group with dyslexia. Additionally, the group with dyslexia showed significantly increased theta oscillations in the left hemisphere. Therefore, the work by Papagiannopoulou and Lagopoulos (2016) showed which brian oscillations were compromised in dyslexia.

The discussed neurophysiological studies of dyslexia found that various frequency bands show abnormal patterns of activity in this disorder. One of the most consistent findings is in the alpha frequency. Alpha activity originates in the thalamus, which regulates the role of normal alpha rhythm in cognitive operations (Bollimunta et al., 2011; Vijayan et al., 2013). Under-activation of the auditory thalamus is a known characteristic in individuals diagnosed with dyslexia (Díaz et al., 2012). Further, alpha oscillations in frontal brain regions

could be descriptive of the processes related to the comprehension and production of language-related information (Drijvers et al., 2016). For instance, frontal alpha is enhanced in response to shortened, relative to complete, forms of words (e.g., yeshay for yesterday; Drijvers et al., 2016), reflecting additional neural resources necessary to process non-standard (i.e., shortened) words. Consistently, dyslexia has been associated with altered cortical oscillations in the alpha band. Klimesch et al. (2001) showed that, relative to healthy controls, participants with dyslexia showed a reduction in alpha power over frontal and central regions when reading words and pseudowords. Based on previous findings in healthy controls, alpha measured over frontal brain regions reflects the degree of attentional involvement and attentional modulation (Misselhorn et al., 2019) and, thus, the reduction of alpha during reading tasks in dyslexia may represent attentional difficulties during encoding of words in these participants (Klimesch et al., 2001). Furthermore, Freunberger et al. (2008) showed that the upper alpha oscillations (9-13 Hz) recorded over the frontal brain region (Fp1, F7, F3, Fc3, Fp2, F8, F4, Fc4) was associated with semantic access and retrieval of information from long-term memory. Similarly, Klimesch and colleagues (2010) showed that theta - alpha phase coupling is associated with processes in semantic long-term memory. As a short summary, alpha frequency could serve as a marker of various cognitive processes (e.g., retrieval of semantic information, attentional processes and encoding of words) that are affected in dyslexia and therefore may be descriptive of the specific dysfunctions in this disorder.

Likewise, previous studies demonstrated how dyslexia alters the expression of gamma frequencies (Lehongre et al., 2013). Gamma oscillations reflect the integration of sensory information (e.g., perceptual binding of visual and auditory word representation; Brovelli et al., 2005; Jensen et al., 2007; Sokolov et al., 2004). Flinker et al. (2015) demonstrated that individual gamma frequencies measured at Broca's area (IFG, frontal brain region) were

positively correlated with performance in the reading of pseudowords in participants with dyslexia. Therefore, the reduced power of gamma in frontal brain regions can be associated with hindered reading performance in dyslexia.

Finally, my recent work (see Study 1) indicated that participants with dyslexia had altered brain activations over various brain regions and frequency bands. Specifically, I used resting-state EEG recordings (eyes open, closed) in a large group of dyslexia and control participants, and found that relative to healthy controls, participants with dyslexia exhibited reduced power in the delta, theta, alpha1, alpha2, alpha3, beta1, and beta2 frequencies when measured over frontal (Fp1, Fp2, F7, F3, Fz, F4, F8) and temporal (T3, T4, T5, T6) electrodes. This pattern of activities was reversed in the central (C3, Cz, C4) and parietal-occipital areas (P3, Pz, P4, O1, O2) and results indicated that delta, theta, alpha1, alpha2, alpha3, beta1, and beta2 activity was enhanced in those regions. On the other hand, gamma resulted in a reduced pattern of activity in all brain regions. In other words, and to summarize the findings described so far, it seems that, relative to control participants, children with dyslexia show alterations in normal brain functioning across a range of different frequency bands and electrode sites.

Various interventions have been developed to treat dyslexia, including training of phoneme awareness, reading fluency, reading comprehension, and word analysis techniques, (Snow et al., 1998). Based on the child's specific deficits, an individual plan that combines these treatments is developed, and the therapies are usually given in the form of extra-curricular tutoring, which is the current best form of treatment available. The effectiveness of the treatments might depend on the time of intervention onset, with better outcomes for treatments that start earlier in life (Wanzek & Vaughn, 2007). One of such treatments for dyslexia is neurofeedback.

Neurofeedback Training

Neurofeedback is a training method in which participants are fed back information regarding their brain activity in real-time on a computer monitor, or via sound or touch, thus providing participants with a proxy of their current brain oscillatory activation. For instance, a proxy could be expressed as a visual image presented to participants that will change its colour, shape, or luminance (e.g., becomes brighter or darker) depending on a specific activity (e.g., alpha frequency compared to reference parameters) in the specific brain region (e.g., left IFG). Therefore, the goal of the treatment is to gradually improve participants' brain activity in a specific task by using the principles of operant conditioning (Sherlin et al., 2011). Notably, the ability to regulate one's brain activity can also be translated into improved cognitive and behavioural performance (Enriquez-Geppert et al., 2017). More specifically, neurofeedback training has shown to improve working memory (Hsueh et al., 2016), long-term memory (Guez et al., 2015), as well as executive functioning (Enriquez-Geppert et al., 2014, 2017).

An advanced neurofeedback training method/protocol is the qEEG guided Low-Resolution Electromagnetic Tomography (LORETA) z-score neurofeedback protocol (e.g. Budzynski et al., 2009). As previously discussed in Chapter 2, the LORETA provides a real-time 3D image of participants' brain activity by plotting current source densities of each of the voxels. LORETA is able to provide the researchers with a real-time description of participants' brain activations (e.g., measures of coherence, asymmetry, and amplitude), which allows for training of activity in specific brain areas (see Table 1 and Methods section below for more details; Krigbaum & Wigton, 2014; Thatcher, 2010).

The activity in specific brain regions that are selected for training in participants with dyslexia could be evaluated in z-score deviations from an objective healthy controls' baseline (hence the z-score neurofeedback; Cannon et al., 2006; Collura, 2010). In other words, the

information from each brain area (power, coherence) can be statistically compared against a normative database (e.g., NeuroGuide) of highly-matched healthy controls (Thatcher et al., 2005; Thatcher et al., 2003). Thus, LORETA is able to improve the spatial resolution of EEG substantially (as precise as 7 mm^3; Pascual-Marqui et al., 2002) and also to train patient's performance in the desired direction (i.e., that of healthy controls).

QEEG-guided neurofeedback therapy has been shown to have a beneficial effect on dyslexia. For instance, Breteler and colleagues (2010) tested 19 participants with dyslexia who were split into either a testing group (10 participants) that received the neurofeedback treatment or a control group that had no neurofeedback treatment (9 participants). Frequency bands and coherence at a number of electrode sites (T3, T4, T6, FC7, FC3) associated with dyslexia were measured, and sites where the participant's own activation pattern was 1.5 z-scores deviant (above, below) from an expected norm, were identified. During neurofeedback therapy, if there was a deviation observed at the corresponding site, the researchers trained delta oscillations at electrode T6, coherence in the alpha- and/or beta band at F7–FC3 or F7–C3 and coherence in all frequencies at T3–T4 in the testing group. Results indicated that the neurofeedback group showed significantly improved performance in a spelling task, but there was no significant improvement in reading. Further, no changes in the EEG power and coherence over frontocentral or temporal electrodes were reported. On the other hand, they found a significant increase of alpha coherence, which they interpreted as facilitating attentional processes that could account for the improvements in spelling.

In a different study, Walker and Norman (2006) conducted neurofeedback training with 12 participants with dyslexia (but no control group). Participants received 30 to 40 neurofeedback sessions of 10 minutes each. The goal of the treatment was to reduce any abnormalities during a baseline qEEG session. Additionally, the participants were trained to increase 16-18 Hz activity at T3 (left mid-temporal area), which was linked to reading

performance and word-non word discrimination in the past (Binder & Price, 2002; Walker & Norman, 2006). As a result, the study observed significantly improved reading performance in all participants. Specifically, all trained participants significantly improved reading performance in 30 to 35 sessions.

Nazari and colleagues (2012) trained 6 participants with dyslexia to decrease delta and theta and to increase beta at T3 and F7 electrodes. These electrodes were selected as previous dyslexia studies found decreased grey matter density of the temporal lobe (around T3; e.g., Brown et al., 2001). The frequency bands were also selected based on previous studies that reported abnormalities in these oscillations in dyslexia (Arns et al., 2007; Rippon & Brunswick, 2000). Nazari and colleagues reported that 20 sessions of neurofeedback training improved reading and phonological awareness skills in all 6 participants with dyslexia (Nazari et al., 2012). On the other hand, the EEG analysis revealed no training-related improvements in the power of the frequency bands of interest (delta, theta, and beta). Thus, in this study, there was a therapy-related normalization of coherence in the theta band at T3-T4, delta band at Cz-Fz, and beta band at Cz-Fz, Cz-Pz, and Cz-C4. It should be noted that there was no control group in this study design, which could have confounded the results since this approach did not account for the effects of procedural learning in behavioural results (i.e., the effect of the same tests being administered before and after the therapy). Specifically, as shown in Study 1 of this dissertation, when tested repeatedly, participants with dyslexia do show slightly improved raw testing scores on many behavioural measures. Although this improvement was smaller for participants with dyslexia than their peers (see Study 1), this should still be tested by a comparison with a healthy control group, which was lacking in the work by Nazari et al. (2012).

Finally, Li and Chen (2017) used neurofeedback on a group of 40 participants with dyslexia who were randomly split equally into therapy and control groups (i.e., 20

participants in each). The goal of the therapy was to strengthen beta waves (15 ~ 18 Hz) and suppressing delta waves (1 ~ 4 Hz) and theta waves (4 ~ 8 Hz) at T3 (temporal region in the left hemisphere; see Walker & Norman, 2006 and Nazari et al., 2012 for comparable approaches). After 20 neurofeedback sessions (30 minutes each, three times per week), participants in the therapy group, relative to control group, exhibited reduced levels of aggression when reading words and text (but no improvements in reading performance per se). These results demonstrate that neurofeedback can also improve disorder-unspecific properties (e.g., level of aggression) and may have a beneficial effect on future reading performance. That is, the effect of neurofeedback could have been expressed at a later time-point after the end of the therapy due to modulation of the soft-skills.

To summarize, few studies have examined the effect of neurofeedback on dyslexia. These studies showed that neurofeedback improved spelling tasks, but not reading task performance (Breteler et al., 2010), significantly improved reading performance (Walker & Norman, 2006), improved reading and phonological awareness skills (Nazari et al., 2012), as well as reduced levels of aggression (Li & Chen, 2017). On a neurophysiological level, neurofeedback for dyslexia improves alpha coherence (Breteler et al., 2010) and normalizes coherence of the theta, delta and beta bands (Nazari et al., 2012).

Note, however, that most previous studies that examined the effectiveness of neurofeedback in dyslexia either used relatively small samples (6 – 12 participants) and/or included no healthy controls. Additionally, previous neurofeedback and EEG studies discussed above ignored the fact that dyslexia is not a homogeneous disorder and that it may be decomposed into subtypes. As outlined in Chapter 1, there are a number of subtyping schemes. These include dysphonetic and dyseidetic subtypes (Boder, 1973), phonological and surface subtypes (Castles & Coltheart, 1993), subtypes with and without verbal language deficit (Leonard et al., 2002), as well as visual attention span and phonological subtypes

(Bosse et al., 2007; Ramus et al., 2018). This lack of control of dyslexia subtypes could result in the observed lack of consistency in EEG and neurofeedback studies of dyslexia. These previous studies also used a limited number of fixed electrode sites and frequency bands for all participants that were used for the purpose of neurofeedback, which could, of course, limit the effectiveness of previous therapies.

Therefore, the current study tested a sample that was either comparable or slightly larger relative to previous works and included both treatment and control groups, ensuring that the study had enough power to detect significant results. Additionally, to account for the heterogeneity in dyslexia subtypes, in the current work, all participants with dyslexia had a statistically significant deficit in phonological skills (see methods section below). Specifically, I ensured that all participants with dyslexia in the current sample had substantial difficulty in phonological task performance (phonological dyslexia), which was selected because hindered phonological processing is an integral part of all the theories of dyslexia (e.g., rapid auditory processing theory, magnocellular theory, cerebellar hypothesis, see Chapter 1 for more details). Therefore, although the phonological subtype was selected due to the efficiency of classification and ease of interpretation, I can not assert with certainty that the participant sample did not belong to mixed subtypes, but accounting for phonological difficulties was an attempt to ensure at least partial homogeneity of my dyslexia sample.

Given the results of Study 1, which indicated rather global electrical dysfunction in the participants with dyslexia, compared to the control group, the use of the LORETA z-score neurofeedback therapy allowed for the selection of a wide range of brain regions (see Table 1) that were examined to identify deviations in all frequency bands (alpha, beta, theta, gamma, delta) in the treatment sample. The current approach was superior to previous neurofeedback studies, which used a fixed and more limited number of electrodes and frequency bands to train all participants with dyslexia. In other words, LORETA z-score

approach allowed for a more fine-tuned selection of electrodes and frequency bands to account for inter-individual differences in the dyslexia sample.

Finally, an important component of the current study design is that all children included in the study were recruited from the Specific Learning Difficulties Association of South Australia (SPELD SA) Literacy Clinic, which provides one on one tutoring once a week and is the best form and recommended behavioural treatment currently available to treat dyslexia (The Australian Dyslexia Association Inc., 2020). As both the therapy and control group will be in receipt of the current best behavioural therapy, any differences seen between groups can be attributed specifically to neurofeedback therapy. In other words, the fact that all participants received standardized remedial training also controls for the homogeneity of the test and control samples. It thus emphasizes the behavioural and neurophysiological changes that come primarily from the neurofeedback therapy and that cannot be accounted for by other variances in the group.

To summarise, the goal of the current study was to investigate the role of neurofeedback in dyslexia by using an advanced LORETA z-score technique and a homogeneous sample of participants with dyslexia. For this purpose, I randomly split 29 participants with dyslexia into therapy and control groups and tested their reading, phonological, and spelling performance before and after the therapy (the timeframe of testing was identical for the waitlist group). Based on the findings from Study 1, I expected that the therapy would result in enhanced activity in the alpha, theta, delta, and gamma frequencies over the frontal and temporal regions, and reduced alpha activity over the central and parietal-occipital regions. In other words, I hypothesized that neurofeedback should "reverse" the disorder-related differences in oscillatory brain activity.

Additionally, based on previous findings in the neurofeedback literature, I hypothesized training-related improvements in spelling performance (Breteler et al., 2010). It

was not clear whether neurofeedback would also facilitate reading and phonological task performance since previous literature produced inconsistent findings. Nevertheless, Study 1 indicated a significant positive correlation between oscillatory activity in frontal brain regions (e.g., alpha 2, alpha 3, beta1) and behavioural performance on the reading and phonological tasks. Therefore, given the results that neurofeedback increased the power of oscillatory brain activity over the frontal brain region, I hypothesized that participants with dyslexia should show improved reading and phonological task performance.

Materials and Methods

Participants

A total of 29 participants who were diagnosed with dyslexia by a provisional psychologist (N females = 15; N males = 14) took part in this study. They were chosen randomly from the group with dyslexia in Study 1 and randomly divided into two subgroups: a therapy group and a control (i.e., waitlist) group. The age range of all participants was a min = 7.03 years, the maximum age a max =14.15 years, with a mean age of 10.83 years (*SD*=2.17) at the beginning of the study. The therapy group consisted of 15 participants (range 7.03 to 14.15 years), and the waitlist group consisted of 14 participants (range 7.77 to 13.95 years). There was no significant age difference between the two groups ($p > 0.9$).

Given that all participants with dyslexia in the current work also participated in Study 1, they all were diagnosed with dyslexia. As described in Study 1, all participants completed a series of test batteries, including the cognitive and achievement tests (Differential Ability Scales, Second Edition; DAS-II), a phonological awareness test (the Woodcock-Johnson: Third Edition (WJ III) Achievement Test 21) and a reading comprehension test (York Assessment of Reading for Comprehension (Form A) Australian Edition [YARC-Australian]). Phonological dyslexia was diagnosed if there was a significant discrepancy

between intellectual abilities measured by DAS-II[3] (i.e., an IQ score of >80 Elliot, 2007; or a Full-Scale IQ score of >80 from the Wechsler Intelligence Scale for Children – Fourth Edition, WISC-IV, Wechsler, 2004), Verbal IQ as measured either via the Verbal Composite scale of the DAS-II or on the Verbal IQ scale of the WISC-IV (a score of >80) and performance on Verbal Composite or Verbal IQ scales. The discrepancy between the observed (DAS-II, Verbal IQ) and predicted (Verbal Composite, Verbal IQ) scales scores should have been at least 1 *SD* (i.e., observed is smaller than predicted). The final sample consisted of participants who: a) had a diagnosis of dyslexia with phonological impairment, b) had English as a first language, c) had significantly lower reading abilities than what was expected based on IQ (i.e. > 1 *SD* difference), d) were of primary - mid-high school age (approx. age range: 7 – 15 years), and c) were currently receiving remedial reading instruction from SPELD SA's literacy clinic which included 1:1 remedial instruction once a week.

Further exclusion criteria were: a) deficits in hearing or visual acuity, b) oral language impairment (score of <80 on either the Verbal Composite scale of the DAS-II or on the Verbal IQ scale of the WISC-IV), c) IQ < 80 - to exclude "garden-variety poor reader" arising from low IQ, d) motor impairment, e) personal or family history of neurological, psychiatric or psychological impairments (e.g. epilepsy, traumatic brain injury, chronic ill health) and f) current psychoactive medication.

Procedure

This study used a randomized pretest-posttest design, in which behavioural and physiological testing of the participants was performed at two different time points T1 (within ~ 1 week before the treatment onset) and T2 (within ~ 1 week after the treatment was

[3] Note that the WISC was only performed by another psychologist in cases in which a dyslexia participant already had a confirmed diagnosis and provided the report.

over). The therapy group received a total of 20 sessions of LORETA z-score training at a private local psychology clinic (Brain Health Clinics). The goal was to conduct two sessions per week, between 8.30 am – 6 pm, Monday - Saturday, for 10 weeks. The participants in the control group were put on a waitlist for 10 weeks and did not receive LORETA z-score therapy; however, both the therapy and control groups continued to receive remedial reading instruction throughout these 10 weeks. All participants of the therapy and waitlist groups were subject to qEEG and to behavioural testing for their phonological, reading, and spelling skills, at time points T1 (before therapy/wait) and T2 (post-therapy/post-wait period).

Following treatment or wait period, all participants were invited to complete a second assessment (post-treatment assessment) in one session lasting up to three hours. This assessment evaluated the efficacy of behavioural and EEG performance relative to pre-treatment measures. Thus, the total time commitment associated with full participation in this study approximated to be 28 hours each.

Behavioural Tests

Consistent with Study 1, a battery of eleven behavioural tests was used to assess participants' reading, phonological, and spelling performance. The specific tests were chosen because they have been frequently used to assess behavioural symptoms of dyslexia and have high validity and reliability (McGrew & Woodcock, 2001). The reading section of the tests consisted of the letter/word identification and passage comprehension tasks, reading fluency, reading accuracy, passage comprehension, and passage fluency tasks (see Supplementary material section and Methods chapter for discussion on the reliability of tests used). The phonological section of the behavioural tests consisted of the reading of non-words task, sound awareness and phonemic decoding efficiency tasks. Finally, the spelling section of the test consisted of a spelling test and spelling sounds test (see the Methods chapter for a detailed description of each of the psychological tests).

The test scores were analysed both as raw test values (i.e., a 10-year-old pupil gets a score = 10 in a case in which their reading performance is adequate to their age or < 10 if their reading performance is hindered) as well as using an aged-matched-to-performance method. In more detail, the raw test scores (TS) were adjusted for age by subtracting the chronological age (CA) from participants' raw score (age-related metric) on each of the tests (i.e., TSCA; see Study 1 for the comparable analysis). Briefly, the age-corrected test score, TSCA=TS-CA, corresponds to the difference of the test score, TS, and the chronological age, CA, of the participants. The TSCA values are independent of chronological age and represent a direct measure of any gains or deficits with respect to the chronological age of the participants (i.e. 10-year-old pupil performs at the level of 8-year-old normative peers; therefore TSCA=8-10=-2).

LORETA Z-Score Neurofeedback Training

Each participant had an individualized LORETA z-score neurofeedback training protocol based on the regions and frequency bands that were shown to be deviant in each individual participant (Thatcher, 2013). As explained in the Methods chapter, LORETA neurofeedback therapy using Neuroguide allows for the selection of Brodmann areas to be selected and targeted for comparison to the normative database and subsequent therapy (however, see Amunts & Zilles, 2005 for limitations of the use of Brodmann areas). In more detail, each participant's resting-state EEG was first recorded for ~ 5 minutes, and subsequently, the recorded EEG activity for individual participants was compared against the normative database (NeuroGuide, Thatcher et al., 2003) to identify those brain regions that were deviant in each participant. Importantly, the comparison (i.e., amplitude, coherence, phase) was made within a selected subset of brain regions (e.g., Brodmann areas) that were implicated in aspects of language dysfunction, based on the extant literature (see Table 4.1 for the list of Brodmann areas with corresponding named areas). Specifically, a specific brain

area was considered to be deviant if its activity in the dyslexia participant was ≥2 *SD* from parameters of the normative database (see Thatcher et al., 2003). The identified deviant brain regions were then consistently trained during neurofeedback sessions.

Table 4.1

Regions of the brain reported as being involved in language dysfunction.

Brodmann Area (left and right)	Acquired from (Rationale)	Cortex (Electrodes)	Corresponding brain area
6 *L*	Nicolson & Fawcett, 2010	Central	Premotor cortex and Supplementary Motor Cortex
7 *L, R*	Kassubek et al., 2001	Parietal	Somatosensory Association Cortex
9 *L, R*	Kovelman et al., 2012	Frontal	Dorsolateral and medial prefrontal cortex
10 *L, R*	Zinchenko et al., 2018	Frontal	Anterior prefrontal
17 *L, R*	Sprenger-Charolles et al., 2013	Occipital	Primary visual cortex (V1)
18 *L, R*	Sprenger-Charolles et al., 2013	Occipital	Secondary visual cortex (V2)
19 *L*	Horwitz et al., 1998	Occipital	Associative visual cortex (V3, V4, V5)
21 *L, R*	Krafnick et al., 2014	Temporal	Middle Temporal Gyrus
22 *L, R*	Coltheart, 2000	Temporal	Superior temporal gyrus
37 *L*	Centanni et al., 2019	Temporal	Fusiform gyrus
39 *L*	Hampson et al., 2006	Parietal	Angular gyrus
40 *L*	Conway et al., 2008	Parietal	Supramarginal gyrus
41 *L*	Dole et al., 2013	Temporal	Auditory cortex
42 *L, R*	Dole et al., 2013	Temporal	Auditory cortex

44 *L, R*	Saralegui et al., 2014	Frontal	Inferior Frontal Gyrus (IFG) - Pars opercularis - part of Broca's area
45 *L, R*	Saralegui et al., 2014	Frontal	Inferior Frontal Gyrus (IFG) - Pars triangularis - part of Broca's area
46 *R*	Shaywitz et al., 1998	Frontal	Dorsolateral prefrontal cortex
47 *L, R*	Shaywitz et al., 1998	Frontal	Pars orbitalis

As discussed in detail in Chapters 1 and 2, neurofeedback therapy uses a brain-computer interface to feedback information to participants about their current brain electrical activity. When the electrical activity in the areas of interest (see Table 1) changes in the desired direction, participants will receive a reward. Upon arrival at the clinic, participants selected a movie that would later be used during the therapy (either among movies available in the clinic or a movie they could bring from home). The personal selection ensured that participants would be interested in and motivated to watch the movie and would, therefore, be motivated to earn the reward provided. Specifically, dependent upon participant brain activity in the selected brain regions that need to be trained, the brightness of the monitor displaying the movie would adjust and, as such, the child was able to watch the movie at a comfortable brightness level only when a certain reward threshold was met. Each therapy session consisted of 8 rounds at 5 minutes each. The clinician's goal was to ensure that the participant would be rewarded 45 to 55% of the time on average each round. The training strategy was to reduce the z-threshold by 0.1 *SD* when the average per cent reward for the 5 minute round would exceed 55% and to increase it by 0.05 *SD* when the average per cent reward would fall below 45%. For example, if the child started at $z = 2.7$, then the goal for the round would be to train the brain activity down to 2.6 for 55% of the time. Once $z = 2.6$ was achieved for >55% of the round, the z-threshold would be further reduced to 2.5 etc. On the other hand, if

the z-threshold was reduced from 2.7 to 2.6 (please note that individual z-score was dependent upon initial EEG activity) and the reward threshold dropped significantly (below 45% reward), the z-threshold would then be increased. Therefore, in the event that this change of 0.1 *SD* was too difficult (i.e., the success rate at the end of the round was < 45%), then 0.05 *SD* was used (e.g. $z = 2.65$ in the example given above). The training goal is to reduce this z-score as much as possible while staying within these parameters. The end goal of therapy was to have a z-threshold below 0.5 *SD* for eight consecutive rounds (see Kropotov, 2009). Therefore, the feedback supported participants in a reduction of z-scores specifically for those brain regions that were selected for training, thus, normalizing neural activity in the selected brain networks.

A typical LORETA z-score neurofeedback training session then started with the application of the electro-cap. The child sat in a comfortable chair during the head preparation and during the whole training session. Once the child was set up with the cap, the lights were dimmed in the testing room, and the movie started. Note that although the brightness of the screen was manipulated for reward, the volume of the video was not manipulated and was kept constant so as not to disturb engagement. The therapy itself was provided by a provisional psychologist trained in Neurotherapy or certified neuro-therapist.

EEG Registration (at T1 and T2)

Like Study 1, EEG recording of both the therapy and control groups was accomplished using a Mitsar-EEG-201, a portable and battery-powered (4 x AA rechargeable batteries) 25 channel EEG amplifier (Mitsar Ltd., Russia). An electrode cap (Electro-Cap International Inc.) containing tin electrodes was fitted and continuous EEG recorded from the 19 sites (Fp1, Fp2, F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, O1 and O2) of the International 10–20 System (Jasper, 1958). Impedances of all electrodes were kept even and below 5.0 kOhms. The input signals were referenced to the linked earlobes, amplified

and sampled at the rate of 500 Hz. EEG recordings were obtained during 'eyes open' (EO) and 'eyes closed' (EC) resting states. The EEG data were recorded for 5 minutes during 2.5 minutes of EO and 2.5 minutes of EC.

Analysis of Behavioural Tests

All statistical analyses in this study were performed using SPSS software, version 25. The design of this study was based on a randomized controlled pretest-post-test design (Breteler et al., 2010). To analyse the data, I used a multivariate repeated measures analysis of variance (rm ANOVA) comparing the two groups with respect to the behavioural tests: reading, phonological, and spelling. This analysis was carried out for the test scores of all participants by the factors Group (therapy and control) and Time (T1: pre, and T2: post). Further analysis of the data was carried out on age-corrected test scores. The test scores of the behavioural tests represent an equivalent test age of the participants for the particular test.

EEG Data Analysis

Data pre-processing and analysis were identical to Study 1 (see also the Methods section for a detailed description of data pre-processing steps) and was performed using EEGLAB (Delorme & Makeig, 2004) and Matlab (MathWorks, 2012). Additionally, the EEG recordings from Study 1 served as a baseline in Study 2. As discussed in detail in Chapter 1, I followed the procedure described in Babiloni et al. (2012) in order to account for inter-individual differences in individual alpha peak frequencies (IAF). With reference to the IAF, frequency bands were described as: delta (IAF-8 to IAF-6 Hz), theta (IAF-6 to IAF-4 Hz), alpha 1 (IAF-4 to IAF-2 Hz), alpha 2 (IAF-2 to IAF Hz), and alpha 3 (IAF to IAF+2 Hz). For example, with an IAF of 10 Hz in the range of 8-15 Hz, the frequency bands of interest were as follows: 2–4 Hz (delta), 4–6 Hz (theta), 6–8 Hz (alpha 1), 8–10 Hz (alpha 2), 10–12 Hz (alpha 3). Consistent with Study 1, I have selected three additional fixed bands for the higher frequencies: beta 1 (13–20 Hz), beta 2 (20–30 Hz), and gamma (30–40 Hz; see

Babiloni et al., 2012 and Study 1 for a similar approach). The 19 electrodes were split into several clusters to increase statistical power and reduce the number of factors (see Table 4.2; see also Kanske & Kotz, 2010; 2011; Luck & Gaspelin, 2017 for similar approaches and motivation).

Table 4.2

Electrodes grouped into regional clusters for statistical analysis.

Region	Electrodes
Frontal	Fp1, Fp2, F7, F3, Fz, F4, F8
Temporal	T3, T4, T5, T6
Parietal-Occipital	P3, Pz, P4, O1, O2
Central	C3, Cz, C4

The EEG data were extracted from EEGLAB and analysed using a 2 x (2 x 4 x 8 x 2) mixed measures ANCOVA with one between-subjects factor, Group (therapy, control) and four within-subjects factors: Condition (eyes closed, eyes open), Region (frontal, temporal, central, parietal-occipital), Frequency bands (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma) and Time (T1, T2). Age and gender of participants were entered as covariates. In a separate analysis, I have additionally included hemisphere as a factor and conducted a 2 x (2 x 2 x 8 x 2) mixed measures ANCOVA with a between-subjects factor: Group (therapy, control), and within-subjects factors: Condition (eyes closed, eyes open), Hemisphere (left, right), Frequency bands (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, and gamma) and Time (T1, T2); age and gender of participants were again used as covariates. Note that in cases in which the sphericity assumption was violated (Mauchly's test of sphericity), Greenhouse-Geisser correction was applied. For the purpose of analyses, 19 electrodes were split into frontal (Fp1, Fp2, F7, F3, F4, F8, Fz), central (Cz, C3, C4), parietal-occipital (Pz, P3, P4, O1, O2), and parietal-occipital (Pz, P3, P4, O1, O2), total left-

hemispheric (Fp1, F3, F7, C3, T7, P3, P7, O1), right-hemispheric (Fp2, F4, F8, C4, T8, P4, P8, O2) and midline (Fz, Cz, Pz) activity. Where necessary, Bonferroni adjustments were applied to account for multiple comparisons.

Results

Behavioural Tests

I submitted the raw and age-corrected data from each group of tests (reading, phonological, spelling) conducted over the two time points (T1, T2) into a 2 x (2 x "i") mixed measures ANCOVA with between-subjects factor group (therapy, control) and within-subjects factors time (T1, T2) and last factor "i" which had a variable number of levels, depending on the number of tests in each section (i.e., reading i = 6, phonological i = 3, spelling i = 2; see supplementary material for the list of tests). Please note that the behavioural results from Study 1 served as a baseline (T1) in Study 2.

In the reading tasks tests, the main effect of Group both in raw data, $F(1,18) = 0.97$, $p > 0.3$, $\eta_p^2 = 0.051$, and in age-corrected data, $F(1,18) = 0.85$, $p > 0.3$, $\eta_p^2 = 0.045$, was not statistically significant. Further, the time x group interactions in the raw data, $F(1, 18) = 2.42$, $p > 0.1$, $\eta_p^2 = 0.12$, and age-corrected data, $F(1, 18) = 3.06$, $p = 0.097$, $\eta_p^2 = 0.15$, and the time x group x reading conditions in both forms of data, raw = $F(5, 14) = 1.18$, $p > 1.5$, $\eta_p^2 = 0.29$, corrected = $F(5, 14) = 1.19$, $p > 0.3$, $\eta_p^2 = 0.29$ were not statistically significant.

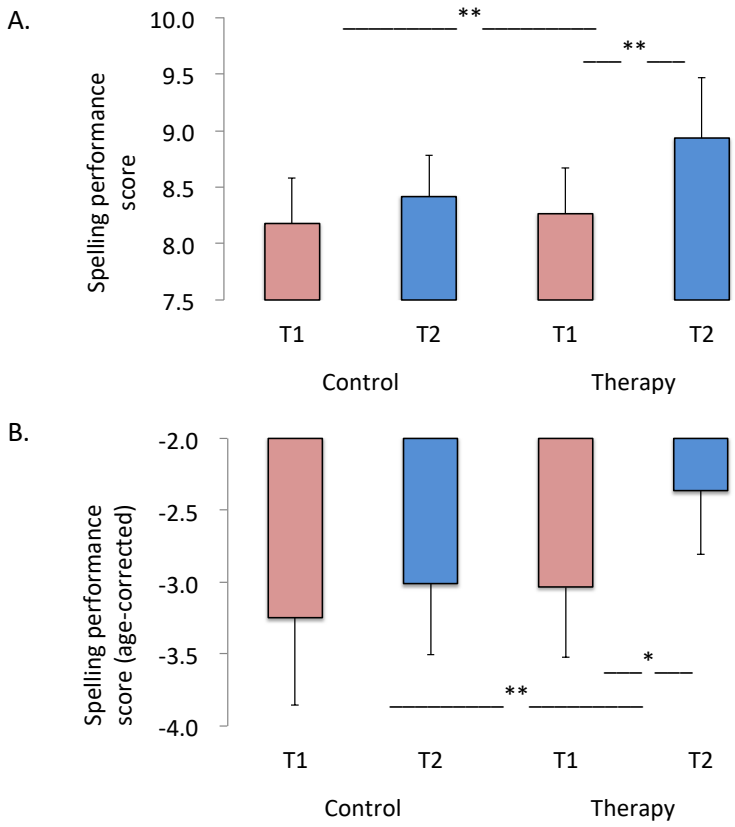
In the phonological task condition, there were two missing points in two participants of the therapy group (in the reading of non-words [participant 8] and sound awareness [participant 36] phonological tasks). To account for these missing values, I performed a mean imputation procedure, substituting the missing value with a mean performance score for that specific test and subgroup. Consequently, 2 scores were filled-in in the corresponding phonological tests. There was a statistically significant Time x Group interaction in the age-corrected data, $F(1, 26) = 5.34$, $p = 0.029$, $\eta_p^2 = 0.17$. I resolved this interaction by group and

further separate analyses over the two groups showed a statistically significant main effect of time in the therapy group (T1 = -3.34, T2 = -2.83; $F(1, 14) = 10.12$, $p < 0.01$, $\eta_p^2 = 0.42$), but not in the control group (T1 = -3.44, T2 = -3.28; $F(1, 12) = 0.97$, $p > 0.3$, $\eta_p^2 = 0.08$).

In the raw data for the spelling (see Figure 4.1), there was a statistically significant three-way interaction of time x spelling x group, $F(1, 25) = 4.48$, $p = 0.044$, $\eta_p^2 = 0.152$. Subsequent analysis separately over the two spelling tests revealed a non-significant two-way Time x Group interaction, $F(1, 25) = 0.105$, $p > 0.7$, $\eta_p^2 = 0.004$, but it was marginally significant for the phonological spelling test, $F(1, 25) = 4.135$, $p = 0.053$, $\eta_p^2 = 0.142$. In the phonological spelling test the main effect of time was further examined separately in the two groups. Consistent with the predictions of improved performance at T2 relative to T1, there was a statistically significant difference between test scores in the therapy group (pre = 8.7, post = 9.76; $t(14) = -2.68$, $p = 0.018$), but not control group (T1 = 8.77, T2 = 8.87; $t(12) = -0.282$, $p = 0.783$).

Figure 4.1

Mean test scores of the phonological spelling task.



*Note***.** The figure represents [uncorrected] mean test scores in the phonological spelling task of Control and Therapy participants tested pre- (T1) and post-training (T2). ** $p < 0.05$. * $p = 0.083$. Error bars indicate standard error of the mean (SEM).

In the age-corrected data for the spelling task, a comparable pattern emerged. There was a statistically significant three-way interaction of time x spelling x group, $F(1, 25) = 4.48$, $p = 0.044$, $\eta_p^2 = 0.152$. Further analyses across the two spelling tasks resulted in non-significant two-way time x group interaction for the spelling test, $F(1, 25) = 0.141$, $p > 0.7$, $\eta_p^2 = 0.006$, but a statistically significant interaction for the phonological spelling test, $F(1, 25) = 4.22$, $p = 0.05$, $\eta_p^2 = 0.145$. Subsequent planned (i.e., one-way) comparisons indicated a marginally significant difference between scores of T1 and T2 testing sessions in the therapy

group (pre = -1.53, post = -2.10; $t(14) = 1.45$, $p = 0.083$), but not control group (T1 = -2.55, T2 = -2.16; $t(12) = -1.19$, $p = 0.127$).

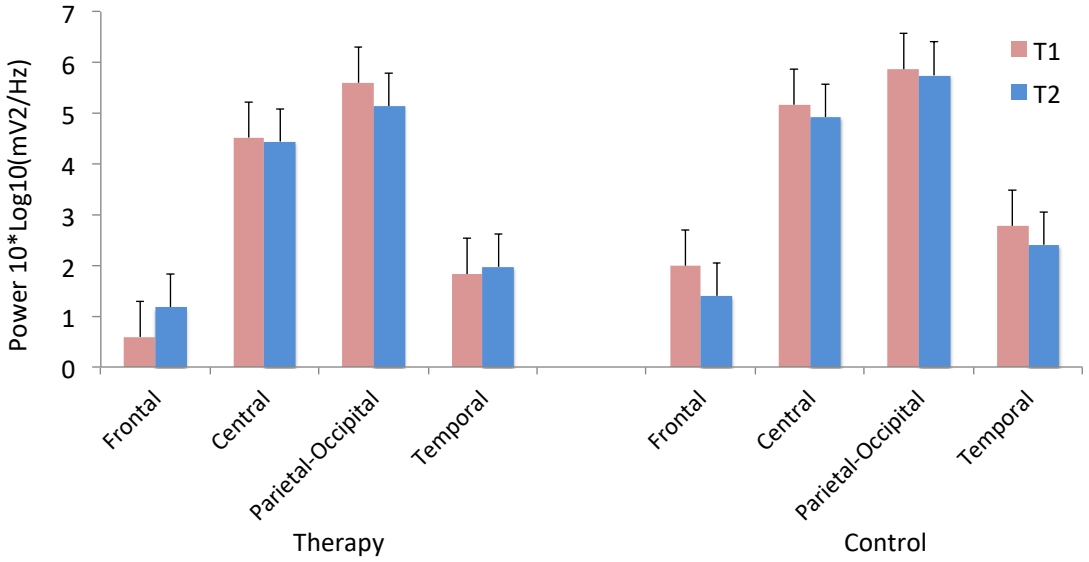
EEG Power Spectra

In the first step, I submitted the data into a 2 x 2 x 2 x 4 x 8 repeated measures ANCOVA with between-subjects factor Group (therapy, control) and within-group factors Time (T1, T2), Condition (eyes closed, eyes open), Region (frontal, central, parietal-occipital, temporal) and Frequency (delta, theta, alpha 1, alpha 2, alpha 3, beta 1, beta 2, gamma).

There was a statistically significant interaction of Time x Region x Group, $F(3, 22) = 5.06$, $p = 0.008$, $\eta_p^2 = 0.41$ (see Figure 4.2). Further analysis across the two groups revealed a two-way interaction of Time x Region in the therapy group, $F(3, 12) = 4.4$, $p = 0.026$, $\eta_p^2 = 0.52$, but not in the control group, $F(3, 10) = 1.23$, $p > 0.3$, $\eta_p^2 = 0.27$. In the therapy group, the main effect of region was significant both in the T1, $F(3, 12) = 127.09$, $p < 0.001$, $\eta_p^2 = 0.97$, and T2, $F(3, 12) = 106.7$, $p < 0.001$, $\eta_p^2 = 0.96$, testing sessions.

Figure 4.2

Power plots as a function of region, group and time points.



Note. The figure represents overall power values (merged over all frequency bands) plotted separately over the four regions of interest (central, frontal, parietal-occipital, temporal), groups (control, therapy) and separately for the two time points (T1, T2). Error bars indicate standard error of the mean (SEM).

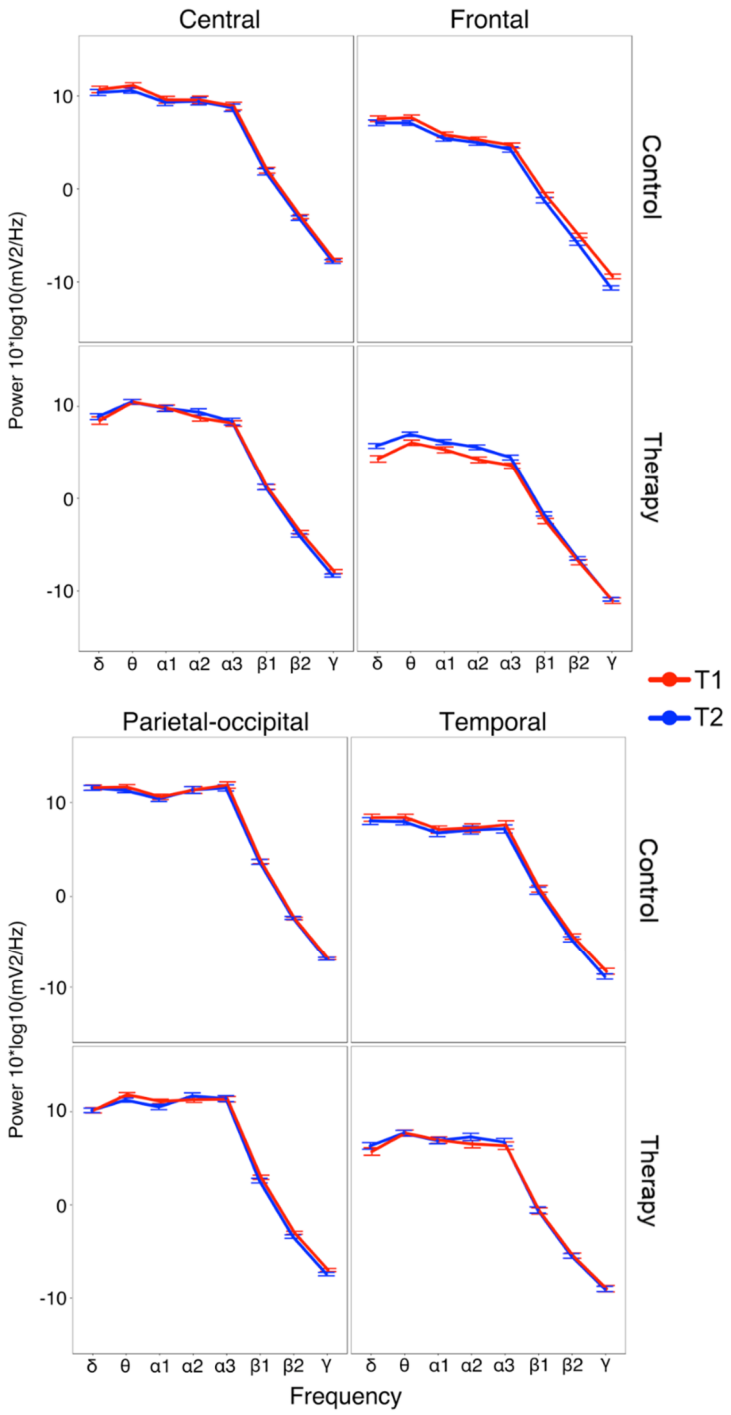
As can be seen from Figure 4.2, there was overall higher mean power in central relative to frontal brain regions and this difference was larger in the T1 testing session, $F(1, 14) = 231.8$, $p < 0.001$, $\eta_p^2 = 0.94$, relative to T2 testing session, $F(1, 14) = 152.8$, $p < 0.0001$, $\eta_p^2 = 0.92$. Similarly, the frontal region resulted in lower overall mean power relative to parietal-occipital region and this difference was larger in the T1 testing session, $F(1, 14) = 294.4$, $p < 0.001$, $\eta_p^2 = 0.95$, relative to T2 testing session, $F(1, 14) = 157.2$, $p < 0.001$, $\eta_p^2 = 0.92$. Finally, the parietal-occipital region resulted in higher overall mean power relative to the temporal brain region and this difference was stronger in the T1 testing session, $F(1, 14) = 317.8$, $p < 0.001$, $\eta_p^2 = 0.96$, relative to T2 testing session, $F(1, 14) = 128.04$, $p < 0.001$, $\eta_p^2 = 0.90$. Note that there was no interaction with the Frequency factor, which implies that the described pattern above was present across all frequency bands.

In a separate step, the time x region interaction within individual groups was split by region and the differences in each of the regions was compared at T1 vs. T2. In the therapy group, there was a significant main effect of time: the alpha power was larger at T2 relative to T1 ($F(1, 14) = 8.79$, $p < 0.01$), while this difference was not significant for any other regions (all p's > 0.1). In contrast, and as was shown above, the time x region interaction was not significant in the control group ($F(3, 10) = 1.23$, $p > 0.3$).

No other main effects or interactions involving theoretically important factors group and time resulted in significant effects (all p's> 0.1; see Figure 4.3). In short, the most important finding here is that there was an overall higher mean power in frontal electrodes at T2 relative to T1.

Figure 4.3

Power plots as a function of region, group, and time points.



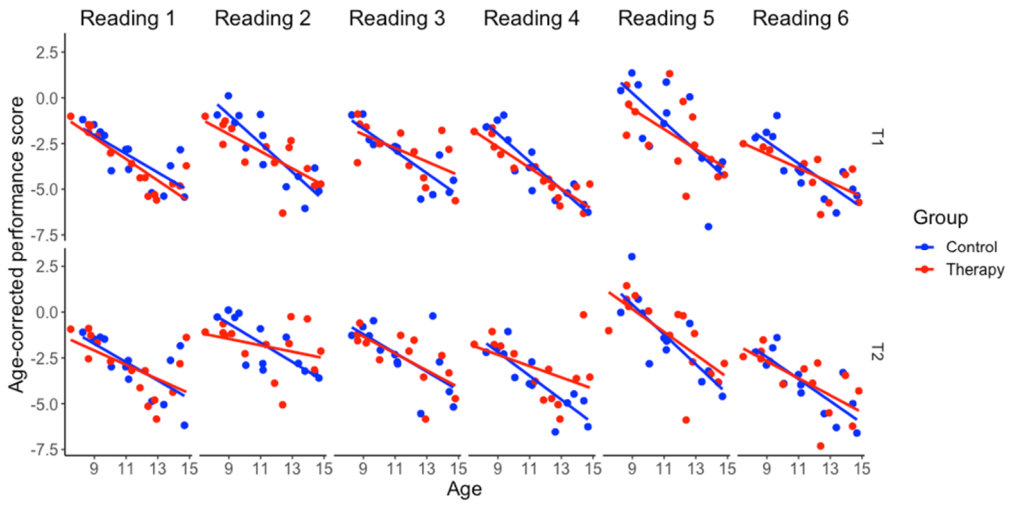
*Note***.** The figure represents mean power values plotted over various frequency bands separately for the control and therapy groups in the pre- (T1) and post-training (T2) sessions. Error bars indicate standard error of the mean (SEM).

Correlational Analysis

When examined separately, the therapy group showed a negative correlation between age of participants and their performance on the letter/word identification task (i.e., reading task), $r = -0.58$, $p < 0.05$, reading fluency, $r = -0.69$, $p < 0.01$, passage comprehension (reading task), $r = -0.71$, $p < 0.01$, and passage fluency (reading task), $r = -0.68$, $p < 0.01$, (see Figure 4.4 and Figure 4.5), but not in passage comprehension (Woodcock and Johnson reading task), $r = -0.31$, $p > 0.2$, or in reading accuracy, $r = -0.48$, $p > 0.1$. Similarly, there was a non-significant negative correlation between the therapy participants' age and performance on reading of non-words task (i.e., phonological task), $r = -0.32$, $p > 0.2$, sound awareness (phonological task), $r = -0.45$, $p > 0.1$, phonemic decoding efficiency task, $r = -0.9$, $p < 0.001$, as well as spelling test, $r = -0.56$, $p < 0.05$, and spelling sounds test, $r = -0.58$, $p < 0.05$.

Figure 4.4

Correlation plots of age-corrected performance scores for reading tests.

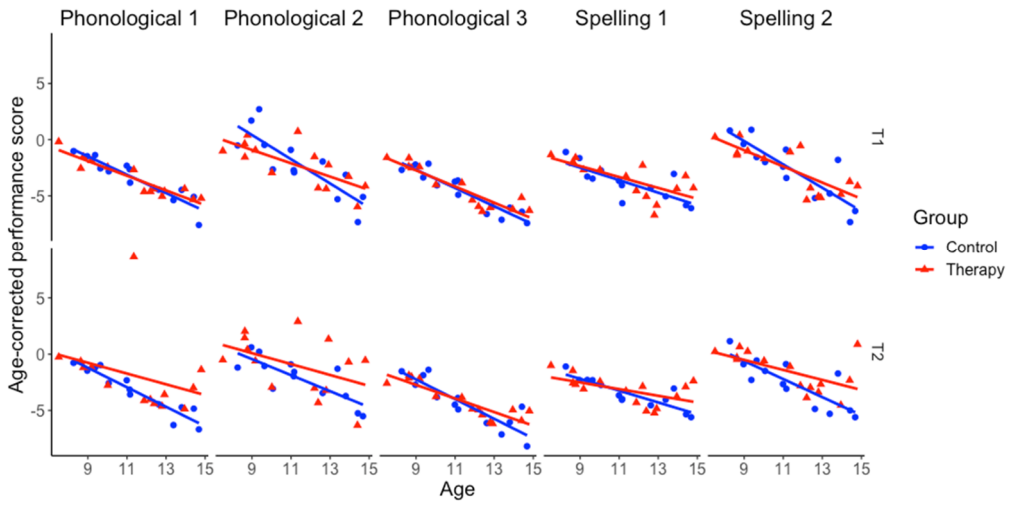


Note. The figure represents correlations of the chronological age of participants with age-corrected performance scores in six different reading tasks plotted separately for pre (T1) and post-therapy (T2). The red line represents the best fitting line of control participants' performance, while the red line is the best fitting line of the therapy group.

In the control group (when examined separately), there was a negative correlation between age of participants and their performance on letter/word identification task (i.e., reading task), $r = -0.68$, $p < 0.05$, passage comprehension (Woodcock and Johnson reading task), $r = -0.78$, $p < 0.01$, reading fluency, $r = -0.64$, $p < 0.05$, reading accuracy, $r = -0.84$, $p < 0.01$, passage fluency, (reading task), $r = -0.82$, $p < 0.001$, and passage comprehension (reading task), $r = -0.79$, $p < 0.01$. There were also negative correlations between control participants' age and performance on reading of non-words task (i.e., phonological task), $r = -0.94$, $p < 0.001$, sound awareness (phonological task), $r = -0.81$, $p < 0.01$, phonemic decoding efficiency task, $r = -0.883$, $p < 0.001$, and in the spelling sounds test, $r = -0.86$, $p < 0.001$, as well as in the spelling test, $r = -0.821$, $p < 0.01$.

Figure 4.5

Correlation plots of age-corrected scores for phonological and spelling tests.



Note. The figure represents correlations of the chronological age of participants with age-corrected performance scores in three different phonological tasks, and two spelling tasks plotted separately for pre (T1) and post-therapy (T2). The red line represents the best fitting line of control participants' performance, while the red line is the best fitting line of the therapy group.

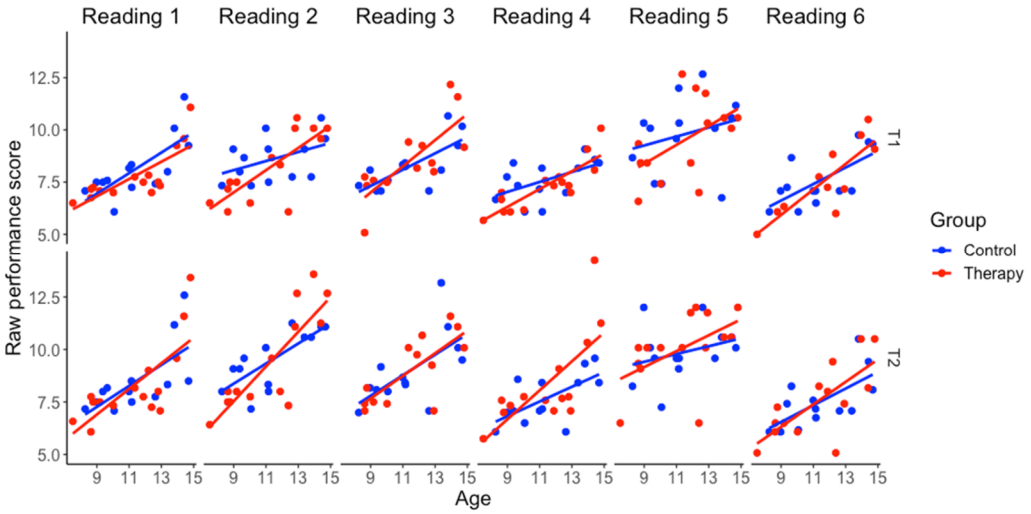
There was a statistically significant positive correlation (see Figure 4.6 and Figure 4.7) between age of participants and their [raw scores] performance on the letter/word identification task (i.e., reading task), $r = 0.71$, $p < 0.0001$, passage comprehension (reading task), $r = 0.69$, $p < 0.0001$, reading fluency, $r = 0.7$, $p < 0.001$, reading accuracy, $r = 0.66$, $p < 0.0001$, passage comprehension (reading task), $r = 0.41$, $p < 0.01$, and passage fluency (reading task) $r = 0.72$, $p < 0.0001$. In addition, there was a positive correlation between participants' age and raw scores on reading of non-words task (i.e., phonological task), $r = 0.34$, $p < 0.02$, sound awareness (phonological task), $r = 0.36$, $p < 0.01$, and phonemic decoding efficiency, $r = 0.58$, $p < 0.0001$, as well as spelling test, $r = 0.77$, $p < 0.0001$, and spelling sounds test, $r = 0.38$, $p < 0.01$. In short, these results indicate that performance of participants with dyslexia did improve from T1 to T2 and they are continuously fell behind their peers at a near constant rate.

When examined separately, the therapy group showed a positive correlation between age of participants and their performance on the letter/word identification task (i.e., reading task), $r = 0.72$, $p < 0.001$, reading fluency, $r = 0.77$, $p < 0.001$, passage comprehension (YARC reading task), $r = 0.76$, $p < 0.001$, and passage fluency (reading task), $r = 0.71$, $p < 0.001$, in passage comprehension (Woodcock Johnson reading task), $r = 0.5$, $p < 0.01$, and in reading accuracy, $r = 0.77$, $p < 0.1$. Similarly, there was a positive correlation between participants' age and performance on reading of non-words task (i.e., phonological task), $r = 0.37$, $p < 0.05$, sound awareness (phonological task), $r = 0.48$, $p < 0.01$, the correlation was

also significantly in the phonemic decoding efficiency task, $r = 0.73$, $p < 0.001$, as well as spelling test, $r = 0.78$, $p < 0.001$, and spelling sounds test, $r = 0.55$, $p < 0.01$.

Figure 4.6

Correlation plots of raw scores for reading tests



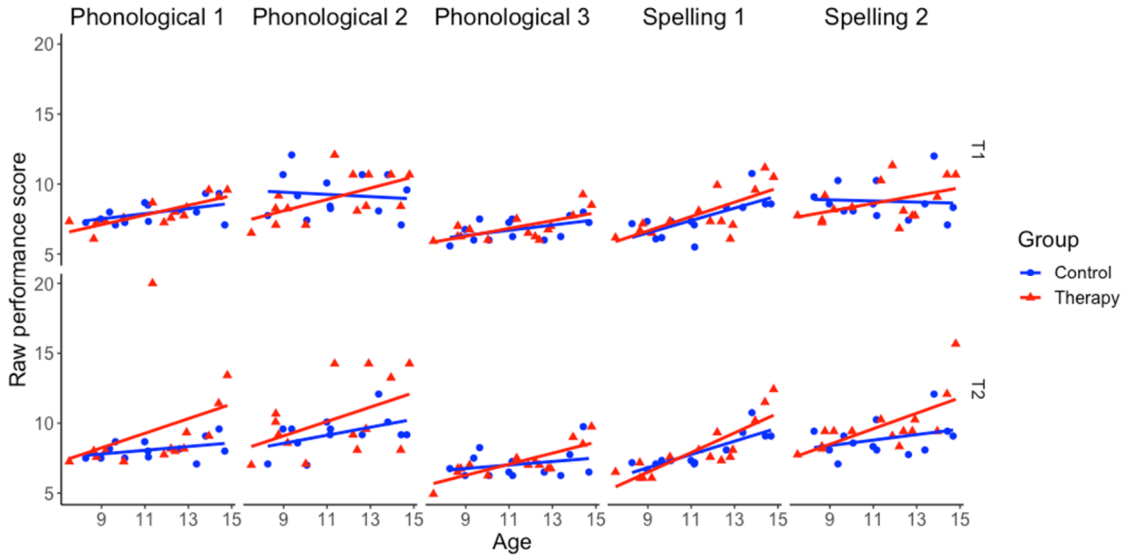
Note. The figure represents correlations of the chronological age of participants with raw performance scores in six different reading tasks plotted separately for pre (T1) and post-therapy (T2). The red line represents the best fitting line of control participants' performance, while the red line is the best fitting line of the therapy group.

The control group also showed a positive correlation between age of participants and their raw performance scores on letter/word identification task (i.e., reading task), $r = 0.37$, $p < 0.05$, passage comprehension (Woodcock and Johnson reading task), $r = 0.48$, $p < 0.01$, reading fluency, $r = 0.73$, $p < 0.001$, reading accuracy, $r = 0.79$, $p < 0.001$, passage fluency (reading task), $r = 0.55$, $p < 0.001$, and passage comprehension (Yarks reading task), $r = 0.12$, $p = 0.53$. There were also non-significant positive correlations between participants' age and performance on reading of non-words task (i.e., phonological task), $r = 0.44$, $p < 0.03$, sound awareness (phonological task), $r = 0.16$, $p = 0.43$, phonemic decoding efficiency task, $r =$

0.35, $p = 0.073$, and in the spelling sounds test, $r = 0.76$, $p < 0.001$, as well as in the spelling test, $r = 0.13$, $p = 0.53$. Note also that I ran a correlation between participants' performance scores at each of the individual tests and the time-interval in days between T1 and T2. As a result, none of the correlations were significant (all p's > 0.05). In other words, these latter findings show that the time interval between the two testing sessions alone is not associated with the behavioural outcomes.

Figure 4.7

Correlation plots of raw scores for phonological and spelling tests



Note. The figure represents correlations of the chronological age of participants with raw performance scores in three different phonological tasks, and two spelling tasks plotted separately for pre (T1) and post-therapy (T2). The red line represents the best fitting line of control participants' performance, while the red line is the best fitting line of the therapy group.

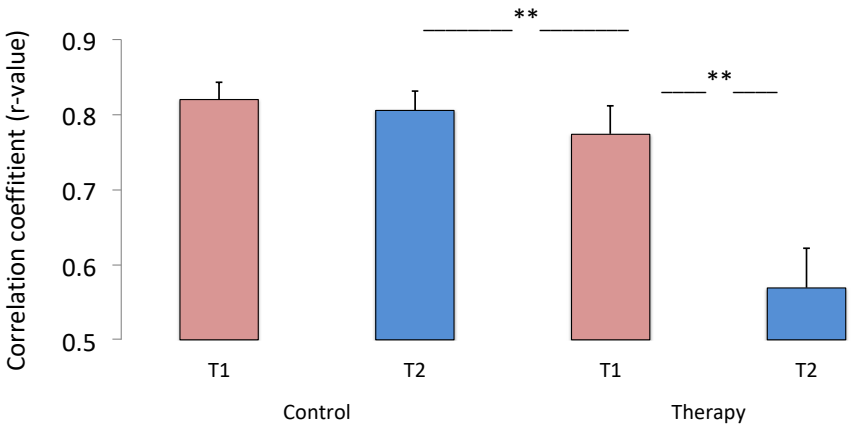
In the final step, the *r*-values of the two groups (therapy, control) were compared over all 11 tests (6 reading tasks, 3 phonological and 2 spelling tasks) tested separately at two time-points (T1, T2). For this purpose, a 2 x 2 repeated-measures ANOVA with factors time

(T1, T2) and group (therapy, control) was run. Note that this is not performing yet another analysis on the same data but rather constitutes a meta-analysis of correlation results. As a result, I found a significant time x group interaction, $F(1, 10) = 6.56$, $p = 0.028$, $\eta_p^2 = 0.396$. In the first step, group differences as a function of time were analysed: no significant difference was found between therapy (mean $r = 0.77$) and control groups at T1 (mean $r = 0.82$), $F(1, 10) = 2.3$, $p > 1.5$, $\eta_p^2 = 0.187$. However, at T2, after therapy, the therapy group resulted in significantly lower r-values (mean $r = 0.57$) relative to control group (mean $r = 0.81$), $F(1, 10) = 13.56$, $p < 0.01$, $\eta_p^2 = 0.576$.

Furthermore, differences between the two time points were analysed separately within each group. There was no r-value difference between T1 ($r = 0.82$) and T2 ($r = 0.81$) in the control group, $F(1, 10) = 0.28$, $p > 0.61$, $\eta_p^2 = 0.027$ (see Figure 4.8). In contrast, the therapy group showed a significant difference between T1 ($r = 0.77$) and T2 ($r = 0.57$), $F(1, 10) = 13.28$, $p < 0.01$, $\eta_p^2 = 0.57$.

Figure 4.8

Correlation between chronological age and behavioural test performance.



Note. The figure represents the mean correlation coefficient (*r*-value) averaged across all psychological tests of Control and Therapy participants tested pre- (T1) and post-training (T2). ** $p < 0.05$. Error bars indicate standard error of the mean (SEM).

The comparable 2 x 2 mixed-measures ANOVA with factors time (T1, T2) and group (therapy, control) was performed over *r*-values of raw test performance scores. There was a statistically significant main effect of group; participants in the therapy group had better overall performance (mean performance score = 65.4) relative to the control group (score = 49.2), $F(1, 10) = 11.54$, $p < 0.01$, $\eta_p^2 = 0.54$. Although the group difference was numerically two times larger before the therapy (therapy group = 70.4, control = 44.2, difference = 26) relative to after the therapy (therapy group = 66.9, control = 53.9, difference = 13), the time x group interaction did not reach statistical significance, $F(1, 10) = 1.99$, $p = 0.18$, $\eta_p^2 = 0.2$. These latter findings suggest that the rate of decline in overall task performance (i.e., averaged over reading, phonological, and spelling tasks) reduced after neurofeedback training (i.e., results in weaker negative correlation). In other words, although participants with dyslexia were still performing worse relative to healthy controls, the rate of their decline was reduced after the therapy.

Discussion

The current work examined the effect of qEEG-guided LORETA z-score neurofeedback training in children with phonological dyslexia. To this end, a power spectrum analysis of EEG data was performed as well as an analysis of eleven behavioural test scores as a function of the chronological age of the participants. Overall, the current results demonstrated the effectiveness of neurofeedback therapy both at the oscillatory and behavioural levels.

Discussion of Behavioural Tests

Study 1 was a "baseline" experiment in which the performance in the dyslexia sample that would later undergo neurofeedback therapy was examined. One of the key findings of Study 1 were the positive correlations between alpha and beta spectral power in frontal regions and performance on several reading tasks (letter/word identification test, passage comprehension and reading fluency test, as well as York assessment of reading comprehension performance) and phonological tasks (word attack test and sound awareness test). Therefore, and based on the findings in Study 1, the primary hypothesis in Study 2 was that the neurofeedback therapy would not only modulate oscillatory brain activity in the frontal brain region but would also improve participants' performance on the corresponding behavioural tests. As a result, and in line with the predictions, analyses of the eleven behavioural test scores (reading, phonological, spelling) showed that the therapy group performed better in the phonological spelling task as well as in the phonological awareness task when tested post-therapy, whereas the control group showed no performance changes when tested after a comparable amount of time on the waitlist. In contrast, the group-related differences in reading task performance were not statistically significant.

The observed improvements in performance on two types of tasks were related to participants' phonological abilities (phonology proper task and phonological spelling task). The tasks require participants to represent words using sound knowledge and relate this sound knowledge to the typical spelling patterns. These findings may not be surprising, given the fact that the sample consisted of participants with confirmed phonological deficits. Although I could not with certainty classify participants into a specific dyslexia subtype, one of the strict inclusion criteria to participate in this study was a substantial difficulty in phonological task performance. Therefore, deficient phonological processing was a consistent feature of all participants with dyslexia in the sample. The phonological theory posits that

children with dyslexia experience difficulties in clearly representing the smallest units of speech sound (Klein & Shaywitz, 2005; Shaywitz & Shaywitz, 2005). In other words, dyslexia is thought to hinder one's ability to connect the sounds of language to letters, which results in delays of reading abilities. Thus, it makes sense that the observed neurofeedback-related improvements are shaped by the specific composition of the group with dyslexia, and it is possible that neurofeedback may not modulate the phonology-related task performance per se (i.e., across all people with dyslexia in general) but are indicative of the fact that the current therapy protocols were specifically tailored to target this deficit.

In general, the research on the efficacy of neurofeedback on behavioural manifestations of dyslexia includes mostly inconclusive results. For example, previous research indicated that neurofeedback therapy improved spelling, but not reading performance (Breteler et al., 2010), reading performance (Walker & Norman, 2006), auditory vigilance and phonological awareness (Au et al., 2014), and both reading and phonological abilities (Nazari et al., 2012). Importantly, these and other previous studies did not control for the inter-individual differences in the expression of dyslexia, and it is, therefore, difficult to know how homogeneous the participant sample was in those studies. In the current study, it was found that neurofeedback results in significant improvements in all reading, spelling and phonological task performance.

The sample composition may also be a plausible explanation for the inconsistent findings in the past and for the absence of therapy-related improvements in reading performance in the current work. As mentioned in the introduction, dyslexia is not a homogeneous disorder and had been previously classified into dysphonetic and dyseidetic subtypes (Boder, 1973), phonological and surface subtypes (Castles & Coltheart, 1993), subtypes with and without verbal language deficit (Leonard et al., 2002), as well as visual and phonological subtypes (Bosse et al., 2007; Ramus et al., 2018). Although there is a consensus

that dyslexia may be expressed in many ways, there is no standard classification that is generally accepted by all researchers (Ramus et al., 2018). Therefore, it would be essential to keep in mind the heterogeneity of dyslexia when using neurofeedback and researchers should potentially explore the role of inter-individual disorder-related differences in the efficacy of neurofeedback therapy. Previous results provide a rationale for the use of LORETA z-score therapy as opposed to non-individualized Neurotherapy protocols (as were used in many of the above samples). LORETA z-score therapy allows for inter-individual differences in expressed symptomology and associated brain areas be targeted; therefore, the findings of the current study may be reflective of the therapies ability to target individualized dysfunction. Finally, it is also possible that the effect of the therapy requires time to be expressed and, thus, participants reading performance could improve further if tested at a later time point post- therapy. Therefore, future studies should address this point more systematically and examine the long-lasting effect of neurofeedback on behavioural performance in participants with dyslexia.

Essentially, the correlation results in the current study replicated the pattern of results observed in Study 1 (Chapter 3). Participants with dyslexia in the two groups consistently showed a negative correlation between chronological age and the corrected performance scores, as well as a positive correlation between chronological age and uncorrected raw performance scores. In other words, these results indicate that participants with dyslexia (in both groups) continuously fall behind in reading, spelling, and phonological tasks at a near-constant rate despite receiving the current recommended course of therapy (remedial instruction) and despite showing modest general improvements in reading performance (i.e., uncorrected raw scores). A crucial finding of this study that extended the results of Study1 is the relative strength of these correlations when compared between the therapy and control groups. Specifically, I found that the therapy group, relative to the control group, showed

overall significantly weaker negative correlations between participants' chronological age and age-corrected test performance scores. In other words, the strength of the negative association that was found in Study 1 becomes weaker after neurofeedback therapy: the therapy group showed overall greater age-dependent improvements in performance scores. Therefore, the conclusion is that LORETA z-score neurofeedback can slow down the overall pace of deterioration in dyslexia.

Discussion of Physiological Findings

The results of Study 1 indicated that dyslexia is characterized by changes in spectral brain activity across different brain regions and frequency bands. More specifically, Study 1 revealed a significant reduction in the delta, theta, alpha1, alpha2, beta2 and gamma frequencies in frontal and temporal regions in the group with dyslexia as compared to healthy controls. On the other hand, the alpha 1 and alpha 3 frequencies were enhanced over central and parietal-occipital electrodes in the group with dyslexia. Finally, the gamma activity was consistently reduced in dyslexia in all brain regions. Therefore, in Study 2, I expected that the therapy would result in enhanced activity in the alpha, theta, delta and gamma frequencies over the frontal and temporal regions, with reduced alpha activity over the central and parietal-occipital regions. In other words, I hypothesized that the therapy would "normalize" brain activity, i.e., make it more comparable to that of healthy controls.

As a result, in the overall averages of the EEG power spectrum data, participants who received neurofeedback therapy had more substantial differences between the central and frontal brain regions and frontal and parietal-occipital brain regions before they received neurofeedback therapy. As expected, and as can be seen in Figure 4.2, this difference was caused primarily by increased overall power at frontal electrodes (across all frequency bands) after receiving neurofeedback therapy.

The post-therapy spectral changes were similarly expressed in all frequency bands across frontal electrodes. Consequently, it is not possible to attribute the observed behavioural changes to improvements in some specific frequency band in the therapy group. Therefore, in what follows, the observed spectral changes will be linked to findings in the previous literature in order to provide a theoretical explanation of the consequences for dyslexia and neurofeedback. Note also that it is difficult to make firm assumptions about the underlying sources of EEG activity based on the location of electrodes, given that scalp EEG averaged over many epochs in the spectral analysis may result from deep sources. Therefore, the neuroanatomical discussion in the following section should be treated as theoretical insights that may be tested at a later date rather than as confirmatory evidence.

Generally, regions in the frontal brain play a crucial role in language production and comprehension. Particularly, the inferior frontal gyrus (IFG; BA 44, 45) plays a key role in reading and visual word recognition (Salmelin et al., 2000). For instance, it was found that the IFG activation can be detected as early as 200 ms after reading onset (Cornelissen et al., 2009). Alternatively, it was also suggested that the IFG is activated when participants link a written word to its phonetics (Coltheart et al., 2001). This is consistent with neuroimaging studies that found a relationship between phonological processing and frontal brain regions during the processing of written words (Burton et al., 2005). Furthermore, the IFG (i.e., Broca's area) has anatomical connections with the thalamus and research supports that both brain areas are engaged in language processing (Bohsali et al., 2015). Indeed, research suggests that readers with dyslexia exhibit overactivation in the IFG during reading tasks, reflecting increased effort during reading (Démonet et al., 2004; Pugh et al., 2000; Sandak et al., 2004; Shaywitz & Shaywitz, 2005). Additionally, these findings may be in line with Temple et al. (2003) who found the training of auditory and oral language tasks in dyslexia

resulted in behavioural improvements in reading, as well as resulted, among others, in increased activation in the frontal brain area (e.g., left IFG).

Therefore, the observed therapy-related changes in frontal brain regions seem legitimate and are in line with previous literature on language-related brain areas in dyslexia. The finding of increased activity across all measured frequency bands during resting state in frontal brain regions (possibly, as a result of trained IFG) may be descriptive of an overall improvement in language-related abilities in dyslexia, which could lead to the observed behavioural benefits (Démonet et al., 2004; Pugh et al., 2000; Sandak et al., 2004; Shaywitz & Shaywitz, 2005). More specifically, alpha frequency in the frontal brain areas is sensitive to the processing of linguistic information and was shown to be reduced in the frontal regions in dyslexia. Alpha is usually reduced in response to word manipulations (e.g., pronouncing yeshay for yesterday; Drijvers et al., 2016). Klimesch and colleagues (2001) showed that participants with dyslexia had reduced alpha in the frontal and central electrodes when they were asked to read words and pseudowords. Based on these findings, it appears that the enhanced alpha frequency at frontal electrodes after the neurofeedback training may represent improved linguistic information processing in dyslexia. Note that it is also possible that the observed generalized increase across the frequency bands is a result of multiple, possibly independent processes.

The observed pattern of spectral activity over frontal electrodes may also signal therapy-related improvements in cognitive control in dyslexia (Cavanagh & Frank, 2014). Specifically, frontal brain regions are highly involved in cognitive control and conflict processing (Knyazev et al., 2009). Cognitive control refers to a collection of fundamental cognitive functions, including an ability to select and concentrate on task goals and ignore (i.e., inhibit) task-irrelevant information (Kanske & Kotz, 2010). This mechanism is vital for

the processing and production of spoken and written language (i.e., conceptualization, formulation, and articulation).

Language requires cognitive control to incorporate multiple linguistic sources of information (visual, audio) into a coherent experience to facilitate interpretation of sensory percept (Ye & Zhou, 2009). Control mechanisms are supported by a network of brain structures, most pronounced in the frontal brain region. For instance, improvements in inhibitory control during brain maturation may be supported by age-related enhancements in connectivity between frontal (IFG: BA44 and BA45; dorsal lateral prefrontal cortex: BA9 and BA46) and subcortical regions, where frontal brain regions could exert control over activity in subcortical brain regions (Hwang et al., 2010). Additionally, tasks that require inhibition of irrelevant information (e.g., Stroop, Flanker, Simon tasks) often elicit enhanced activity in the anterior cingulate cortex and dorsolateral prefrontal cortex (Knyazev et al., 2009). The anterior cingulate cortex monitors the environment for conflicts and inconsistencies (Botvinick et al., 2001; Carter & Van Veen, 2007). The dorsolateral prefrontal cortex is thought to activate top-down control and facilitate selection between two or more competing alternatives (MacDonald et al., 2000; Egner & Hirsch, 2005; Mansouri et al., 2009). Furthermore, various structural MRI studies of dyslexia demonstrated that the most consistent disorder-related functional brain alterations are observed in frontal brain areas (i.e., IFG; Brown et al., 2001; Peterson et al., 2013; Pugh et al., 2001; Robichon & Habib, 1998). Therefore, it is possible that [at least parts of] the observed increase in spectral power over the frontal region in dyslexia indicates therapy-related improvements in the functioning of this brain area.

The question of how these functional anatomical differences are represented in physiological patterns of activity remains unanswered. Successful cognitive control is associated with enhanced theta activity in frontal brain areas (medial prefrontal cortex: BA9

and mid-cingulate cortex; Cavanagh & Frank, 2014), as well as with an increase in beta in the medial prefrontal cortex (Buschman et al., 2012; Buschman & Miller, 2007; Schmidt et al., 2019). Theta and beta activities in the frontal cortex are predictive of both cognitive control and language regulation (Kim et al., 2019). As the current results indicated enhanced post-therapy theta and beta activities in frontal brain regions, it is possible that neurofeedback resulted in generally enhanced cognitive control, which in turn resulted in improved performance on cognitive-behavioural tasks. Therefore, disorder-related hypoactivation of frontal brain areas is a crucial determinant of dyslexia. Further, this hypoactivation may reflect a deficit in the ability to be successful on cognitive tasks and could cause the deficiencies in the language network performance observed in dyslexia (Nardone et al., 2011; Varvara et al., 2014; Ye & Zhou, 2009). Note that because the current study did not directly control for cognitive control abilities before and after the neurofeedback training, future studies should investigate this point more directly.

Delta frequency could be a neural marker of speech comprehension. For instance, delta frequency was shown to distinguish cognitive-linguistic differences between word classes (differentiating between concrete vs. abstract nouns). Dyslexia often results in hindered recognition and awareness of speech units, which is reflected in altered delta frequency. Specifically, participants with dyslexia, relative to healthy controls, showed weaker neural entrainment to speech in the delta band (0.5–1 Hz) and hindered delta synchronization in the left IFG (Molinaro et al., 2016). Therefore, increased delta frequency in the frontal brain region in individuals with dyslexia may imply improved language processing post-therapy.

Finally, research revealed that individuals with dyslexia have altered gamma frequencies, which play a crucial role in the integration of sensory information into a coherent [auditory] sensory percept (Brovelli et al., 2005; Jensen et al., 2007; Sokolov et al.,

2004). For instance, Flinker et al. (2015) showed that gamma frequency over Broca's area in participants with dyslexia was positively correlated with their performance on reading of pseudowords task performance. Therefore, gamma frequency in the frontal region may indicate improved integration of sensory [linguistic] information, which contributes to the observed behavioural benefits.

On the other hand, the current study did not result in the expected enhanced delta, theta, alpha1, alpha2, beta2 and gamma activations over the temporal region. Also, there was no reduction in alpha 1 and alpha 3 frequencies over central and parietal-occipital electrodes. Therefore, it is possible that the neurofeedback was the most effective over the frontal areas, possibly because frontal brain regions were targeted more frequently relative to other brain regions (see Table 1). It is also possible that different brain regions require a region-specific number of therapy sessions to find a positive effect. Therefore, this could be seen as a limitation of the current study and future studies should investigate whether different brain areas are more or less sensitive to neurofeedback and how much minimum time they require to observe reliable performance.

Limitations of the Current Study and Directions for Future Research

Although the sample size in the current study was larger than that used in previous research, the sample size of both the therapy and control groups was small and, consequently, reduced the power of the statistical analyses. Specifically, although Study 1 included 47 participants in each of the groups (dyslexia, control), the current work tested ~ 15 participants in each group. It is important to note that this sample size is comparable to previous neurofeedback literature (e.g., Breteler et al., 2010).

Additionally, due to the specifics of the current study, there was a variable time interval between T1 and T2 testing. Therefore, it is possible that the observed effects may be partly related to unequal time intervals between the two testing sessions across participants.

For instance, it is possible that the LORETA z-score training is not effective if performed at low frequencies over a longer time interval. Note, however, that there was no obvious relation between behavioural performance scores and time interval between T1 and T2 testing, as revealed by non-significant correlations. Therefore, the possibility that the time interval between the two testing sessions could influence the result is less likely, although future studies should take this into consideration. A second scenario is that LORETA z-score training, if performed at high frequency over a short period of time, loses its effect sometime after the end of the last session. Despite this possibility, it is important to note that the time differences between the two testing sessions were not significantly different between the two groups ($p > 0.6$). Therefore, these potential effects need to be further studied and are the basis of Study 3, which involves the analyses of data from a follow-up assessment three months post-therapy.

Another potential limitation was the engagement of the participants with the movie. Although the children could select, make requests, or bring movies from home, given the number of neurofeedback sessions, it was difficult to assess the continuous engagement of all participants. Specifically, the effectiveness of neurofeedback could be lower for those participants who were less engaged with the movie. Therefore, future studies could increase the level of engagement by using a video-game neurofeedback approach, which may be more appealing to children (see Schoneveld et al., 2016 for an example). The assumption here is that more exciting and engaging options for the child to choose from may improve the overall and inter-individual levels of engagement in participants.

Summary

To summarize, current findings demonstrated that participants with dyslexia showed increased oscillatory activity in frontal electrodes after, relative to prior to the neurofeedback training across all measured frequency bands. These findings reflect a general improvement

in reading and language performance in participants with dyslexia post-therapy, which is in line with previous fMRI studies that found enhanced activity in the language-related IFG in response to improved behavioural performance. Despite these results, it is also possible that each of the altered frequency bands represents a different improved function as discussed above (cognitive control, language, and integration of sensory input). These results demonstrate that oscillatory activity in frontal brain regions could be used for early diagnostic purposes of dyslexia and to measure the success of the training intervention.

The study also showed that LORETA z-score training might be an effective method to reduce the behavioural symptoms in dyslexia by facilitating normalization of these critical neural correlates of the disorder. Although all participants continued to fall behind their peers on behavioural measures, compared to children only receiving remedial instruction, the speed at which children with dyslexia fell behind appeared to be slowed following receipt of neurofeedback therapy that was given in conjunction with remedial training. This implies that neurofeedback could be a viable treatment for dyslexia (Enriquez-Geppert et al., 2019). Future studies should confirm current results while accounting for potential limitations in the current study. Specifically, an important avenue for future research concerns the lasting effects of neurofeedback. A recent meta-analysis on the efficacy of neurofeedback in participants with ADHD showed that standard neurofeedback protocols might result in sustained effects that last up to 12 months (Arns et al., 2020). However, to my knowledge, little has been done to explore whether the beneficial effects of neurofeedback in dyslexia remains after the end of the therapy. Therefore, in the next chapter, Study 3 was performed to address this point empirically by re-testing therapy participants 3 months after therapy had finished.

Supplementary Material

Reading:

a) Woodcock-Johnson – Letter/Word Identification (Test 1)

b) Woodcock-Johnson – Passage comprehension (Test 9)

c) Woodcock-Johnson – Reading Fluency (Test 2)

d) York Assessment of Reading for Comprehension – Reading accuracy

e) York Assessment of Reading for Comprehension – Passage Comprehension

f) York Assessment of Reading for Comprehension – Passage Fluency

Phonological skills:

a) Woodcock-Johnson – Word Attack (reading of non-words Test 13)

b) Woodcock-Johnson – Sound awareness (identification and manipulation of sounds Test 21)

c) Test of Word Reading Efficiency–Second Edition (TOWRE 2) – Phonemic decoding efficiency

Spelling:

a) Woodcock-Johnson – Spelling (test 7)

b) Woodcock-Johnson – Spelling Sounds (Test 18)

Chapter 5. Study 3

The Lasting Impact of LORETA Z-Score Neurofeedback Training for the Treatment of Dyslexia

Abstract

There is accumulating evidence that neurofeedback therapy may reduce behavioural symptoms of dyslexia (i.e., improve reading, spelling and phonological function); however, it remains unclear how durable this effect may be. To examine this question, the group of participants with dyslexia (N = 18) from Study 2 was re-examined three months after the end of LORETA z-score neurofeedback therapy. Each participant performed several tests (reading = 6 tests, phonological = 3, spelling = 2) collected at three time points: 1 week before the start of the neurofeedback therapy (T1; Study 1), immediately after the end of the therapy (T2; Study 2), and three months after the end of the therapy (T3; current Study 3). Performance on these tests was compared with the time of testing as a within-group factor. Results indicated that children with dyslexia from the therapy group had improved reading, spelling and phonological test scores at T3 and T2 relative to T1, with no statistically significant differences between T3 and T2. These results indicated that participants' performance did not only improve after the treatment but that this improved performance was sustained three months post-therapy. Comparable results were observed both for the raw (uncorrected) performance scores, as well as for the scores that were corrected for chronological age of participants (i.e., reading age – [minus] chronological age). Finally, analysis of parental questionnaires (administered 1 week after the end of therapy) indicated that the majority of participants with dyslexia showed noticeable improvements in the willingness to practice reading, the pace of learning, choosing to read spontaneously, focus and attention on schoolwork, and self-esteem in regards to reading. The parental questionnaire results indicated that the therapy-related improvements were not only

observable in the formal lab tests but were also noticeable subjectively in individual families. Thus, these findings support the idea that neurofeedback can result in clear and visible behavioural improvements in dyslexia. To summarize, the current work provides an important contribution in demonstrating that neurofeedback can improve reading, phonological and spelling abilities in dyslexia and that these effects are lasting.

Keywords: Dyslexia; Robust effects; Neurofeedback; Phonological processing

Introduction

Dyslexia is a specific learning disorder that is primarily manifested through the hindered acquisition of essential skills such as reading, writing, and/or phonological awareness (Fletcher et al., 2011; Gvion & Friedmann, 2010; Sahari & Johari, 2012). Interestingly, dyslexia is not associated with impairment in other cognitive abilities (e.g., mathematical abilities, logical reasoning, problem-solving) and it is estimated that over 10% of the world population could be affected by this disorder (American Psychiatric Association, 2013; De Santana et al., 2012; Klein & Shaywitz, 2005). Therefore, various studies have attempted to elucidate the nature of this disorder and develop therapies and behavioural training interventions (both terms used interchangeably in the current work) to help affected children and adults to overcome learning difficulties in dyslexia.

Such therapies have mainly used rote learning techniques targeted to the core difficulties, including phoneme awareness, reading fluency, reading comprehension, and spelling, that are expressed by most individuals with dyslexia (Snow et al., 1998). Generally, these therapies depend on repetition and rote learning techniques (i.e., memorization). It was established that the success of this behavioural training depends on many factors, one of the most important being the time of onset of intervention, with increased efficacy of early interventions (Wanzek & Vaughn, 2007).

Neurofeedback is a type of therapy that has been used to treat many disorders, including anxiety, depression, epilepsy, ADHD, and dyslexia (Breteler et al., 2010; Walker & Norman, 2006). In essence, neurofeedback methodology allows participants to have a proxy of their brain activity fed back to them in a meaningful way. This can be done via visual representation (via a computer monitor), auditory feedback (such as music or a tone) or even tactile (such as a transcutaneous electrical nerve stimulation machine). This allows for a clinician to select a goal for therapy and reward the participant when a specific, desired neural state is reached (e.g., increase in alpha over a particular electrode site). Specifically, during the training session, participants' EEG is being recorded while they are watching a movie (or receive some other visual, auditory, or tactile stimulation). When participants' EEG activity is within the desired range, they are able to watch the movie without any occlusions. Alternatively, when their neural responses deviate from the therapeutically set parameters, the watched movie is occluded in some way (such as dimming of the screen brightness). Therefore, the "feedback" follows an ongoing measurement of the participant's brain activity (hence, neurofeedback) that is known to be specific for the particular task being trained. Using these methods, participants can train and gradually improve their brain activity relative to an objective and individual-matched baseline in a specific brain area.

There is some evidence that neurofeedback-related improvements can be durable (Nazari et al., 2012; Sherlin et al., 2011). For instance, Nazari and colleagues (2012) tested whether twenty 30-minute sessions of neurofeedback could improve reading and phonological awareness in 6 participants with dyslexia. The participants' resting-state EEG was recorded before and after the training and results indicated a post-training normalization of coherence of the delta, theta, and beta bands. Further, participants with dyslexia also showed improved reading and phonological abilities, with behavioural changes still observable at a follow-up assessment two months after the end of the therapy. In other words,

this study showed that the results of the neurofeedback training could last longer than the training itself.

In Study 2 of this dissertation, a group of 15 participants with phonological dyslexia received 20 sessions of qEEG guided Low-Resolution Electromagnetic Tomography (LORETA) z-score neurofeedback therapy and their performance was compared to 14 participants with dyslexia who did not receive neurofeedback (see Study 2 for details of the procedure and method in general; see also Cannon et al., 2006; Collura et al., 2010 for comparable approaches). In Study 2, participants in both groups (therapy, wait-list control) had confirmed difficulties with phonological skills. All participants completed several tests (reading = 6 different tests, phonological = 3 tests, spelling = 2 tests) prior (T1) and after (T2) neurofeedback training. In Study 2, relative to the control group, participants in the therapy group had improved phonological and spelling (but not reading) performance at T2 relative to T1. This shows that neurofeedback was able to facilitate participants' behavioural (phonological, spelling) performance and reduce symptoms of dyslexia. Participants' test performance scores were also correlated with chronological age separately at T1 and T2. Analysis of Pearson's *r* coefficients indicated that dyslexia symptoms became weaker (less pronounced) after the neurofeedback training as the relationship between age and individual tasks' performance became less negative after the training relative to prior to the training in the therapy group, but not in the control group. In other words, this shows that neurofeedback therapy was successful in slowing down the rate at which children with dyslexia were falling behind their peers after receiving therapy. To summarize, Study 2 indicated that LORETA z-score neurofeedback therapy is an efficient method to treat the symptoms of dyslexia.

Although neurofeedback was found to be an effective method to reduce some of the symptoms of dyslexia, there is still some uncertainty about the efficacy of the technique. For instance, it is not entirely clear if the effects of neurofeedback are long-lasting (Marzbani et

al., 2016), although results from other neurodevelopmental studies are promising. For example, in autism research, neurofeedback-related behavioural improvements could still be observed 12 months after the end of the therapy (Kouijzer et al., 2009). Similarly, relative to the control group that did not receive any training, children with ADHD performed better on measures of impulsivity, inattention, and hyperactivity 6-months post-treatment (Leins et al., 2007; Strehl et al., 2006). Unfortunately, there is still little knowledge about the lasting effects of neurofeedback in dyslexia and previous studies either have not addressed this question or used an insufficient design (i.e., had too few participants and did not include a control group; see Nazari et al., 2012).

Therefore, the current study aimed to examine the behavioural performance of participants with dyslexia from Study 2 three months post-therapy. If the effect of neurofeedback is lasting and does not diminish three months post neurofeedback, the performance at T3 should be comparable to T2 (right after the end of the therapy). Further, improved performance at T3 (3 months post-therapy) relative to T1 (before therapy) would indicate a lasting effect. In contrast, if neurofeedback therapy has no lasting effects, performance at T3 would be lower than at T2, with comparable or reduced age-corrected task performance at T3 relative to T1. If the effects of neurofeedback are only superficial, behavioural performance in dyslexia would be expected to return to baseline or continue deteriorating. In other words, their performance would essentially be identical to or worse than that in the control group at T2.

Based on previous findings, it was hypothesized that participants with dyslexia would perform better at T3 relative to T1, but that there would be no difference between T3 and T2. If neurofeedback can help children with dyslexia overcome the neurophysiological under- or over-activation in specific brain areas that precluded the development of adequate phonological, spelling, and reading skills, it is also plausible to assume that it may still take

some time for the corresponding skills to develop fully. In other words, children with dyslexia may require additional time after the alleviation of neural dysfunctions underlying their disorder to develop the corresponding skills and an even more beneficial effect of neurofeedback may be observable sometime after the end of the therapy once participants have had time to learn the skills in a new, less impaired state. Given that dyslexia is a specific learning disorder and children with other disorders that manifest in childhood, such as ADHD and autism., have shown improvements after neurofeedback therapy, this learning-to-learn hypothesis could be extended to children with dyslexia (see Chapter 1). If the learning-to-learn hypothesis is correct, improved performance at T3 relative to both T1 and T2 would be expected. Therefore, the third hypothesis was that participants with dyslexia would show even further improved behavioural performance at T3 relative to T2. Thus, two opposing hypotheses were tested: (i) similar performance scores at T3 and T2, with higher performance at T3 than T1; or, (ii) higher performance at T3 relative to T2, with a lower performance at T1, relative to T2 and T3. The hypothesis that the therapy group would have a lower performance at T3 relative to T2 and comparable to T1 was also tested. Although all three hypotheses are theoretically plausible, the first two possibilities were given priority based on previous studies.

Materials and Methods

Participants

All inclusion and exclusion criteria were the same as in Study 2, as all participants had participated in that study. A total of 14 participants from the therapy group of Study 2 (females = 7, mean age = 11.62, *SD* = 2.49; see Chapter 4) and four additional participants (total N=18) who were in the control group in Study 2 but were subsequently given neurofeedback therapy (total females = 9 mean age = 11.36, *SD* = 2.37) took part in the follow-up testing three months after the end of the neurofeedback training. The four

additional participants followed the same sequence of events as the other participants with dyslexia (T1- therapy - T2 - three month delay - T3).

Although the lack of a control group could be considered problematic, the within-subjects design provides some control as participants had their own previous results (from Studies 1 & 2) served as a control/baseline, which was based on overall dyslexia-related task performance and therapy-related rate of improvements. It is important to note that participants in the waitlist control group (Study 2) could not serve as a control in this study because they were mandated to undergo therapy by the Flinders Clinical Research Ethics Committee and, thus, were no longer naïve. Further, Study 2 results indicated that the control participants showed no improvements from T1 to T2 and, therefore, it was assumed that those children with dyslexia who did not receive neurofeedback therapy would not show any improvement three months after their last behavioural tests.

Psychological Tests

As in Study 1 (see Chapter 3) and 2 (Chapter 4), 11 psychological tests were used to measure reading, phonological, and spelling performance. In more detail, the reading section of the tests consisted of the letter/word identification task, passage comprehension (Woodcock and Johnson reading task), reading fluency, reading accuracy, passage comprehension (Yarks reading task), and passage fluency tasks. The phonological part consisted of the reading of non-words task, sound awareness and phonemic decoding efficiency tasks. Finally, the spelling section of the test consisted of the actual spelling test and spelling sounds test (see Chapter 2 and 3 for more detail on specific tests).

The test scores of each of the psychological tests represent reading-age equivalent test scores (raw scores). For example, a reading-age score represents each child's reading ability when considered against the expectations for a person of their age. For example, if a 10-year-old child is reading at the level of an average eight-year-old, their reading age is 8, and

chronological age is 10. Additionally, in line with the previous studies, participants' age-corrected tests scores were measured (TSCA scores). In more detail, the TSCA corresponds to the difference of the test score (TS) and the chronological age (CA) of participants with dyslexia (thus, TSCA = TS-CA). This was an explicit measure of any gains or deficits with respect to the chronological age of the subjects; it described not only participants' performance on the test but could also directly assess their progress with respect to an established norm.

Parental Questionnaire

Parents of participants were additionally asked to fill-out a questionnaire (see Appendix E) and indicate whether they could subjectively observe any difference in their child's overall enjoyment for reading, willingness to practice reading, self-esteem in relation to literacy, expressive language skills, understanding verbal instructions, the pace of learning, focus and attention for schoolwork, and whether their child showed a tendency to choose to read spontaneously. Note that expressive language skills and understanding verbal instructions were chosen as control tasks to potentially uncover any accidental benefits that may have resulted from therapy that targeted the language network but are not dyslexia specific. It was hypothesized that there would not be any marked improvement in these skills, given that the aim was to target brain regions associated with phonological dyslexia. All questions were answered via a Likert scale on a range from "much worse" to "much better" (see Table 1).

Results

Psychological Tests

In separate analyses, raw and age-corrected data of each testing section (reading, phonological, spelling) conducted over the three time points (T1, T2, T3) were submitted into a 3 x "i" repeated measures ANOVA with within-subjects factor Time (T1, T2, T3) and

second factor "i" which had a variable number of levels, depending on the number of tests in each section (i.e., Reading i = 6, Phonological i = 3, Spelling i = 2). That is, this last factor could represent either Reading, Spelling and/or Phonological processing with the corresponding number of levels (see above). Finally, Greenhouse-Geisser corrections were applied in cases in which the Mauchly's test of sphericity was statistically significant (i.e., when the variances of the differences between all combinations of related variables were not equal).

There was a significant main effect of Time, $F(2, 20) = 24.15$, $p < 0.01$, $\eta_p^2 = 0.71$, in the raw reading tasks' data results (see Figure 5.1A), but the interaction between Time and Reading was not statistically significant, $F(10, 100) = 1.03$, $p > 0.3$, $\eta_p^2 = 0.093$. In the subsequent steps, the six reading tests across the three time points were contrasted in a pairwise manner. Results indicated a significantly larger test score at T2 (mean = 8.85) relative to T1 (mean = 8.43; $F(1, 11) = 11.97$, $p < 0.01$, $\eta_p^2 = 0.52$), and at T3 relative to T1, $F(1, 10) = 54.26$, $p < 0.01$, $\eta_p^2 = 0.84$, as well as larger T3 scores (mean = 9.19) relative to T2, $F(1, 12) = 7.33$, $p < 0.02$, $\eta_p^2 = 0.38$.

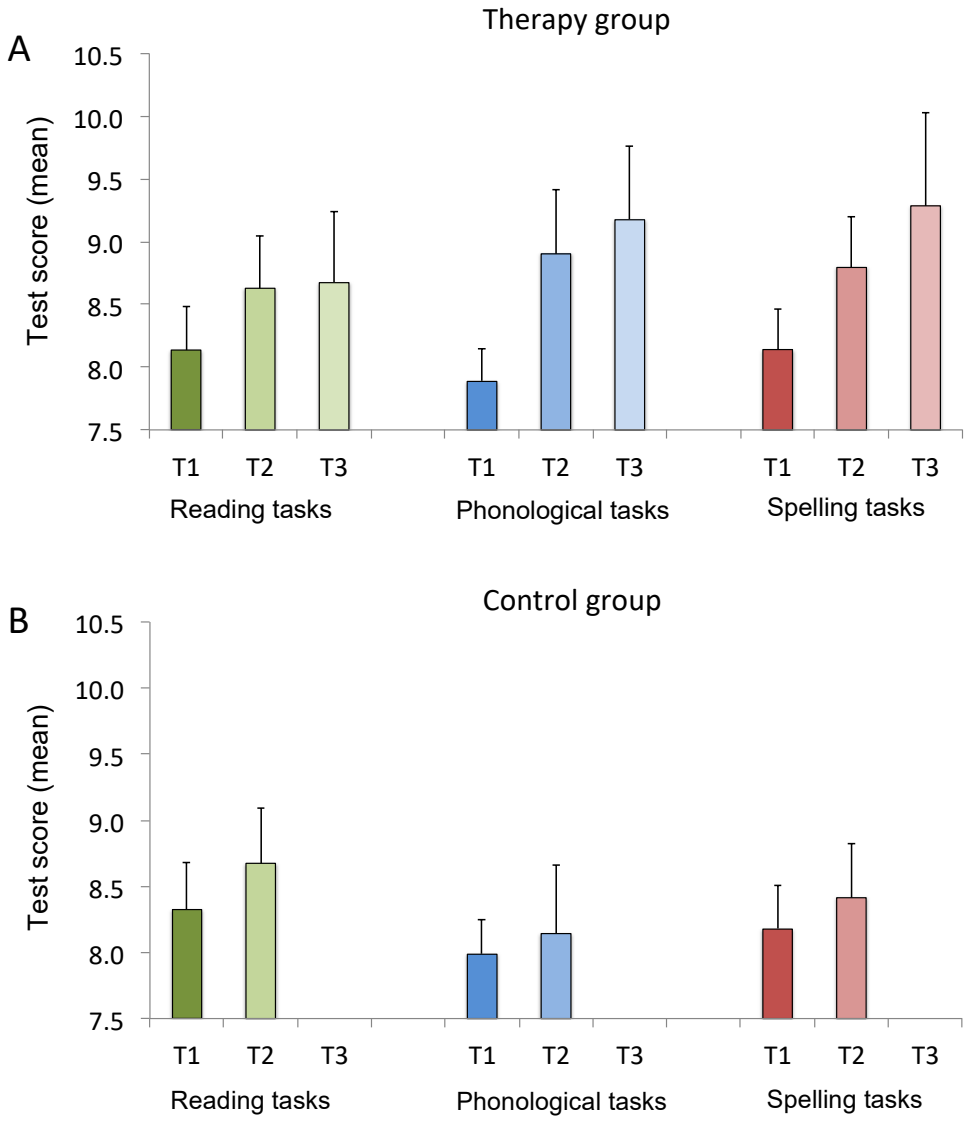
In the raw phonological tasks' data results, there was a statistically significant main effect of Time, $F(2, 30) = 20.68$, $p < 0.01$, $\eta_p^2 = 0.58$, and an interaction of Time and Phonological task, $F(4, 60) = 2.65$, $p < 0.05$, $\eta_p^2 = 0.15$. Each of the phonological tasks was further analyzed separately across the three time points. As a result, it was found that the main effect of Time was significant in the reading of non-words test, $F(2, 32) = 14.81$, $p < 0.01$, $\eta_p^2 = 0.48$. Subsequent pairwise t-tests revealed that there was a significant difference between T1 (mean = 7.87) and T3 (score = 9.0; $t(16) = -4.94$, $p < 0.001$), as well as between T2 (mean = 8.61) and T3, $t(16) = -3.76$, $p < 0.01$, but the T1-T2 difference was only marginally significant, $t(17) = -2.08$, $p = 0.053$. Similarly, there was significant main effect of time in the identification and manipulation of sounds test, $F(2, 32) = 14.14$, $p < 0.01$, $\eta_p^2 =$

0.47. Subsequent pairwise t-tests revealed that there was a significant difference between T1 (mean = 8.65) and T3 (mean = 10.66; $t(16) = -4.89$, $p < 0.001$), as well as between T1 (mean = 8.84) and T2 (mean = 10.21; $t(17) = -3.81$, $p < 0.01$), but only marginally significant between T2 and T3, $t(16) = -1.91$, $p = 0.074$. Finally, the main effect of time was significant in the phonemic decoding efficiency test, $F(2, 34) = 7.24$, $p < 0.01$, $\eta_p^2 = 0.29$. Further pairwise t-tests revealed that there was a significant difference between T1 (mean = 6.85) and T3 (mean = 7.69); $t(17) = -3.29$, $p < 0.01$, as well as between T2 (mean = 7.24) and T3 (mean = 7.69); $t(17) = -2.16$, $p < 0.05$, but only marginally significant between T1 and T2, $t(18) = -1.99$, $p = 0.062$.

Finally, in the raw spelling task's data results, there was a significant main effect of Time, $F(2, 34) = 4.94$, $p < 0.05$, $\eta_p^2 = 0.23$, but no interaction of Time and Spelling task, $F(2, 34) = 1.54$, $p > 0.2$, $\eta_p^2 = 0.083$. In the subsequent analysis the performance in spelling tests across the three time points was compared in a pairwise manner. There was the main effect of Time between T1 (mean = 8.1) and T2 (mean = 8.8), $F(1, 18) = 8.89$, $p < 0.01$, $\eta_p^2 = 0.33$. The difference between the T1 and T3 (mean = 9.29) was also significant, $F(1, 17) = 2.53$, $p < 0.05$, $\eta_p^2 = 0.245$; however, there was no statistically significant difference between the T2 and T3, $F(1, 17) = 2.02$, $p > 0.17$, $\eta_p^2 = 0.11$.

Figure 5.1

Mean cognitive task scores.



Note. The figure represents mean [raw] test scores in the reading tasks (left), phonological tasks (middle) and spelling task (right) of the therapy group (A) and control group (B) at three time-points (T1, T2 and T3) for the therapy group and two time points (T1 and T2) for the control group. The control group figure is given for reference purposes, but these data are not reported in the results section. Note, however, that none of the tests resulted in a

significant difference between T1 and T2 in the control group (all p's > 0.1; see Study 2 for details).

Similarly, in the age-corrected reading results, there was a significant main effect of Time, $F(2, 20) = 9.51$, $p < 0.01$, $\eta_p^2 = 0.49$, and an interaction of Time and Reading, $F(10, 100) = 4.38$, $p < 0.05$, $\eta_p^2 = 0.31$. Again, each of the six reading tests was compared across the three time points of testing (T1, T2, T3) and there was a marginally significant main effect of time in the letter/word identification task, $F(2, 34) = 4.15$, $p = 0.056$, $\eta_p^2 = 0.20$. Follow-up t-tests showed that there was a significant difference between T1 (mean = -4.93) and T2 (mean = -2.81), $t(18) = -2.17$, $p < 0.05$, marginally significant between T1 and T3 (mean = -2.89), $t(17) = -1.94$, $p = 0.069$, but not between T2 and T3, $t(15) = 1.25$, $p > 0.23$. These results show that the improvement in the reading task was comparably better at T2 and T3 relative to T1.

Unlike in the raw test scores, there was a significant main effect of time in the age-corrected scores of the passage comprehension task, $F(2, 32) = 5.21$, $p < 0.05$, $\eta_p^2 = 0.25$. Pairwise comparisons showed a marginally significant difference between T1 (mean = -1.87) and T2 (mean = -1.14), $t(17) = -1.75$, $p = 0.098$, as well as between T1 and T3 (-0.68), $t(16) = -2.68$, $p < 0.02$, but not between T2 and T3, $t(17) = -1.02$, $p > 0.3$. Finally, there was also a significant main effect of Time in the passage fluency task, $F(2, 26) = 4.67$, $p < 0.05$, $\eta_p^2 = 0.26$. Further pair-wise comparisons revealed a marginally significant difference between T1 (mean = -2.73) and T2 (mean = -3.64), $t(14) = 2.1$, $p = 0.054$, as well as between T1 and T3 (mean = -3.73), $t(13) = 2.27$, $p < 0.05$, but not between T2 and T3, $t(16) = 0.62$, $p > 0.5$. This finding shows that performance on the passage fluency task decreased over time (at T2 relative to T1, but this reduction in performance was stabilized three months post-therapy). No other effects (i.e., passage comprehension, reading fluency, and reading accuracy tasks) were significant (all p's > 0.05).

In the age-corrected phonological performance results there was a significant main effect of time, $F(2, 30) = 3.76$, $p < 0.05$, $\eta_p^2 = 0.20$, and an interaction of time and phonological task, $F(4, 60) = 4.53$, $p < 0.01$, $\eta_p^2 = 0.23$. Post hoc comparisons indicated that the main effect of Time was significant in the reading of non-words task, $F(2, 32) = 4.07$, $p = 0.05$, $\eta_p^2 = 0.20$. Subsequent pairwise t-tests revealed that there was a significant difference between T1 (mean score = -3.06) and T3 (score = -2.5), $t(16) = -2.4$, $p < 0.05$, but not between T1 and T2 (mean score = -1.95), $t(17) = -1.68$, $p > 0.1$or between T2 and T3, $t(16) = -0.62$, $p > 0.5$.

Age-corrected identification and manipulation of sounds task performance also revealed a significant main effect of time, $F(2, 32) = 6.1$, $p < 0.01$, $\eta_p^2 = 0.28$. Follow-up pairwise comparisons resulted in significant differences between T1 (mean score = -1.85) and T2 (score = -0.81), $t(17) = -2.8$, $p < 0.05$, and between T1 and T3 (mean score = -0.64), $t(16) = -2.99$, $p < 0.01$, but not between T2 and T3, $t(16) = -1.1$, $p > 0.3$. The main effect of time was not significant in the phonemic decoding efficiency task, $F(2, 34) = 1.52$, $p > 0.2$, $\eta_p^2 = 0.08$. Finally, age-corrected spelling performance showed no main effect of time, $F(2, 34) = 1.18$, $\eta_p^2 = 0.065$, and no interaction of time and spelling tasks, $F(2, 34) = 4.65$, $p > 0.2$, $\eta_p^2 = 0.08$.

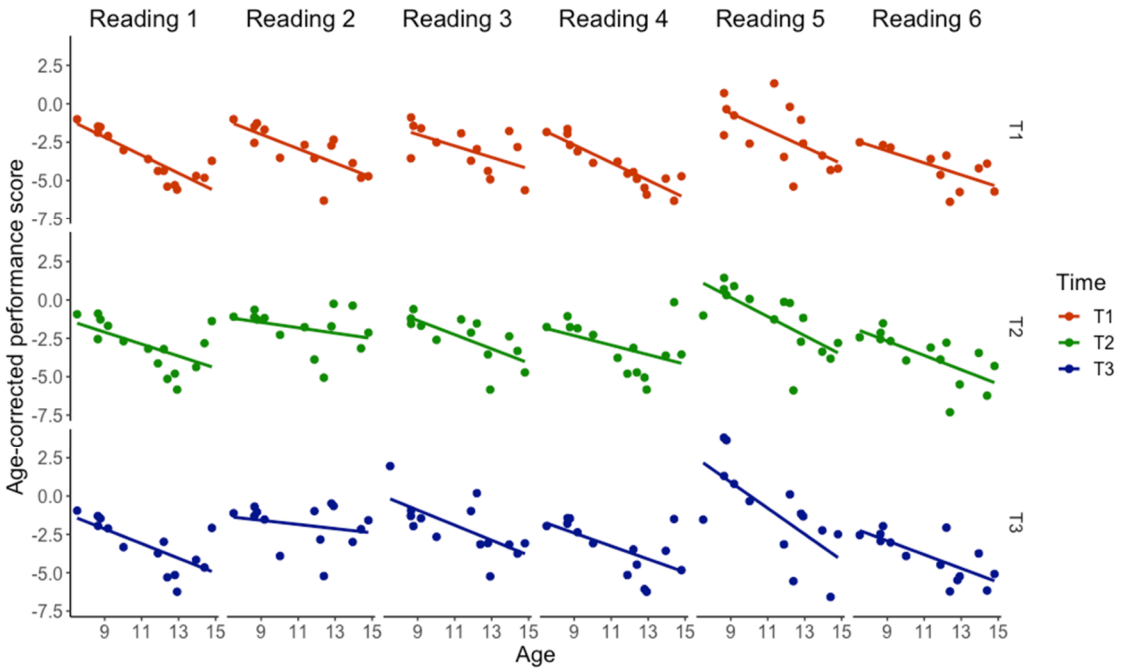
Correlational Analyses

There was a statistically significant negative correlation between age of participants at T3 and their T3 age-corrected performance on the letter/word identification task (i.e., reading task; $r = -0.719$, $p < 0.01$; Figure 5.2), reading accuracy (reading task; $r = -0.67$, $p < 0.01$), passage comprehension (reading task; $r = -0.72$, $p < 0.01$) and passage fluency task (reading task; $r = -0.59$, $p < 0.02$). No other correlation involving the reading tasks reached significance (all p's > 0.05).

Similarly, there was also a negative correlation between participants' age and performance on phonemic decoding efficiency (phonology task; $r = -0.8$, $p < 0.01$; see Figure 5.3), as well as the spelling test (spelling task; $r = -0.79$, $p < 0.01$). These findings show that the participants at T3 were still continuously falling behind normative performance on a number of dyslexia-relevant tests.

Figure 5.2

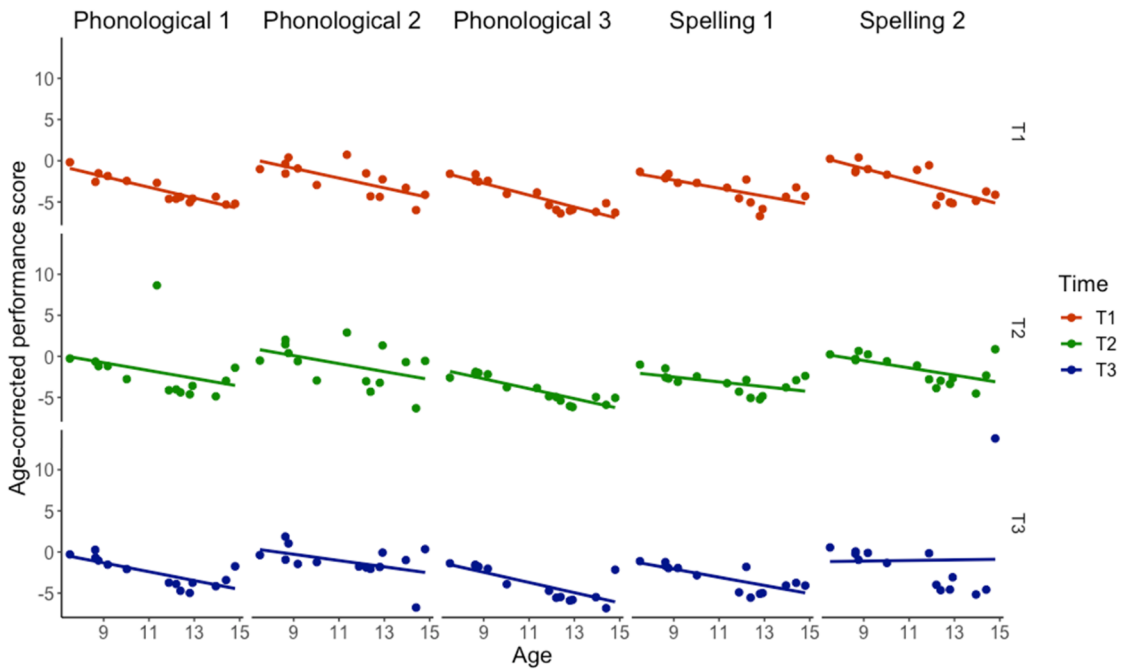
Correlation plots of age-corrected scores for reading tests



Note. The figure represents correlations of the chronological age of participants with age-corrected performance scores in six different reading tasks plotted separately for pre (T1), post-therapy (T2) and once again three months post-therapy (T3). The lines represent the best fitting line of participants' performance.

Figure 5.3

Correlation plots of age-corrected scores for phonological and spelling tests



Note. The figure represents correlations of the chronological age of participants with age-corrected performance scores in three different phonological tasks and two spelling tasks plotted separately for pre (T1), post-therapy (T2) and once again three months post-therapy (T3). The lines represent the best fitting line of participants' performance.

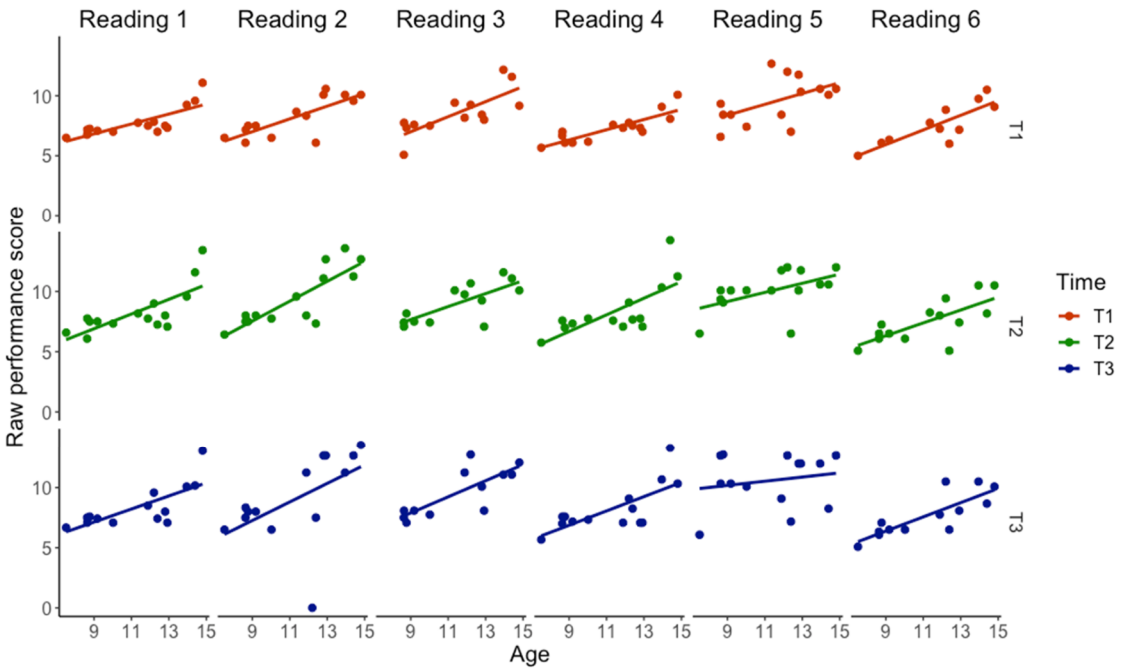
In contrast, there was significant positive correlations of participants age at T3 and raw test performance scores (at T3) on the letter/word identification task (reading task; r = 0.66, $p < 0.01$), passage comprehension (reading task; $r = 0.46$, $p = 0.056$), reading fluency (reading task; $r = 0.49$, $p < 0.05$), and reading accuracy tasks (reading task; $r = 0.68$, $p <$ 0.01). No other correlation involving the reading task reached significance (all p's > 0.05).

Further, there also was found a positive correlation between participants' age and performance on reading of non-words task (phonological task; $r = 0.62$, $p < 0.01$), and phonemic decoding efficiency task (phonological task; $r = 0.53$, $p < 0.05$), as well as spelling

test (spelling task; $r = 0.81$, $p < 0.01$) and spelling sounds test (phonological spelling task; $r = 0.44$, $p = 0.068$; see Figure 5.4 and Figure 5.5).

Figure 5.4

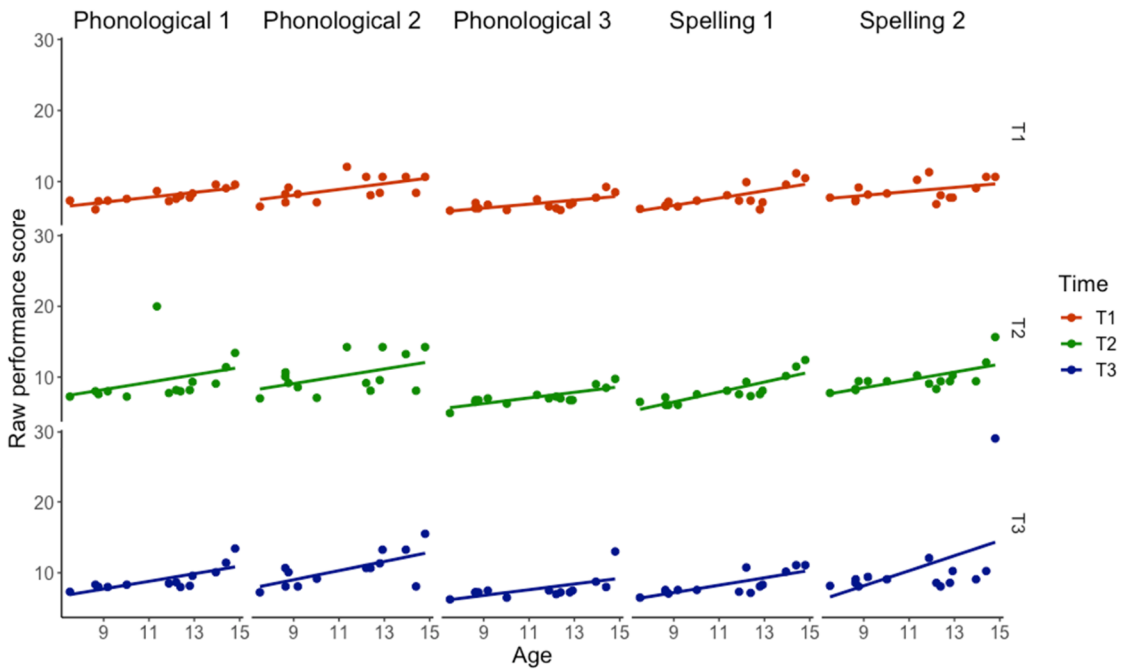
Correlation plots of raw scores of reading tests



Note. The figure represents correlations of the chronological age of participants with raw performance scores in six different reading tasks plotted separately for pre (T1), post-therapy (T2) and once again three months post-therapy (T3). The lines represent the best fitting line of participants' performance.

Figure 5.5

Correlation plots of raw scores on phonological and spelling tests



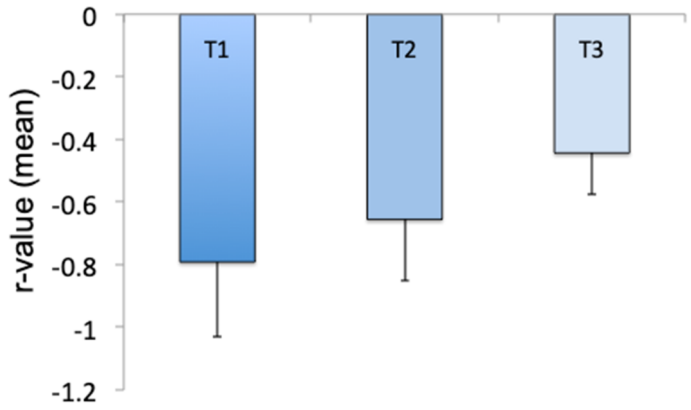
Note. The figure represents correlations of the chronological age of participants with raw performance scores in three different phonological tasks and two spelling tasks plotted separately for pre (T1), post-therapy (T2) and once again three months post-therapy (T3). The lines represent the best fitting line of participants' performance.

In the final step, the *r*-values of the therapy group over 11 tests (6 reading tasks, 3 phonological and 2 spelling tasks) tested separately at three time-points (T1, T2, and T3; see Figure 5.6) were compared statistically. For this purpose, separate repeated-measures ANOVAs were performed with a single within-group factor time (T1, T2, T3). As a result, there was a significant main effect of time, $F(2, 20) = 8.99$, $p < 0.01$, $\eta_p^2 = 0.47$. In the following steps, pairwise comparisons of the three time-points were performed. Results indicated a statistically significant difference in *r*-values between T1, $r = -0.791$, and T2, $r = -$

0.655, $t(10) = -2.97$, $p < 0.05$, between T1 and T3, $r = -0.51$; $t(10) = -3.46$, $p < 0.01$, and also marginally significant between the T2 and T3, $t(10) = -2.17$, $p = 0.056$.

Figure 5.6

The figure depicts correlation coefficients (r-values) between chronological age and age-corrected behavioural test performance plotted for the three time points (T1, T2, T3).

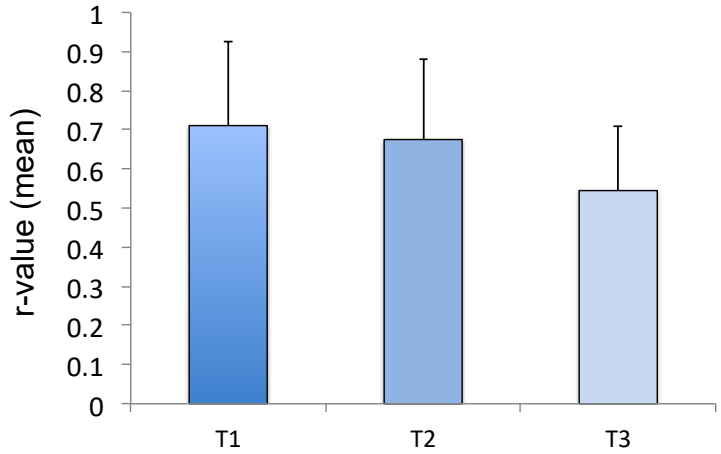


Note. The figure represents the mean correlation coefficient (*r*-value) averaged across all psychological tests ** $p < 0.05$. Error bars indicate standard error of the mean (SEM).

The *r*-values of the therapy group's raw tests' performance tested separately at three time-points (T1, T2, and T3; see Figure 5.7) were also compared. There was a significant main effect of Time, $F(2, 20) = 8.84$, $p < 0.01$, $\eta_p^2 = 0.47$. In the following steps, pairwise comparisons of the three time-points were conducted. As a result, there were no significant differences in *r*-values between T1, $r = 0.71$, and T2, $r = 0.67$, $t(10) = 0.64$, $p > 0.5$, but it was significant between T1 and T3, $r = 0.49$; $t(10) = 4.21$, $p < 0.01$, and also between the T2 and T3, $t(10) = 3.08$, $p < 0.02$.

Figure 5.7

The figure depicts correlation coefficients (r-values) between chronological age and age-corrected behavioural test performance plotted for the three time points (T1, T2, T3).



Note. The figure represents the mean correlation coefficient (*r*-value) averaged across all psychological tests ** $p < 0.05$. Error bars indicate standard error of the mean (SEM).

To summarize, these latter findings suggest that participants with dyslexia continued showing generally hindered performance in overall age-corrected task performance (i.e., averaged over reading, phonological and spelling tasks). Nevertheless, the rate of performance deterioration, as defined by the steepness of the correlation (i.e., *r*-values), was reduced after neurofeedback therapy (i.e., resulted in weaker negative correlation). Most importantly, this parameter was even further reduced three months post-therapy.

Parental Questionnaire

As can be seen from Table 1, the majority of parents (> 60%) indicated at least minimal changes in their child's post-therapy reading ("Has your child's willingness to read, practise reading, practise spelling, etc. changed at all compared to before they began the study?"), self-esteem ("Has your child's confidence or belief in their capabilities in regards to their literacy skills (e.g., spelling, reading comprehension, reading to themselves or out loud) changed compared to before they began the study?") and attention behaviours ("Does your

child find it easier to concentrate on their work? Do they appear to be finishing their homework faster or are better at staying on task?"). The only exceptions are the control categories mentioned above: expressive language skills (Has your child's spontaneous use of words in speech changed at all since they began the study? For example, using new vocabulary words in sentences, etc.) and understanding verbal instructions (Does your child appear to understand verbal instructions better since they began the study?); over 70% of all parents noticed either no changes or only slight changes post-therapy. To summarize, the results of the parental questionnaires indicate that the parents reported post-training changes in some critical, dyslexia-related behaviours, but not on control tasks that were used to control for the social desirability bias (see methods section).

Table 5.1

Results of the parental post-therapy questionnaire

	Much worse	Moderately worse	Slightly worse	No change	Slightly better	Moderately better	Much better
Overall enjoyment for reading	0 %	0 %	0 %	15 %	31 %	23 %	31 %
Willingness to practice reading	0 %	0 %	0 %	38 %	8 %	15 %	38 %
Choosing to read spontaneously	0 %	0 %	0 %	15 %	23 %	38 %	23 %
Self-esteem in relation to literacy	0 %	0 %	0 %	23 %	15 %	31 %	31 %
Expressive language skills	0 %	0 %	0 %	54 %	15 %	23 %	8 %
Understanding verbal instruction	0 %	0 %	0 %	69 %	23 %	0 %	8 %
Pace of learning	0 %	0 %	0 %	23 %	31 %	23 %	23 %
Focus and Attention for school work	0 %	0 %	0 %	8 %	38 %	31 %	23 %

Note. The scores represent the percentage of parents who had chosen the responses listed in column names for categories that are depicted in the row names. See supplementary material for the sample questionnaire.

Discussion

In the current study, the lasting effects of LORETA z-score neurofeedback training on behavioural symptoms of dyslexia were examined. In more detail, the performance of the therapy group on 11 psychological tests was contrasted across the three time points (T1: before the start of training, T2: immediately after training, and T3: three months post-training). It was hypothesized that if the beneficial effects of neurofeedback were robust, one would observe that the performance in participants would remain higher three months following therapy relative to testing prior to the commencement of the therapy. Furthermore, if the learning-to-learn hypothesis were correct, the therapy group would show even better performance three months following therapy relative to both pre- and post-therapy.

Analysis of raw test scores (reading, phonological, spelling) across the three time-points showed that participants better performance in the reading, phonological, and spelling tasks three months post-therapy (T3), relative to prior to the training (T1). Importantly, there was also improved raw performance three months post-therapy (T3) relative to immediately following therapy (T2), specifically in the reading and phonological tasks. This consistency in improved phonological performance both immediately following therapy and three months post-therapy is in line with the findings of training-related changes in brain activity in frontal brain regions discussed in Study 2 (see also Arns et al., 2007). Further, in Study 2, results indicated generalized improved brain activation in frontal brain regions, which particularly the inferior frontal gyrus (IFG; BA 44, 45), are known to play an essential role in phonological processing (Nixon et al., 2004). Therefore, improved phonological performance at T3 and T2 relative to T1 could represent lasting, neurofeedback-related improvements in activity in frontal brain regions.

Importantly, the current work indicated that participants' performance not only improved after the end of therapy but remained significantly higher three months after the

therapy was over. Therefore, the first hypothesis was confirmed, and the effect of neurofeedback was found to be robust. Furthermore, in line with the learning-to-learn hypothesis, reading and phonological task performance improved even further three months post-therapy. In more detail, it was hypothesized that neurofeedback therapy may not only facilitate participants' immediate behaviour but that it could also have durable effects through the improved acquisition of dyslexia-related skills. Therefore, Study 3 was designed to test the potentially lasting effects of neurofeedback by conducting follow-up assessments three months after the end of therapy. Results indicated that neurofeedback does seem to facilitate participants' ability to acquire new skills, and their performance continued improving not only immediately following therapy relative to before therapy but at three months post-therapy relative to immediately following the therapy. Therefore, the second hypothesis was confirmed, as well. Note that these results are consistent with previous findings that showed long-lasting effects of neurofeedback therapy (Kouijzer et al., 2009; Leins et al., 2007; Strehl et al., 2006). It was shown that neurofeedback can improve participants' behaviour when retested 12 months after the end of the therapy (autism; Kouijzer et al., 2009) and 6 months after the end of the therapy (ADHD; Leins et al., 2007; Strehl et al., 2006). Importantly, to my knowledge, this work is first to both use a highly controlled design and also to simultaneously show the long-lasting effects of neurofeedback in dyslexia.

Interestingly, the pattern of findings was somewhat different in the age-corrected performance scores. Specifically, although age-corrected scores also showed consistent improvements in performance in the reading and phonological (but not spelling) tasks, such improvements were most pronounced immediately following therapy (T2) relative to before therapy (T1), but there was no difference between testing immediately post-therapy and the testing three months post-therapy (T3). This implies that although the rate of performance deterioration on individual tasks in dyslexia-related tasks was reduced after the end of

therapy, the rate of reduction on those tasks was constant three months post-therapy. This in itself is a positive finding, which implies that neurofeedback training can modulate task performance of participants with dyslexia by either continuously improving their raw performance scores or reducing the rate of performance deterioration (when compared to chronological age expectations). Note also that the correlational analyses of Pearson *r* scores revealed that the rate of deterioration (i.e., the strength of negative correlation between age-corrected test scores and participants' chronological age) was significantly weaker at the three-month follow-up relative to immediately following therapy. Given that correlations were performed overall all 11 tests, it is possible that testing the performance over individual tests lacked statistical power to detect significant changes three-month post-therapy.

In line with this finding, there were statistically significant positive correlations between chronological age and raw score test performance. In other words, participants seem to accumulate some skills as they get over time; however, the strength of the positive correlation also reduced when examined over the three time points (i.e., before the therapy, right after the therapy and three months after the therapy). This finding implies that although participants' performance does show some improvement with age, such change is also getting weaker as participants grow.

Moreover, it was also found that the therapy group showed overall significantly weaker negative correlations between participants' chronological age and their age-corrected test performance scores. In more detail, it was observed that participants with dyslexia generally showed a negative correlation between their age and performance scores. In line with the analysis of raw performance scores, these results indicate that participants with dyslexia continuously fall behind their peers in reading, spelling, and phonological tasks at a constant rate. However, the strength of this negative relationship was weaker after neurofeedback therapy, which means that in addition to improved child's scores on some

specific tasks (i.e., reading of non-words, identification and manipulation of sounds, decoding efficiency, generally in all reading and spelling tests), neurofeedback therapy is also capable of slowing the rate at which children are falling behind their peers. It is possible to conclude that neurofeedback therapy may indeed have an overall positive and worthwhile effect on combined test performance (i.e., including reading, phonological and spelling tasks). This idea is also consistent with other neurofeedback studies that found a positive effect of neurofeedback training (e.g., Walker & Norman, 2006; see also Van Doren et al., 2019). Notably, the weakening of the relationship between the chronological age and test performance continued even after the end of the therapy (i.e., the difference was also significant between the end of therapy and three-month follow-up).

The current findings are also in line with earlier work on the lasting effects of neurofeedback in dyslexia (Nazari et al., 2012). Nazari et al. reported that 20 sessions of neurofeedback (30 minutes each) could result in improved reading and phonological performance scores in 6 participants with dyslexia. Interestingly, in this study, the achieved improvements were evident even two months after the training was over (i.e., the effects of neurofeedback were durable). Note that although the results of the current study support findings by Nazari and colleagues (2012), they also extend previous results. The current dyslexia sample is three times larger relative to what was used previously (6 vs. 18 participants), which should improve the power of the current findings. Additionally, the results in the current work were contrasted against a control group (see Study 2 in Chapter 4), while the work of Nazari and colleagues did not test whether any of the reported improvements in participants with dyslexia were superior to an appropriate control group. Most importantly, and as discussed above, current results indicated that neurofeedback does not only result in durable changes but that participants with dyslexia may even continue to improve after the therapy is over (e.g., improved reading and phonological awareness

performance three months post-therapy), which is once again consistent with the learning-to-learn account of neurofeedback.

One could argue that the durable positive effect of the therapy could be unrelated to improved neural brain functioning but instead related to the behavioural remedial training in dyslexia (remember that both the therapy and control groups received additional remedial training during the whole duration of the training). Although this possibility remains, it is less likely due to recent findings that behavioural training alone does not seem to maintain lasting effects in dyslexia. For instance, van der Kleij and colleagues (2019) examined whether behavioural training can have a long-lasting effect on word and pseudoword processing in Dutch children with dyslexia. The main finding was that participants with dyslexia produced more errors relative to healthy controls and showed a lack of behavioural improvements, even after they underwent behavioural reading intervention (see also Tam & Leung, 2019). Furthermore, the results of Study 2 (see Chapter 4) showed that those participants with dyslexia who received remedial instructions but no additional neurofeedback training showed no behavioural improvements. In other words, it seems unlikely that behavioural training alone could result in either such a substantial improvement or have any durable effects. Although this reasoning does provide some support for the hypothesis that the neurofeedback resulted in improved behavioural performance in the current study, an interesting question remains; would neurofeedback therapy and a specific behavioural intervention combined show better outcome relative to neurofeedback alone?

It was shown previously that dyslexia is not a homogeneous disorder and that it can be classified into dysphonetic and dyseidetic subtypes (Boder, 1973), phonological and surface subtypes (Castles & Coltheart, 1993), subtypes with and without verbal language deficit (Leonard et al., 2002), as well as visual attention span and phonological subtypes (Bosse et al., 2007; Ramus et al., 2018). Specifically, in the current work, all participants had a

phonological subtype of dyslexia, i.e., all participants with dyslexia must have shown considerable difficulties with phonological task performance to be included in the study. Therefore, it would be interesting whether the effect of neurofeedback would have been more substantial and/or more robust if it was explicitly combined with a structured phonology-oriented intervention program (da Silva & Capellini, 2015) in the phonological dyslexia sample. Note that participants with dyslexia did receive extra tutoring throughout the study (T1-T3) and part of this tutoring included a phonological component; however, an interesting question is whether a much stronger phonological training would advance the effect of the neurofeedback training even further (as in Silva & Capellini, 2015). In contrast, most previous neurofeedback studies not only ignored the existence of dyslexia subtypes but also either provided no remedial training at all or did not follow any structured approach to deliver remedial training. Therefore, future studies should address the synergetic effect of the two types of therapy/training more systematically, considering both dyslexia subtype and type of behavioural intervention (see General discussion chapter for more detail).

The results of the parental questionnaires indicated that, from the subjective parents' point of view, a large proportion of participants with dyslexia showed slight to substantially improved behaviour on several parameters (e.g., overall enjoyment for reading, willingness to practice reading, choosing to read spontaneously etc.). For example, 85% of parents stated that they saw an improvement in overall enjoyment of reading in the child, with 31% stating it was "much improved". Similarly, 92% of parents noted improvements in focus and attention for schoolwork, with 23% who thought it was "much improved" (see Table 1). On the other hand, the improvements were less pronounced for such parameters as "expressive language skills" and "understanding verbal instructions", where over 70% of all parents noticed either no changes or little changes post-therapy. These questions were included as “control” parameters for two main reasons. First, the neurofeedback therapy targeted a wide

range of brain areas implicated in the language network that could result in behavioural improvements that are not exclusive to dyslexia (i.e., the positive effect of neurofeedback could spill over to other language functions). If this were the case, one would have expected to find parent-rated improvements in all language-related parameters, including the "expressive language skills" and "understanding verbal instructions". Therefore, since the questionnaire results demonstrated improvements specifically in dyslexia-related parameters (overall enjoyment for reading, willingness to practice reading, choosing to read spontaneously), it could be concluded that LORETA z-score neurofeedback was successful in targeting disorder-specific alterations in brain functioning (in line with the goal of therapy) and could improve specific behavioural performance.

Additionally, control evaluation points in the parental questionnaire could also account for the parents' social desirability bias. When asked to fill out a questionnaire, parents could have potentially responded in a way that they thought was more desirable given the purpose of the study, rather than providing an unbiased assessment (Mortel, 2008). In other words, if parents reported substantial improvements in all parameters (i.e., questions that were related to language functions but that were not targeted by the therapy), one could have suspected such a social desirability bias and the results of the questionnaire could have been compromised. In contrast to this, participants with dyslexia showed substantial improvements in dyslexia-related functions, but not in language functions that were not targeted by the therapy (e.g., expressive language skills, Carroll & Myers, 2010). To summarize, the results from the parental questionnaire results were in line with the idea that the LORETA z-score neurofeedback therapy was developed to address specific, dyslexia-related behaviours. The pattern of results suggests that current findings did not stem from parents' response biases or general, therapy-unrelated, and task-unspecific maturation of participants with dyslexia.

Another interesting finding from the parental questionnaire concerns the self-esteem parameter, in which over 75% of parents observed improvements in their child's behaviour. Research has shown that children with dyslexia can often experience frustration, depression and low self-esteem due to the inability to meet their parents' expectations (Livingston et al., 2018). For instance, Wilson et al. (2009) examined a large group of people with self-reported learning problems (15 to 44 years old) and found that relative to healthy controls, these participants showed significantly increased levels of depression, anxiety and even suicidal thoughts. Additionally, Cosden, Patz, and Donahue (2012) found that, besides obvious learning difficulties, people with dyslexia are disproportionally at higher risk for low self-esteem, poor social communication, and substance abuse. Consequently, neurofeedback therapy may not only reduce the deterioration in reading and spelling performance in children with dyslexia, but may also improve their overall self-esteem and possible other emotion-related characteristics. To my knowledge, this is first demonstration that besides objective improvements in formal test performance, neurofeedback also results in changes in informal dyslexia-specific behaviour that can still be observed months after the end of the therapy.

Limitations of the Current Study

One clear limitation of the current work is the absence of a control group at T3. This was a result of the study design because control participants with dyslexia on a waiting list started receiving neurofeedback training before the follow-up testing three months post-therapy (i.e., testing these participants would be confounded by their neurofeedback training). The presence of a control group could assure that the observed improvements three months post-therapy were indeed unique to the neurofeedback and not due to their remedial tutoring (see above). Note, however, that the control (in contrast to the therapy) group showed no difference between T1 and T2 in Study 2 while they were also receiving the remedial

training, thus it would be unlikely that their performance would be changed three months later.

Another problem is the lack of control for school holidays/vacation when testing participants with dyslexia. In more detail, the study did not consider the time of school holidays, which means that some children may not have been receiving the same level of extra tutoring or even regular schooling throughout therapy, making the group potentially more heterogeneous in terms of neurofeedback outcome. Future studies could take this into account and either make the therapy less extended (i.e., by increasing the frequency of test sessions) or plan the study in such a way as to avoid lengthy and uncontrolled breaks from therapy/ training.

Summary

The current work was a follow up of Study 2 results that indicated that neurofeedback-related changes in resting-state neural activity in frontal brain regions and significantly higher performance on behavioural tasks (spelling, writing, phonology) post-therapy. This study was designed to examine whether the facilitated improvements were robust and could still be observed three months post-treatment. I hypothesized that if the effect of neurofeedback were robust, performance three months post-therapy (T3) would be higher than performance immediately post-therapy (T2). Additionally, if the learning-to-learn hypothesis were correct and neurofeedback improved one's ability to acquire previously hindered skills, improved performance three months post-therapy (T3) relative to both prior to therapy (T1) and immediately post-therapy (T2) would be expected. Results indicated that the LORETA z-score neurofeedback training was an effective method to improve behavioural symptoms of developmental dyslexia. Most importantly, likely due to the acquisition of learning skills in dyslexia and slowing down of disorder-related deterioration of relevant task performance, the positive effect of neurofeedback could last at least three

months after the end of the therapy. Finally, these results suggest that in addition to noticeable behavioural improvements, neurofeedback may lead to overall psychological benefits in dyslexia (i.e., improved self-esteem and motivation to learn), as observed via parental questionnaires.

Chapter 6. Discussion on the Role of Neurofeedback in Dyslexia

Discussion

Dyslexia accounts for almost 80% of all specific learning disorders (American Psychiatric Association, 2013) and affects 5 to 20% of the world population (De Santana et al., 2012), with up to 11% of individuals in Australia affected (Smythe et al., 2005). The best behavioural therapies for dyslexia that are currently available have limited effectiveness, with even the most advanced practices not allowing for a full recovery of reading and phonological performance (e.g., Breteler et al., 2010; Nazari et al., 2012).

Additionally, these therapies are time-consuming and require much effort from both the children and their parents. Therefore, the current work of three experiments attempted to further examine the behavioural and neural correlates of this disorder. In addition, given that LORETA z-score neurofeedback therapy has been shown effective in the treatment of ADHD and autism (Arns et al., 2020; Kouijzer et al., 2009), the efficacy of this treatment was examined in a sample of children diagnosed with dyslexia.

The ability to assess the effectiveness of neural markers of dyslexia after neurofeedback therapy is complex and requires an in-depth understanding of the EEG processes in this disorder (Babiloni et al., 2012). Unfortunately, previous studies provided inconsistent results due to low sample sizes (Nazari et al., 2012), lack of consideration of dyslexia subtypes (Arns et al., 2007; Li & Chen, 2017; Rippon & Brunswick, 2000;), and control of remedial training (Binder & Price, 2002; Walker & Norman, 2006). Therefore, in Study 1 of the current dissertation, a large and homogeneous sample of participants with phonological dyslexia (N = 47) were tested, and their behavioural and EEG brain activity was compared to a gender- and an age-matched group of healthy controls (N total = 94). The goal of the study was to identify dyslexia-related changes across a range of EEG frequency bands: low, medium, and high alpha frequencies, and the delta, theta, beta1, beta2, and gamma

bands. Treatment related changes in these identified neural markers were used as one of the measures of effectiveness of neurofeedback therapy in Study 2. In this study, the averaged brain activity was recorded and then compared across four electrode regions: frontal (sites Fp1, Fp2, F7, F3, Fz, F4, F8), temporal (sites T3, T4, T5, T6), parietal-occipital (sites P3, Pz, P4, O1, O2), and central (sites C3, Cz, C4).

*Discussion of study 1*Given that previous findings in research on EEG correlates of dyslexia produced inconsistent results, Study 1 was more exploratory in nature. Nevertheless, it was expected that the participants with dyslexia could potentially show reduced power in the three alpha frequency bands at parietal, occipital, and temporal brain areas (Babiloni et al., 2012). It was also expected to find increased theta, delta, and beta in the frontal and right temporal brain region (Arns et al., 2007). Gamma frequency power was expected to be reduced in the frontal region (Flinker et al., 2015; note, however, that these authors used intracranial EEG and thus their method is not fully compatible with the current work) as a marker of hindered functioning in dyslexia of the language-related Broca's area (Kennison, 2017). Finally, reading, phonological and spelling tasks' performance was expected to be worse in dyslexia.

Study 1 results indicated a strong negative dependency of age-corrected test scores on the chronological age of participants in the group with dyslexia, with older subjects showing significantly lower age-corrected scores than younger subjects. The observed effect indicated that children with dyslexia at all age ranges tested in this study (7 to 15 years) continuously fell behind their normal peers at a similar rate. Importantly, in the sample of children with dyslexia, there was a negative correlation between the test scores and chronological age in all measured tasks. Relative to children without dyslexia, the performance of children with dyslexia was lower across all behavioural tasks (6 reading tests, 3 phonological tests and 2 spelling tests; see the methods section for more details about the structure of these tests).

Although previous studies were inconsistent regarding the exact frequency of oscillations that are affected in dyslexia, it was still shown that reading, writing and spelling deficiencies in dyslexia are characterized by abnormal oscillatory neural mechanisms in cortical networks involved in the corresponding cognitive tasks (Klimesch, 1999; Pfurtscheller & Lopes Da Silva, 1999). These assumptions were subsequently tested in Study 1 in order to analyses resting-state EEG activity.

In the analysis of EEG data from Study 1, when measured at frontal (Fp1, Fp2, F7, F3, Fz, F4, F8) and temporal (T3, T4, T5, T6) electrodes, dyslexia relative to control participants showed reduced power of delta, theta, low-, medium- and high- alpha bands, reduced power in low- and high- beta frequencies. In contrast, these frequency bands resulted in an enhanced pattern of activations in the central (C3, Cz, C4) and parietal-occipital (P3, Pz, P4, O1, O2) electrodes. Finally, gamma frequency was consistently reduced in all brain regions.

The significantly reduced oscillatory activity across all frequency bands in the frontal brain regions is characteristic of some of the known dyslexia-related brain alterations. Frontal brain regions are involved in cognitive control and inhibition of motor actions (Cavanagh & Frank, (Cavanagh & Frank, 2014), as well as functions that aggregate information from the brain's language networks (Ye & Zhou, 2009). Participants with dyslexia typically show reduced cognitive and executive control abilities (Dhar et al., 2010), hindered performance on tasks that require control over verbal and phonological fluency, auditory attention, and visual and verbal working memory (Varvara et al., 2014). Therefore, it is plausible that the abnormal pattern of activity over the frontal regions in dyslexia is indicative of deficient language-network functioning and hindered cognitive control abilities in this disorder. The observed altered oscillatory activity replicates previous work that also observed dyslexia-related differences in the frontal brain region (Ahn et al., 1980; Martin Arns et al., 2007;

Colon et al., 1979; Fonseca et al., 2006; Sklar et al., 1972). In addition, the current work tested a large sample of participants and showed disorder-related changes across all frequency bands frontally, thus extending previous findings.

Reduced power of frequency bands in the frontal brain region can also reflect hindered phonemic encoding in dyslexia (Lehongre et al., 2011). This is because apart from cognitive control, a number of frontal areas are also directly linked to speech production (Broca's area; Kennison, 2017), language comprehension (Goswami et al., 2011) and language processing (Kim et al., 2019; Nardone et al., 2011). For instance, gamma activity measured intracranially in Broca's area was shown to be highly correlated with the reading task performance during the reading of pseudowords in dyslexia (Flinker et al., 2015).Reduced frontal delta frequency reflects deficient processing of slow-rate speech information (Goswami et al., 2011) and reduced frontal theta is associated with reading difficulties (Arns et al., 2007; Goswami, 2011; Klimesch, 1999; Penolazzi et al., 2008). Collectively, the results of Study 1 support results indicating hindered functioning of Broca's area in dyslexia (Lehongre et al., 2013) and reflect dyslexia-specific dysfunctions in the core neurophysiological correlates of linguistic processing (understanding of phonological information; Flinker et al., 2015), as well as semantic (Goucha & Friederici, 2015), and syntactic processing (Rumsey et al., 1992).

This claim is additionally supported by the results of the correlational analysis that indicated that the alpha and beta frequencies in the frontal cortex correlated positively with reading tasks (reading fluency and comprehension). Thus, reduction in these areas was directly associated with worse reading performance. These correlational results further advanced the understanding of the links between cognitive tests and disorder-related brain alterations by showing that the strength of peak alpha frequency can be directly associated

with the successful performance on these cognitive tasks (Bornkessel et al., 2004; Cecere et al., 2015).

Much like the pattern of results observed over the frontal brain regions, there was also a comparable reduction in oscillatory activity in the temporal regions. The reason for the observed reduction in this brain area could be related to the thalamocortical language network (Bollimunta et al., 2011; Vijayan et al., 2013). The thalamus connects sensory organs to areas of primary sensory processing. Furthermore, thalamic nuclei form a hub connecting language-specific brain structures: the frontal cortex (including the Broca's region) and medial-temporal lobes (Ketz et al., 2015). The thalamus is also thought to be one of the origins of alpha oscillations, and thalamocortical structures modulate alpha's involvement in cognitive functions (Bollimunta et al., 2011; Vijayan et al., 2013). Therefore, reduced low-, middle- and high-alpha frequency in temporal (and frontal) brain regions in dyslexia symbolizes the disrupted link between language-related frontal and temporal brain regions through the thalamic hub described above. In line with this proposition, children with dyslexia were shown to have hindered activity in the auditory thalamus in response to phonemes (Díaz et al., 2012).

Interestingly, and in contrast to the pattern of results observed in frontal and temporal regions, there was increased low- and high-alpha power at central and parietal-occipital brain regions. Although the pattern of results was qualitatively different relative to those observed over the frontal and temporal regions (i.e., increase vs. decrease in activation), it is possible that these results are comparably associated with neural abnormalities in dyslexia. For instance, an increase in alpha power in parietal and occipital brain regions is associated with enhanced cognitive demands (Haegens et al., 2014). Such an increase in cognitive demand at rest (i.e., when measured at resting state) is in line with hindered inhibitory and cognitive control in dyslexia (Dhar et al., 2010). In other words, current findings suggest that children

with dyslexia have an abnormal level of cognitive demand even when they are not performing a task. That is, children with dyslexia appear to require an increased level of cognitive control and neuronal activity just to maintain normal brain functioning during rest.

Additional hemisphere analysis showed that healthy controls had higher alpha power activity in the right relative to the left hemisphere in frontal and parietal-occipital brain regions. In contrast, the participants in the dyslexia sample showed no such asymmetry. The findings in the control group are consistent with previous observations of higher alpha amplitudes over the right than left posterior regions (Louis et al., 2016). It is possible that the group with dyslexia did not show such a hemisphere-specific asymmetry because of the overall increased level of alpha in this group in this area. In other words, the participants with dyslexia could have reached a ceiling level of alpha in both hemispheres and therefore showed no cross-hemispheric asymmetry.

One of the advantages of the current work was the use of individual alpha peak frequencies (IAFs) to set the ranges of oscillatory activity that were used to define individual frequency bands. The IAF refers to the frequency of peak EEG power within the alpha range: 8 – 15 Hz (Klimesch, 1999). Thus, to find an IAF, it is necessary to identify the frequency at which the power spectral density is maximal within the frequency range of 8-15 Hz (Klimesch, 1999; Kropotov, 2016). Inter-subject variance in IAFs have explained the variability in participants' performance in various perceptual (Cecere et al., 2015; Samaha & Postle, 2015) and cognitive tasks (Bornkessel et al., 2004; Klimesch et al., 2006). The IAF is thought to be particularly relevant when working with patients (e.g., dyslexia, PD, ADHD) who have an average IAF that may be different from healthy controls (e.g., Arns et al., 2012).

Given that rigidly applied frequency ranges may not capture the inter-individual differences across participants, this may influence the individual frequency band definition by making it less precise. To overcome this problem, previous work used IAF as a reference

point from which to define all frequency bands of interest (e.g., Babiloni et al., 2012). For example, the delta frequency band was defined in a frequency range of IAF - (minus) 8 to IAF-6 Hz, theta as IAF-6 to IAF-4 Hz etc. Using this method, the selected frequency ranges were different for each participant and could also account for IAF variability.

In contrast to other disorders (Arns et al., 2012), Study 1 indicated that children with dyslexia and controls had statistically comparable IAFs, and there was no disorder-related statistically significant shift in IAF between groups. These findings are comparable to Babiloni and colleagues (2012) who also did not observe a statistically significant IAF shift in dyslexia. Taken together, it seems that dyslexia may not affect the IAFs per se. Nevertheless, the IAF approach to frequency ranges definition accounted for any inter-individual variance, which results in possibly more precise and therefore robust findings.

Additionally, the current work accounted for another important factor that was not accommodated previously in dyslexia research: the type of resting-state recordings, with eyes either open or closed. Although this question was previously unexplored in dyslexia research, there was consistent evidence from neuroimaging research that the two resting-state conditions (eyes open and closed) may result in different connectivity patterns in various brain networks (Agcaoglu et al., 2019), as well as have a different influence on various frequency bands (Boytsova & Danko, 2010). Furthermore, Barry and colleagues (2007) showed that the two resting-state conditions could result in different EEG topography and power levels across all frequency bands. Therefore, the two conditions should be considered when evaluating EEG research (Barry et al., 2007); however, the current results revealed neither main effect of the eyes factor (open, closed) nor an interaction of this factor with any other factors of interest. Therefore, it was concluded that this resting state condition (eyes open, closed) is not critical in dyslexia research and future studies could concentrate on only one of the two options, which would naturally reduce the number of conditions necessary for

participants. This would not only be less time consuming for researchers but would also reduce the cognitive load for participants during testing.

Note also that all participants with dyslexia in both the treatment and waitlist groups received identical remedial training for the duration of the studies. The amount and intensity of behavioural training the groups received was controlled to account for the homogeneity of the sample in terms of additional extracurricular reading, writing and phonological learning, and experience. However, even considering the additional behavioural training, the reading, writing and spelling abilities of the participants with dyslexia continuously fell behind their age-matched peers (negative correlation with age-corrected performance scores) despite improvements in absolute performance scores (positive correlation with raw performance scores). These results demonstrate clearly that the best remedial treatment currently available for children with dyslexia is not able to compensate for disorder-related deterioration of behavioural symptoms fully. Although children with dyslexia continue gaining relevant skills, the gains occur at a significantly reduced rate than gains made by their peers. Therefore, it is reasonable to search for alternative or additional therapies to improve the learning rate in children with dyslexia, which was done in Study 2.

To summarize, the results of Study 1 provided important information regarding neurophysiological correlates of developmental dyslexia and how these are associated with the behavioural symptoms of the disorder. In short, I found reduced activity in frontal and temporal regions across all frequency bands and increased activity across all frequency bands (except for gamma) in central and occipital-parietal areas. Both patterns of findings signal reduced executive control and hindered language-related (reading, phonological) processing. It was also possible to track how behavioural task performance in children with dyslexia deteriorates, regardless of an increase in chronological age and despite some minor improvements in raw performance scores. The next question is whether neurofeedback

therapy would be able to alter the observed behavioural and neural correlates of dyslexia. Study 2 further tackled this question.

Discussion of study 2

Due to its relatively high prevalence and impact on society, many studies have attempted to develop effective treatments for dyslexia and introduced different behavioural training protocols to reduce the symptoms of this disorder (Habib, 2000; Yampolsky & Waters, 2002). For instance, children with dyslexia show substantial improvements in reading and spelling performance after training to match letter-speech sounds (González et al., 2015). In a different study, participants with dyslexia showed improved reading comprehension after phonological awareness training (Pape-Neumann et al., 2015). Other training methods include training of phoneme awareness, reading fluency, reading comprehension, word analysis techniques and others (Snow et al., 1998). It is important to note that participants with dyslexia equally benefit from vision-concentrated reading training and compared to phonological awareness training (Pape-Neumann et al., 2015). In other words, because phonology-unrelated (i.e., vision-based) training protocols could as well remediate reading performance in children with dyslexia with phonological deficits, behavioural training methods may not be specific or effective enough. Finally, behavioural training protocols are lengthy and time consuming. This time and financial commitment require much mental and physical effort and may not be attainable by many families with children with dyslexia. To summarize, despite its moderate effectiveness and being the best form of training available currently, behavioural approaches have serious limitations (i.e., time-consuming, financially costly, does not reach the level of healthy controls). Therefore, it makes sense to explore other training methods to advance therapy for the treatment of dyslexia.

One alternative treatment option that has gained popularity in the last decade is neurofeedback (Binder & Price, 2002; Walker & Norman, 2006); however, the disadvantage

of neurofeedback therapy in past research and practice was the limited and rigid protocols (Fadzal et al. 2012; Gunkelman, & Johnstone, 2005; Mohammadi et al., 2015). Specifically, the majority of studies that investigated the efficacy of neurofeedback in dyslexia used a fixed number of prior-selected electrodes and frequency bands that were targeted during the training (e.g., theta and delta waves at F7; Raesi et al., 2016). Given the wide variety of regions and frequency bands that are affected in dyslexia (Binder & Price, 2002; Hampson et al., 2006; Shaywitz et al., 1998; Walker & Norman, 2006) and confirmed by the results of Study 1, this approach may not be optimal. The current results of Study 1 indicated abnormal activity in frontal, temporal, central and parietal-occipital regions across all frequency bands in dyslexia. Similarly, previous studies also showed disorder-related abnormal brain activity across various brain regions and frequency bands (e.g., slower theta and delta bands over frontal and right temporal regions, Arns et al., 2007; enhanced beta activity over central and parietal electrodes, Fadzal et al., 2012 etc.). To summarize, given the wide variety of topography and frequency composition of dyslexia-related dysfunctions, using a rigid set of electrode sites and frequency bands is not optimal since it cannot encompass the entire spectrum of abnormalities.

In contrast, LORETA z-score neurofeedback therapy allows the selection of individualized and precise training protocols to account for the observed variability of affected areas and frequencies (Thatcher et al., 2015). Briefly, LORETA z-score neurofeedback offers a real-time approximation of activity (coherence, asymmetry, and amplitude) in participants' specific brain regions via a method of EEG source localization from scalp recordings, which source localises the signals within a 3 dimensional modelled space representing the brain. Consequently, it is then possible to compare the activity in certain brain areas to a normative database of healthy controls and, in the case of abnormalities, target those brain areas by means of neurofeedback training (Krigbaum &

Wigton, 2014; Thatcher, 2010). To conclude, the use of individualized testing protocols is one of the major advantages of the LORETA z-score neurofeedback over other more traditional, standardized therapy protocols.

Therefore, Study 2 aimed to explore further whether LORETA z-score neurofeedback therapy could help normalize neural correlates and improve behavioural performance in children that tested positive for phonological dyslexia. In this study, 29 participants with dyslexia from Study 1 were randomly split into the therapy and control groups. The reading, phonological, and spelling performance of these participants were tested again after the end of the neurofeedback training. Importantly, both the therapy and control group received remedial reading, spelling, and phonological training during the time of the therapy, which, as mentioned above, is the current recommended "best therapy" for dyslexia. Therefore, the goal of the study was to test whether the neurofeedback could help normalize statistically significant neural dysfunctions in participants with dyslexia and measure whether any normalization was associated with the behavioural performance beyond the effect of the remedial training alone.

Importantly, Study 2 used EEG guided LORETA z-score neurofeedback. Based on previous findings in the literature, a number of brain areas known to be implicated in dyslexia, as well as broadly related to language functioning, were selected to check for anomalies, most consistently in the frontal brain region (IFG, Broca's area, dorsolateral prefrontal cortex etc.; Kovelman et al., 2012), but also in the temporal region (auditory cortex, fusiform gyrus, middle temporal gyrus; Hampson et al., 2006), parietal region (angular gyrus; Krafnick et al., 2014) and occipital region (V1, V2; Sprenger-Charolles et al., 2013). Table 1 of Study 2 and the Methods chapter provide more detail about the inclusion of these regions. I hypothesized that neurofeedback would "reduce" the pattern of abnormalities observed in Study 1, bringing the therapy group closer to the activity seen in the population

of normally developing children. Specifically, I expected that the training would result in an enhanced activity pattern over the frontal and temporal regions across alpha, theta, gamma, delta, and beta frequencies. Additionally, the central and parietal-occipital regions were expected to show an opposite pattern and result in reduced power in alpha, theta, delta, and beta. As gamma is reduced in all areas when compared to the normative database, it was hypothesized that gamma would be increased. Finally, it was hypothesized that the therapy group would show behavioural improvements in all reading, spelling, and phonological tasks over and above any benefits from remedial training.

As a result, analyses of behavioural test scores (reading, phonological, spelling) indicated that, compared to the control participants, the performance of the therapy group was improved for the phonological and spelling tasks after neurofeedback training. In other words, the therapy group, but not the control group, showed behavioural improvements after receiving neurofeedback therapy. Furthermore, and in line with the overall trend, relative to the control group, the therapy group showed overall significantly weaker negative correlations between chronological age and age-corrected (i.e., age-matched performance score minus chronological age of participants) test performance scores. These results indicated that participants with dyslexia (in both groups) continuously fell behind in reading, spelling, and phonological tasks at a near-constant rate (i.e., the discrepancy between the two scores increased linearly with age); however, the slope the negative association was weaker in the therapy relative to the control group, indicating that the rate of decline in performance was reduced in the therapy group. Thus, although the children with dyslexia in both groups continued to fall behind their peers, the rate at which the children were falling behind was reduced when children were given LORETA z-score neurofeedback therapy, implying that the therapy was successful.

Interestingly, the behavioural improvements in Study 2 were related to phonological awareness and phonological spelling tasks. That is, the phonological component of both tasks showed the most pronounced results. Phonological tasks tested participants' ability to represent words using sound knowledge and knowledge of typical spelling patterns (participants were required to listen to and spell non-words). Therefore, the current findings may support the phonological theory of dyslexia and contribute to numerous findings of hindered phonological processes in dyslexia (e.g., Klein & Shaywitz, 2005; Shaywitz & Shaywitz, 2005). In other words, dyslexia appears to hinder the ability to connect the sounds of language to letters, which results in delays of reading abilities.

The phonological account of dyslexia posits that individuals with dyslexia experience difficulties in learning to separate individual word sounds and then match those sounds with their visual letter representations (Carroll et al., 2003; Pfost, 2015). In other words, these individuals have problems with phonemic awareness (i.e., matching of sounds and corresponding letters), which could be tested via a non-word decoding test. In this type of test, participants are presented with meaningless non-existing words that could still be processed using common rules of letter-sound correspondence (e.g., salder, poot, dar; Turner, 1994). Importantly, performance on phonological awareness tests was shown to be a reliable predictor of future reading abilities in dyslexia (Carroll et al., 2003; Pfost, 2015). Although problems with phonology are most likely not the only cause of the disorder, there is still some clear neuroimaging evidence indicating that phonological impairments in dyslexia are associated with abnormalities in cerebral connectivity, as well as alterations in cortical structure of the language network in the left hemisphere (Hampson et al., 2006; Xia et al., 2016), showing a direct link between phonology and symptoms of dyslexia (i.e., phonological awareness deficit plays a causal role in dyslexia; Peterson et al., 2013; Ziegler & Goswami, 2005a). Therefore, the behavioural results from Study 2 showed that LORETA z-score

neurofeedback therapy has a measurable increase in the phonological abilities of the participants.

Analysis of EEG recordings revealed therapy-related increases in power, specifically in the frontal brain region across a number of frequency bands (alpha, beta, theta, gamma, and delta) when measured post-therapy. The results of Study 2 showed that the LORETA z-score neurofeedback had the most pronounced effects in the frontal brain region. As also discussed earlier, this region is known to have direct and indirect links to language-related processes that are highly relevant in dyslexia (e.g. Peterson et al., 2013; Flinker et al., 2015; Kim et al., 2019; Nardone et al., 2011). Therefore, it is possible to conclude that neurofeedback could normalize activity in this brain area.

The frontal lobe (specifically, the IFG; BA 44, 45) is highly related to proficiency in silent reading (with no motor component involved; Shaywitz et al., 2002), as well as reading and visual word processing (Salmelin et al., 2000). The IFG is activated when participants are required to associate a written word with its phonetics (Coltheart et al., 2001). The IFG (specifically Broca's area) is highly connected with the thalamus, which plays an important role in language processing (Bohsali et al., 2015). Therefore, the results of Study 2 point to the possibility of neurofeedback-related improvements in children with dyslexia in known dysfunctional areas in the language network, specifically in frontal brain regions.

The frontal brain regions play a key role in executive functions and in cognitive control of attention and memory (Dhar et al., 2010; Varvara et al., 2014). Frontal brain regions integrate information from the language network and impacts performance in participants with dyslexia (Ye & Zhou, 2009). Cognitive control refers to the human ability to prioritize certain sources of attention, memories, or motor actions and inhibit irrelevant sources of information, memories or reflexive responses (Kanske & Kotz, 2010) and control mechanisms are crucial for production (i.e., motor component) and understanding (attention,

memory) of spoken and written language. This is because cognitive control can enable multiple linguistic sources of information (visual, audio) to be merged into a coherent and meaningful sensory percept (Ye & Zhou, 2009). Studies showed that development and maturation of frontal brain areas, such as the inferior frontal gyrus (IFG; BA44 and BA45) and dorsal-lateral prefrontal cortex (BA9 and BA46), are directly related to successful inhibitory control (Hwang, Velanova, & Luna, 2010). Consistently, participants with dyslexia showed hindered performance on various cognitive control tasks (e.g., Go-Nogo task; Dhar et al., 2010; auditory attention, visual and verbal working memory tasks; Varvara et al., 2014). Therefore, it is possible that neurofeedback facilitated the performance of otherwise hindered frontal control areas in dyslexia.

Indeed, there is accumulating evidence that frontal brain regions are some of the most functionally affected (i.e., as revealed by fMRI research) brain regions in dyslexia (Brown et al., 2001; Peterson et al., 2013; Pugh et al., 2001; Robichon & Habib, 1998). Based on this information, as also discussed above, most potential neurofeedback-targeted brain regions in Study 2 were located frontally (IFG, Broca's area, dorsolateral prefrontal cortex, Pars orbitalis, Pars triangularis etc.). Consequently, the observed increase in spectral power at frontal electrodes in dyslexia could signal the modulation of frontal brain region activity after neurofeedback therapy. This conclusion is additionally supported by the correlational analysis of behavioural performance and oscillatory activity in frontal brain regions. Specifically, Study 1 showed that alpha and beta frequencies in frontal regions were positively correlated with reading and phonological task performance. Consistently, in Study 2, there was increased power of oscillatory activity in frontal brain regions along with improved behavioural performance in these tasks. When taken together, this correlational evidence supports my conclusion of the functional relationship between activity in frontal brain regions and dyslexia-related behavioural performance.

Note, however, that the exact functional role of frontal brain regions in dyslexia is not fully elucidated and conflicting results have been reported in previous literature. For instance, although some fMRI studies showed increased brain activations over frontal regions (e.g., overactivation in the IFG; Démonet et al., 2004; Pugh et al., 2000; Sandak et al., 2004; Shaywitz & Shaywitz, 2005) in readers with dyslexia, relative to healthy readers, other studies found reduced activation (i.e., under activation) over frontal regions in participants with dyslexia as compared to healthy controls (Corina et al., 2001; Georgiewa et al., 1999; Paulesu et al., 1996). Additionally, EEG activity may not be easily and straightforwardly linked to underlying brain structures and future studies may couple LORETA z-score neurofeedback therapy with functional and/or structural MRI measurements (see below for the outlook of future research).

The observed improvement in neural and behavioural performance after neurofeedback has strong clinical implications. Specifically, the current findings imply that LORETA z-score neurofeedback therapy should be applied as an additional therapeutic option in combination with behavioural remedial training. The current research has provided strong evidence via a well-controlled randomized control trial that neurofeedback therapy is able to compensate for the rather imprecise effect of behavioural training and can result in additional improvements beyond the remedial learning alone. Additionally, an interesting avenue for future research is whether LORETA z-score neurofeedback could be applied to children who are at risk of developing the disorder but have not yet reached clinically diagnosed levels. The rationale for this is that neurofeedback delivered in advance could mitigate the effect of dyslexia to the extent that there would be no observable difference between the at-risk group and healthy control with the onset of formal education. In other words, this study suggests that LORETA z-score neurofeedback therapy can significantly reduce the rate of deterioration of the acquisition of skills in children with dyslexia. Study 1

also showed that this gap in performance is significantly smaller when children are younger. Therefore, if LORETA z-score neurofeedback therapy was given prior to this deterioration, it may slow down this deterioration before large performance discrepancies occur. This idea is supported by previous studies that showed a negative relation between the age of intervention onset and its effectiveness (the earlier, the better, Wanzek & Vaughn, 2007).

Interestingly, it was shown that the risk of dyslexia could be assessed as early as six months of age (Leppänen et al., 2002). For instance, at-risk infants have structural differences in the left arcuate fasciculus (Langer et al., 2017), which is crucial for reading and language processing (Catani & Mesulam, 2008). Other researchers could predict the onset of dyslexia at the age of 8 by measuring these same children's neural responses to speech and non-speech sounds when they were newborns (Molfese, 2000). Finally, infants with a family history of dyslexia also show different activation levels in the left hemisphere in responses to language sounds (Leppänen et al., 2002). Therefore, it seems indeed possible to identify those children who are at risk of dyslexia and apply LORETA z-score neurofeedback in a preventive manner. Also, as LORETA z-score neurofeedback allows for the creation of individualized therapy protocols for each child, the risk is minimal as only areas of the brain that are already showing statistically significant anomalies would be targeted.

To conclude, Study 2 showed that 20 sessions of LORETA z-score neurofeedback therapy can result in improved behavioural performance and correspondingly modulated oscillatory EEG activity in frontal brain regions in participants with dyslexia, which were found to be dysfunctional in Study 1. Specifically, I showed that neurofeedback could slow down the rate at which children with dyslexia fall behind their peers when performing various cognitive tests and that neurofeedback can normalize the neural correlates of the disorder. More explicitly, neurofeedback therapy changed the pattern of brain activity in children with dyslexia towards normalization, which was also accompanied by reduced behavioural

symptoms of the disorder. This means that neurofeedback should serve as an effective treatment option for children with dyslexia (Enriquez-Geppert, Smit, Pimenta, & Arns, 2019); however, despite its positive effects as measured immediately following the end of the therapy, the question remained whether neurofeedback could result in sustained changes. As neurofeedback is based on the principles of operant conditioning, it is possible that it may be susceptible to the principles of extinction. That is, that once the reward is no longer presented, that the desired outcome (oscillatory activity closer to the norm) would disappear. It is important to note that extinction principles are applied in terms of a stimulus, behaviour, reward sequence in which the participant is actively engaged. The fundamental advantage of neurofeedback therapy is that participants are unaware of the modulations being made in their oscillatory activity without being provided feedback. Therefore, in Study 3 I hypothesized that neurofeedback could be less susceptible to extinction once therapy has stopped and those therapy effects should still be present months later (Martijn Arns et al., 2020; Marzbani et al., 2016).

Discussion of Study 3

In Study 3, I examined whether the observed reduction in the behavioural symptoms of dyslexia would remain three months after cessation of the LORETA z-score neurofeedback. To test the stability of the reduction observed in Study 2, the therapy group from Study 2 was invited back and re-examined three months after the end of the therapy. Specifically, these participants' performance on the psychological tests was contrasted across the three time points (T1: before the start of therapy, T2: immediately after the end of therapy, and T3: three months post-therapy). If the effect of neurofeedback was robust, the improved performance seen after the therapy in Study 2 would be maintained at the three months follow-up. On the other hand, it was also possible that neurofeedback would enable the children with dyslexia to learn at the same rate as healthy children. As the behavioural

symptom measures in dyslexia require the acquisition of skills to be measurable, it is possible that bringing the neural correlates of dyslexia closer to the norm would result in an increased ability of children with dyslexia to acquire the skills necessary for reading and, thus, the participants in the Study 2 therapy group may show even further improvements 3 months post-therapy. Finally, if the effect of training were superficial or subject to the extinction phenomenon, the performance of the children with dyslexia at T3 would be comparable to T1 performance, representing a performance decrease relative to T2. In this scenario, the effect of the therapy would disappear soon after the end of the training. Note that based on previous literature, which although not vast specifically in dyslexia, did provide evidence based on the treatment of other disorders, therapy should be just as effective 3 months following therapy as it was immediately following therapy (Leins et al., 2007; Strehl et al., 2006).

Analysis of test scores (reading, phonological, spelling) across the three time-points showed that the therapy group had better performance in the reading, phonological and spelling tasks three months post-therapy (T3), relative to prior to the training (T1). Additionally, there was no significant difference between T2 and T3 performance. Finally, when the r-values of the therapy group in all tests were compared across the three times points, there was a significant difference between T3 and T1, as well as a marginally significant positive effect between T3 and T2. When taken together, these results suggest that performance not only improved after the end of therapy but that this result remained significant (or even further improved) three months after the therapy was over. In other words, the effect of neurofeedback does not appear to be subject to extinction and is maintained for at least three months after initial training.

Additionally, the negative relationship between participants' chronological age and their age-corrected test performance scores (i.e., worsening of performance as they age) became weaker after neurofeedback therapy in both Study 2 and Study 3. This once again

shows that the neurofeedback indeed had an overall positive effect on combined test performance (i.e., including reading, phonological and spelling tasks). Importantly, this weakening of the relationship between the chronological age and test performance seems to continue even after the end of the therapy as much as three months later.

This finding is in line with the enable-to-learn view of neurofeedback training in dyslexia. Specifically, it was proposed that by altering the underlying neural markers of the disorder, one can facilitate the ability to acquire the specific skills (i.e., reading, phonological, spelling) at an improved rate in children with dyslexia. In other words, their ability to learn the tasks is improved, but the skills still take time to be acquired and measured on behavioural tasks. Figuratively speaking, if neural dysfunction in dyslexia were to be compared to children wearing metaphorical headphones with loud music that distracts them and hinders their phonological abilities and reading abilities, then neurofeedback would be a mechanism that reduces this music's intensity or, ideally, something that removes the distracting music altogether. In this context, although neurofeedback cannot reverse the time and recover information that was missed or not previously encoded previously due to the allegorical headphones, it enables children with dyslexia to now learn on equal terms with healthy controls. Study 3 focused on the longer-term effects of neurofeedback, and I hypothesized that if neurofeedback therapy could improve participants' capabilities to learn and acquire information that was hindered previously by dyslexia-related alterations in brain functioning, there would be even further improved performance at T3 relative to T2 and T1. In line with this, the results of Study 3 showed some support for the enable-to-learn account by demonstrating that the participant's performance continued improving 3 months after the end of the training.

To my knowledge, this is the first study that examined this hypothesis and the potential lasting effect of neurofeedback in dyslexia. Although there was some limited work

on the role of neurofeedback in dyslexia previously (Breteler et al., 2010; Li & Chen, 2017; Walker & Norman, 2006), the findings in previous studies lacked consistency (Omejc et al., 2019). Most importantly for the results of Study 3, all previous studies examined performance only once right after the end of the training in children with dyslexia and could therefore not assess whether the observed improvements would be lasting. In contrast to dyslexia, there is some evidence from other disorders (e.g., ADHD, epileptic seizures) that neurofeedback can have pronounced and lasting effects (6 months, Engelbregt et al., 2016; Gevensleben et al., 2010; Heinrich et al., 2004; at least 3 years, Leins et al., 2007; or even 10 years, Lubar, 1997). Contrary to this, other studies do not show long-term effects for individuals with autism spectrum disorder (Kouijzer et al., 2009) or ADHD (Wadhwani et al., 1998). Finally, given that neurofeedback therapy is still relatively new, there are also mixed results presented in the latest review papers (Holtmann et al., 2014; Sitaram et al., 2017). Therefore, in the future, researchers should confirm and further study the long-lasting effect of neurofeedback by, for instance, examining the efficacy of the therapy 6 to 12 months post-training.

Study 3 also indicated that apart from objective parameters, such as reading and phonological tasks performance, neurofeedback was associated with notable improvements in informal dyslexia-specific behaviour. Specifically, as rated by the parents, participants with dyslexia showed improved behaviour on several related parameters (e.g., overall enjoyment for reading, willingness to practice reading, choosing to read spontaneously etc.). These results point to a different facet of dyslexia that is less frequently addressed in training and intervention-based research: the psychological well-being impact of the disorder. Specifically, approximately 40% of people with dyslexia experience psychological difficulties, a number that is higher than the prevalence of psychological disorders in the general population, which, depending on the diagnostic criteria, is reported to be between 5%

and 18% (Ravens-Sieberer et al., 2008). Ravens-Sieberer and their colleagues suggested that children with dyslexia have more negative thoughts, higher occurrence of depression, as well as school-related anxiety starting from primary school. For instance, Yang et al. (2018) measured the self-reported level of anxiety and depression in Chinese children with developmental dyslexia and in healthy controls. As a result, the children with dyslexia showed overall higher levels of depression, as well as higher levels of school phobia when compared to the control group. Moreover, correlation analysis revealed that participants' anxiety and depression scores were negatively correlated with the speed of digital rapid naming. In other words, dyslexia not only results in increased anxiety, depression, and school phobia, but these psychological factors also hinder reading performance and possibly other dyslexia symptoms. My findings from Study 3 suggested that neurofeedback also improves psychological factors in dyslexia that are not directly linked to the disorder but which may also indirectly contribute to improved symptoms (Wu et al., 2018). This is consistent with previous work by Li and Chen (2017) who showed that 20 sessions of neurofeedback (30 minutes each, three times per week) reduced the level of aggression in participants with dyslexia relative to a control group of participants with dyslexia who did not receive neurofeedback.

Finally, the results of the parental questionnaires indicated that, from the subjective point of view of the parents, over 50% of participants with dyslexia showed slight to substantially improved behaviour on several reading-related outcomes, including overall enjoyment for reading, willingness to practice reading, and choosing to read spontaneously. However, and as expected, this was less pronounced for such parameters as "expressive language skills" and "understanding verbal instructions", in which more than 50% of participants seem to show no visible improvements. Note that given that the sample of children with dyslexia included in the study were required to have an average performance on

verbal IQ but significantly lower performance on phonological testing scores to be included in the study, this finding was expected. Overall, the results of these questionnaires indicated that, besides objective improvements in formal test performance, neurofeedback also resulted in improvements in informal dyslexia-specific behaviour that can also be observed months after the end of the therapy. To summarize, the results of Study 3 indicated that neurofeedback has a beneficial and lasting effect on some characteristics of dyslexia, including reading and phonological task performance, as well as overall enjoyment for reading, willingness to practice reading, and choosing to read spontaneously.

Outlook on Future Research

The results of the current thesis not only contribute to and extend previous findings but may also provide important directions for potential future research. One of the primary directions could be the use of more fine-grained tools to describe and measure performance in individuals with dyslexia. Although administering regular tests of developmental dyslexia (Woodcock-Johnson reading performance tests, York Assessment of Reading for Comprehension etc.) is a popular and effective way to diagnose and track the disorder before and after the therapy, because participants would have built certain expectations about test questions and could develop some procedural learning over time, multiple (i.e., three times) administration of the same test within approximately eight months could bias the test performance. . One way to increase the sensitivity of the test would be to employ additional neuropsychological and physiological measures to track more implicit (i.e., less conscious) disorder related correlates of test performance both before and after the therapy. For example, eye-tracking methodology could be used to measure the pattern of eye movements during reading, spelling, or phonological task performance. Unlike screening methods that are based on explicit oral or written tests, eye tracking does not require verbal responses from participants and thus provides a natural means to objectively assess the reading process

(Benfatto et al., 2016; Wu et al., 2018). For instance, Benfatto et al. (2016) compared a sample of participants with word decoding difficulties and a control group. The authors used predictive modelling and statistical resampling techniques and created a classifier that was able to successfully differentiate between participants with word decoding difficulties and healthy controls by analysing their eye movements. Benfatto and colleagues showed that it is possible to identify children at risk of reading difficulties by using eye-tracking during reading.

Eye-tracking in future dyslexia research

Interestingly, eye tracking can also be used to classify the performance of participants with dyslexia, even in dyslexia-unspecific tasks. For instance, Wu and colleagues (2018) asked a group of participants with dyslexia and a group of healthy controls to perform a Stroop Color and Word Test (SCWT). In this study, participants had to judge the colour of a written word and ignore either congruent (word RED written in red font) or incongruent (word RED written in green font) semantic meaning of the word. Simultaneously, the researchers recorded eye movements in both groups of participants. Compared to the control group, participants with dyslexia had lower accuracy, slower responses, and larger conflict effects (i.e., reaction time and error rate differences between the processing of congruent and incongruent Stroop word-font combinations). Furthermore, participants with dyslexia demonstrated a lower frequency of fixations, greater numbers of saccades, and shorter mean saccade distance. To summarize, although the phonological and language abilities are fundamental to dyslexia, eye movements in reading and non-reading tasks alone can be highly predictive and efficient in identifying children at risk of long-term reading difficulties. Importantly, eye movements are highly automatic and difficult to manipulate or consciously adjust. Therefore, future studies could use these sensitive measures (frequency of fixations

and eye movements, saccade length etc.) to determine if they could be associated with any of the EEG correlates of dyslexia prior to or after the therapy (including the long-term effects).

Neuroimaging in future dyslexia research

Although LORETA improves the spatial resolution of EEG recordings, the source localization in the EEG signal is much poorer relative to that of fMRI methodology (Lystad & Pollard, 2009). Therefore, fMRI could provide valuable information about therapy outcome measures, especially for disorders that focus on training detailed networks, such as the treatment for dyslexia. For example, due to the highly interconnected nature of the brain, the therapy-induced modulation of activity recorded at frontal electrodes in EEG could potentially stem from improved performance in other brain regions (e.g., temporal areas). In other words, fMRI would allow not only the assessment of the functional performance in dyslexia, but also the monitoring of specific brain locations and specific changes in performance on dyslexia-related tasks before and after the neurofeedback therapy. Further, fMRI methodology could inform, in much greater detail, specific information about spatial localization of disorder-related malfunctions, as well as about neural changes as a function of the therapy. For instance, in a recent work, Prasad et al. (2020) examined the pattern of brain activations in a group of participants with dyslexia and in a group of age- and gender-matched controls. Results indicated that during semantic tasks processing, the occipital-temporal (fusiform) gyrus was less activated in dyslexia relative to control participants. Therefore, it was shown that dyslexia might result in some disorder-specific alterations in brain functioning, which was possible to track via fMRI and could be used as an objective and precise measure of therapy efficacy (see Table 1 in Study 2 for more brain regions that are known to show abnormal activation patterns in dyslexia).

FMRI may, in fact, be a great tool to measure the outcome of therapy in participants with dyslexia. For instance, Richards and Berninger (2008) tested a group of children with

dyslexia and a group of matched healthy controls in an fMRI study. Both groups of participants took part in a three-week training program that provided instruction in linguistic awareness, alphabetic principles, decoding, and spelling. Importantly, before and after the end of the training, participants had their brains scanned while they performed a phoneme-mapping task. There was a significant disorder-specific difference in fMRI connectivity between several brain regions (e.g., left inferior frontal gyrus and left middle frontal gyrus) reported. Most importantly, after the end of the treatment, the children with dyslexia did not differ from the children without dyslexia in any of the measured brain areas, indicating that functional connectivity in this area may normalize following instructional treatment. Therefore, fMRI methodology could be an additional tool to study further the neural correlates of behavioural changes (both short- and long-term) after the neurofeedback therapy.

As briefly discussed above, another important and interesting avenue of future research concerns the potential long-lasting effect of neurofeedback on dyslexia. Currently, relatively little known about whether the effect of neurofeedback to treat dyslexia is long-lasting and how often the training should be repeated for the effects to be sustainable. Study 3 demonstrated that participants with dyslexia given neurofeedback therapy showed improved performance three months after the end of the therapy; however, it remains unclear whether this effect would still be observable 6- and 12-months post-therapy. Thus, future research could focus on determining the optimal frequency of neurofeedback (1-2 times a year, every 3 months etc.) that would be necessary to achieve a noticeable and sustainable improvement in performance in dyslexia. As was shown in Study 3, neurofeedback therapy may enable children to acquire skills at a more rapid pace following the normalization of certain dysfunctional oscillatory activity. Therefore, an interesting research avenue could focus on

intensive remedial training following LORETA z-score neurofeedback therapy to "take advantage" of the child's newly improved abilities to acquire these skills.

Dyslexia and inter-individual variability

Future studies could also benefit from collecting additional information about participants' interpersonal characteristics before including them in their study, such as levels of depression, anxiety, and social or school phobias. An interesting question is whether these and other interpersonal characteristics (e.g., coping strategies, level of motivation etc.) could further modulate the beneficial effects of neurofeedback in children with dyslexia. In other words, the idea would be to correlate participants' interpersonal characteristics with the level of therapy-related improvements in behavioural and neural performance. This is particularly relevant in dyslexia research because children with dyslexia may have difficulties with motivational factors, as well as with cognitive control of attention.

For instance, Kikkert (2015) explored whether the effect of neurofeedback training was dependent upon interpersonal characteristics such as learning style, cognitive style, locus of control, and others. They found evidence via EEG that increases in beta correlated with individuals' learning style, cognitive style, and locus of control. On the other hand, theta inhibition was correlated with factors such as mindfulness and reward sensitivity. These results show that differences in cognitive characteristics should be considered when giving neurofeedback therapy as they may help or hinder the therapy/learning process. For instance, it would be interesting to test whether people who are reward-sensitive would be able to benefit more from the neurofeedback versus those who are not. On the other hand, it is also possible that the LORETA z-score neurofeedback could overcome or ignore such inter-individual differences, given its individualistic approach (see below for a detailed discussion).

In a different work, Kadosh and Staunton (2019) reviewed 21 neurofeedback manuscripts that investigated interpersonal characteristics and factors that modulated individual success rates of neurofeedback training. The researchers identified several main categories of factors, including attentional control, motivation, and mood, as reliable predictors of success of the neurofeedback training and concluded that there is a need for further research to understand how psychological variables may impact participants during neurofeedback training. Accordingly, I propose that future studies concentrate on the identification of those factors that could predict the success of neurofeedback therapy in dyslexia. This information could possibly be helpful to predict the future success of the therapy in dyslexia and/or to decide the necessity of such an approach for a specific patient.

Event-related Neurophysiology in Dyslexia

Although the current work concentrated on the resting state EEG brain activity, it would also be meaningful to examine how neurofeedback modulates brain activity (event-related potentials, frequency bands) in children with dyslexia during dyslexia-relevant task performance (reading, spelling, phonological processing). For example, Gonzalez and colleagues (2016) trained a group of children with dyslexia to perform a letter-speech sound mapping task. Additionally, they recorded event-related EEG potentials (ERPs) that were elicited in responses to visually presented written words before and after the training. As a result, the visual presentation of words elicited enhanced ERP negativity approximately 200 ms after stimulus onset (also known as N170) in participants with dyslexia relative to control participants. The N170 is a well-studied ERP component that, among other things, is related to the processing of words (Rossion et al., 2003). Most importantly, participants with dyslexia who showed behavioural improvements after the training also showed a substantial reduction in the N170 amplitude post-training relative to prior to training, indicating that these children required fewer neural resources to process written words. On the other hand,

less successful participants with dyslexia in the training program showed no changes in the N170. When taken together, these results indicated that behavioural training could improve reading performance in some but not all participants with dyslexia. Additionally, results indicated that behavioural improvements (or lack of thereof) could also be traced via specific neural marker of word processing (i.e., N170). To conclude, ERPs could be used as an assessment tool for the outcome of behavioural therapy in future studies. Additionally, future studies could measure neural responses in dyslexia during the actual task performance.

Finally, neurofeedback training in Study 2 resulted in significant changes in the frontal brain region of the children with dyslexia. On the other hand, this training did not alter resting-state activity in the central, temporal, and parietal-occipital regions that were also found to be deviant in the group with dyslexia in Study 1. Therefore, future studies should test whether increasing the number of neurofeedback session ($N > 20$) could potentially result in changes in these other brain regions. Future studies should examine empirically the optimal number of neurofeedback sessions that would be enough to result in reliable and sustainable neural changes in all deviant neural markers and whether improvements in these further areas results in increased behavioural performance in children with dyslexia.

Discussion of Strengths

One of the advantages of the current work is its highly controlled sample of participants. As discussed previously, dyslexia is not a homogeneous disorder and could be classified into dysphonetic and dyseidetic subtypes (Boder, 1973), phonological and surface subtypes (Castles & Coltheart, 1993), subtypes with and without verbal language deficit (Leonard et al., 2002), as well as dyslexia with visual attention span and phonological deficits (Bosse et al., 2007; Ramus et al., 2018). Despite these classification attempts, there is still no consensus regarding clear definitions of dyslexia subtypes. Therefore, previous studies that explored the efficacy of neurofeedback in dyslexia did not control that all participants with

dyslexia constituted a homogenous sample, and this may have resulted in a dilution of the measured outcomes.

To account for this heterogeneity, one of the strict inclusion criteria to participate in the current study was a substantial difficulty in phonological task performance. Consequently, all participants with dyslexia in the sample had deficient phonological processing. In more detail, the phonological account of dyslexia assumes that children with this disorder experience difficulties comprehending the smallest units of speech sound (Klein & Shaywitz, 2005; Shaywitz & Shaywitz, 2005). According to this theory, dyslexia hinders the link between letters and their auditory representation, resulting in delayed reading acquisition. Therefore, the findings in the current work should also be interpreted keeping the sample specificity in mind.

Future studies could also examine whether neurofeedback training would have a different impact in samples with predominantly surface or visual attention span subtypes of dyslexia; however, following the logic of the current findings, it could be hypothesized that LORETA z-score neurofeedback would be equally effective regardless of the specific subtype. In more detail, LORETA z-score neurofeedback therapy could specifically and precisely target each child's individual dysfunction (i.e., abnormal brain activity). Therefore, although it is possible that different dyslexia subtypes show subtype-specific patterns of brain abnormalities, LORETA z-score therapy should overcome these potential discrepancies by using individualized therapy protocols. This approach contrasts with most previous neurofeedback studies that relied on fixed and inflexible therapy protocols.

Many previous works concentrated on rather rigid neurofeedback protocols that used only small and fixed brain regions and specific frequency bands for the purpose of the training (e.g., T6, T3/T4, F7, FC3; Breteler et al., 2010). In contrast, the LORETA z-score approach in the current work was able to localize disorder-specific brain regions for each

dyslexia participant and these individualized brain areas were then targeted during the neurofeedback training (Cannon et al., 2009; Collura et al., 2010). In other words, LORETA z-score neurofeedback training provides the possibility to individually tailor the feedback to the participant's specific dysfunction. This is especially important given the great variability of brain areas and frequency bands that have been shown by researchers (including Study 1 in the current work) to be associated with dyslexia.

Collectively, the current work supports the use of LORETA z-score neurofeedback in clinical settings. It provides the potential for the development of individualized therapy protocols specifically tailored to the individual clients, while still following strict, standardized procedures that are identical across different participants. In other words, although this type of neurofeedback relies on common and standard conditioning principles that are known to modulate the expected behavioural and neural performance via reward and by gradually increasing the difficulty of the therapy, there is still a large, individualized component of this therapy. Specifically, only those brain regions are targeted during the neurofeedback training that show an abnormal pattern of activity relative to a normative database. Therefore, given its cost-efficiency (only 20 sessions were enough to elicit lasting behavioural changes) and individualized approach that makes it a universal tool for various dyslexia subtypes and inter-individual differences between participants, I propose that LORETA z-score therapy should be made more accessible to children with dyslexia.

The current work also controlled for group homogeneity regarding the remedial training. In more detail, it was shown that behavioural training alone is able to achieve moderate but significant improvements in reading and spelling performance (González et al., 2015), phonological awareness (Pape-Neumann et al., 2015), reading fluency and reading comprehension (Snow et al., 1998). Therefore, it was important to ensure that all dyslexia and control participants received identical and standardized remedial training to measure the

specific effect of neurofeedback. In other words, controlling for training homogeneity in the two groups provides more confidence that the observed behavioural and neurophysiological changes stem from the neurofeedback therapy and cannot be accounted for by other group variances.

Another strength of the current work is related to the definition and selection of individual EEG frequency bands. Specifically, individual alpha frequencies were used to define the frequency bands of interest. As was also discussed earlier, alpha frequency shows a high degree of variability and inter-subject heterogeneity in individual's peak alpha frequency (IAF), which were shown to be predictive of individuals' performance on various perceptual tasks (Cecere et al., 2015; Samaha & Postle, 2015) and cognitive tasks (Bornkessel et al., 2004; Klimesch et al., 2006).

General heterogeneity of IAFs becomes problematic for the "traditional" definition of frequency bands in EEG research (Klimesch et al., 2007). For instance, although alpha frequency is usually defined as an oscillatory brain activity observed within a certain relatively strict frequency range (e.g., 8-14 Hz) because individual participants could have slight-to-moderate differences in the range of oscillatory activity that is traditionally believed to be the alpha frequency the observed variances in the IAFs suggest that such a strict definition is not always possible. This could be especially relevant for clinical populations, as was shown in Parkinson's disease and Attention-Deficit Hyperactivity Disorder (see Arns et al., 2012). Note also that almost all previous dyslexia EEG studies did not account for IAFs, which could have potentially skewed previous findings (but see Babiloni et al., 2012). Therefore, to account for these inter-individual differences in the IAFs, the current work used IAF as a functional reference point to define all frequency bands of interest (see Babiloni et al., 2012 for the same approach). This approach accounted for the individual heterogeneity across participants, which reduced the risk of observing spurious main effects. Restated, it is

possible that the inconsistency in previous literature on EEG markers of dyslexia could at least partially stem from heterogeneity in the definition of individual frequency bands. The current EEG work took this into account, which should produce more reliable results.

The current work was also the first to test whether the power of different frequency bands would vary as a function of the resting-state condition (i.e., eyes open, eyes closed). Previous research suggested that the two resting-state conditions may result in different connectivity patterns in various brain networks (Agcaoglu et al., 2019) and have a different influence on various frequency bands (Boytsova & Danko, 2010). Nevertheless, it was unknown whether resting-state recordings would vary in dyslexia sample when recorded with eyes open and closed conditions. The results of both Study 1 and 2 revealed that there were no significant group differences as a function of eyes condition.

Most of the previous studies had underpowered samples and/ or did not have adequate control groups. Specifically, only a few studies tested more than between 5 and 10 participants, which could have resulted in spurious (false positive and false negative) findings. Therefore, the generalization of such findings to other samples is difficult, which results in inconsistency in previous research. In contrast, the current work tested a large sample of participants (total N = 94 participants for Study 1, N=29 for study 2, and N=18 for study 3), which should have resulted in more reliable measurements and statistical results.

Finally, and in contrast to the majority of dyslexia studies in the past (Babiloni et al., 2012; Nazari et al., 2012; Walker & Norman, 2006), another strength of the current work is its within-subjects design in Study 3. Specifically, this is the first work that tracked the neural and behavioural performance in participants with dyslexia at three different time-points: before the therapy onset, after the end of the therapy and then once again three months post-therapy. Within-subjects design is much more sensitive in terms of statistical analysis and could provide more reliable results (Charness et al., 2012). It also allowed tracking the

evolution of neural and behavioural performance in children with dyslexia and examined this performance in relation to neurofeedback training.

To summarize, despite a common goal to test the role of neurofeedback as a treatment alternative for dyslexia, previous studies used different sample sizes, different number and duration of training sessions and different cognitive tasks necessary to test the effect of neurofeedback. They also did not control for group homogeneity in terms of dyslexia subtypes and remedial training. Therefore, the strength of the current work is that it accounted for all these limitations, thus resulting in more robust findings. Most importantly, the current work is the first to examine the advanced LORETA z-score neurofeedback therapy in children with dyslexia, which localized disorder-specific brain regions in each participant and thus provided an individualized training protocol. The work is also unique since it had a combination of large sample size and employed a randomized control study design. This improved the specificity and precision of the applied training and resulted in potentially better behavioural improvements, thus providing a valuable contribution to the current body of knowledge.

Discussion of Limitations

The current work may have several potential limitations. One of the limitations is the relatively small size of both the therapy and control groups in Study 2 and, consequently, the power of statistical analyses. Specifically, while Study 1 tested 47 participants in each of the groups (dyslexia, control), the neurofeedback Study 2 relied on ~ 15 participants in each group. Note, however, that, although relatively modest, this sample size is comparable or larger than previous neurofeedback literature (e.g., Breteler et al., 2010). Further, the effect sizes of critical findings in the current work were moderate to large, which also indicates that the sample sizes tested were adequate to capture the true effect.

Another clear limitation is the absence of a control group in Study 3. Due to the study design, participants with dyslexia who were placed on a waiting list and served as controls in Study 2, had already started receiving neurofeedback training by the time the main therapy group was invited for a follow-up testing 3 months after the end of Study 2. Therefore, Study 3 did not have an adequate control group. Although it was still possible to meaningfully compare these participants' performance across the three time points (T1, T2 and T3), presence of a control group could assure that the observed improvements three months post-therapy were indeed specific/ unique to the neurofeedback and not due to their remedial instruction.

Another potential problem is the lack of control for school holidays/vacation when testing participants with dyslexia. The current study did not take into account the timing of school holidays, which means that some children may not have been receiving the same level of extra tutoring or even normal schooling throughout the therapy or during the 3 months before follow up, making participants potentially more heterogeneous in terms of neurofeedback outcome. Although this was somewhat expected given the personal schedules of participants and the clinic availability, future studies could take these points into account and either make the therapy less extended (i.e., by increasing the frequency of test sessions or by standardizing the times between testing sessions) or plan the study in such a way as to avoid long and uncontrolled breaks from therapy and remedial tutoring.

There are several limitations related to the methodology and interpretation of the neurofeedback-related findings. For instance, the use of Neurofeedback could not, unfortunately, provide information about the nature of the cause of dyslexia or necessarily about the specific neural mechanisms of this disorder. That is, although we could assess whether neurofeedback influenced the psychophysiological correlates of dyslexia and what these correlates were, one cannot support or argue against any of the existing theories of

dyslexia. Additionally, the neurofeedback parameters that were used in the therapy were based on one 5-minute EEG recording. This may be potentially problematic, as results may vary depending on the individual's state on that day (e.g. child having good/bad day, time of day, good/poor previous night's sleep, etc.). Therefore, future studies should consider whether the neurofeedback parameters should be selected based on an averaging across multiple recordings, which would facilitate a more stable and reliable understanding of their EEG profile.

One should also note that the results of Study 1 (Chapter 3) relied on EEG and behavioural data from a database control group. Although the use of the Neuroguide database allowed to save time and resources that would have otherwise been necessary for the data collection of healthy controls, as well as allowed to precisely match the dyslexia group in terms of gender and age, it is important to keep in mind that the database was collected in a foreign culture with a different language and cultural background relative to the sample of dyslexia participants in the current work. On the other hand, the most critical findings in the current work (Studies 2 and 3) were based on the sample of participants who were homogeneous in terms of language and cultural background.

Lastly, there is also some scepticism in the EEG research community about the adequacy of LORETA Z-score neurofeedback for research and clinical use (see Coben et al., 2019 for an overview). For instance, it is argued that in order to increase the reliability of the LORETA approach, it may require a higher number of electrodes (128 relative to 19 used in the current work; Kim et al., 2006). Since the therapy sets in the current work had only 19 electrodes, further work is necessary to confirm that the LORETA protocols with this number of electrodes is enough to adequately localize deviant brain regions. Note, however, that LORETA Z-score neurofeedback remains a state-of-the-art approach in the field of neurofeedback and was shown to be more advanced relative to the other neurofeedback

methodologies (see Coben et al., 2019). To summarize, the current work had some potential limitations (sample size, adequate control group for Study 3 and controlled level of residual learning in Study 3) that could potentially bias the results. Therefore, future studies should take these points into account in future work.

Summary

The overarching goal of this dissertation was to investigate the behavioural and neural correlates of LORETA z-score neurofeedback therapy on developmental dyslexia. Dyslexia affects the educational success and psychological wellbeing of millions of affected children worldwide and, as such, has a dramatic impact on society. The current work supports the use of LORETA z-score neurofeedback as an effective therapy that, in combination with behavioural remedial training, is able to reduce the deterioration rate of reading, spelling and phonological functions in dyslexia and result in lasting behavioural improvements. This neurofeedback approach could also be immune to factors that hindered the development of successful neurofeedback therapies in the past (subtype specificity, rigidity in therapy protocols). Given the results of this thesis, I recommend that both clinical therapists and researchers concentrate on LORETA z-score neurofeedback therapy to facilitate learning and successful development in children with dyslexia going forward.

References

Aaron, P. G. (2012). *Dyslexia and hyperlexia: Diagnosis and management of developmental reading disabilities* (Vol. 1). Springer Science & Business Media.

Abu-Hamour, B., Hmouz, H. Al, Mattar, J., & Muhaidat, M. (2012). The Use of Woodcock-Johnson Tests for Identifying Students with Special Needs-a Comprehensive Literature Review. *Procedia - Social and Behavioral Sciences*, 47, 665-673. https://doi.org/10.1016/j.sbspro.2012.06.714

Ackerman, P. T., Dykman, R. A., Oglesby, D. M., & Newton, J. E. (1995). EEG power spectra of dysphonetic and nondysphonetic poor readers. *Brain and language,* 49(2), 140-152. https://doi.org/10.1006/brln.1995.1025

Adlard, A., & Hazan, V. (1998). Speech Perception in Children with Specific Reading Difficulties (Dyslexia). *Quarterly Journal of Experimental Psychology Section A: Human Experimental Psychology*, 51(1), 153-177. https://doi.org/10.1080/713755750

Adrian, E. D., & Matthews, B. H. C. (1934). The berger rhythm: Potential changes from the occipital lobes in man. *Brain*, 57(4), 355-385. https://doi.org/10.1093/brain/57.4.355

Agcaoglu, O., Wilson, T. W., Wang, Y. P., Stephen, J., & Calhoun, V. D. (2019). Resting state connectivity differences in eyes open versus eyes closed conditions. *Human Brain Mapping*, 40(8), 2488-2498. https://doi.org/10.1002/hbm.24539

Ahissar, M., Protopapas, A., Reid, M., & Merzenich, M. M. (2000). Auditory processing parallels reading abilities in adults. *Proceedings of the National Academy of Sciences of the United States of America*, 97(12), 6832-6837. https://doi.org/10.1073/pnas.97.12.6832

Ahn, H., Prichep, L., John, E. R., Baird, H., Trepetin, M., & Kaye, H. (1980). Developmental equations reflect brain dysfunctions. *Science*, 210(4475), 1259-1262.

https://doi.org/10.1126/science.7434027

Akin, M. (2002). Comparison of wavelet transform and FFT methods in the analysis of EEG signals. *Journal of Medical Systems*, 26(3), 241-247. https://doi.org/10.1023/A:1015075101937

Aldosari, M., Joswig, H., Marti, A. S., Parrent, A., & Mirsattari, S. M. (2018). F122. Non-lesional eating epilepsy with mesial temporal and inferior insular onset: A stereo-EEG study. *Clinical Neurophysiology*, 129, e112-e113. https://doi.org/10.1016/j.clinph.2018.04.285

Alexander, A. W., & Slinger-Constant, A. M. (2004). Current status of treatments for dyslexia: Critical review. In *Journal of Child Neurology*, 19(10), 744-758. https://doi.org/10.1177/08830738040190100401

American Psychiatric Association. (2013). American Psychiatric Association, 2013. Diagnostic and statistical manual of mental disorders (5th ed.). In *American Journal of Psychiatry*, https://doi.org/10.1176/appi.books.9780890425596.744053

Amunts, K., & Zilles, K. (2015). Architectonic mapping of the human brain beyond Brodmann. Neuron, 88(6), 1086-1107.

Aoki, F., Fetz, E. E., Shupe, L., Lettich, E., & Ojemann, G. A. (1999). Increased gamma-range activity in human sensorimotor cortex during performance of visuomotor tasks. *Clinical Neurophysiology*, 110(3), 524-537. https://doi.org/10.1016/S1388-2457(98)00064-9

Ardila, A., Bernal, B., & Rosselli, M. (2015). Language and visual perception associations: meta-analytic connectivity modeling of Brodmann area 37. *Behavioural neurology*. doi: http://dx.doi.org/10.1155/2015/565871

Arnal, L. H., & Giraud, A. L. (2012). Cortical oscillations and sensory predictions. In *Trends in Cognitive Sciences*, 16(7), 390-398. https://doi.org/10.1016/j.tics.2012.05.003

Arnal, L. H., Wyart, V., & Giraud, A. L. (2011). Transitions in neural oscillations reflect prediction errors generated in audiovisual speech. *Nature Neuroscience*, 14(6), 797. https://doi.org/10.1038/nn.2810

Arns, Martijn, Clark, C. R., Trullinger, M., deBeus, R., Mack, M., & Aniftos, M. (2020). Neurofeedback and Attention-Deficit/Hyperactivity-Disorder (ADHD) in Children: Rating the Evidence and Proposed Guidelines. In *Applied Psychophysiology Biofeedback*, 45(2), 39-48. https://doi.org/10.1007/s10484-020-09455-2

Arns, Martijn, Drinkenburg, W., & Leon Kenemans, J. (2012). The effects of QEEG-informed neurofeedback in ADHD: An open-label pilot study. *Applied Psychophysiology Biofeedback*, 37(3), 171-180. https://doi.org/10.1007/s10484-012-9191-4

Arns, Martin, Peters, S., Breteler, R., & Verhoeven, L. (2007). Different brain activation patterns in dyslexic children: Evidence from EEG power and coherence patterns for the double-deficit theory of dyslexia. *Journal of Integrative Neuroscience*, 6(01), 175-190. https://doi.org/10.1142/S0219635207001404

Arnsten, A. F. T., & Jin, L. E. (2014). Molecular influences on working memory circuits in dorsolateral prefrontal cortex. In *Progress in Molecular Biology and Translational Science*, 122, 211-231 https://doi.org/10.1016/B978-0-12-420170-5.00008-8

Au, A., Ho, G. S. M., Choi, E. W. M., Leung, P., Waye, M. M. Y., Kang, K., & Au, K. Y. (2014). Does it help to train attention in dyslexic children: Pilot case studies with a ten-session neurofeedback program. *International Journal on Disability and Human Development*, 13(1), 45-54. https://doi.org/10.1515/ijdhd-2013-0005

Authors, F. (2005). Guide for Authors For Authors. *NeuroImage*, *175*, 1–6.

https://doi.org/10.1016/S0303-2434(04)00078-9

Babiloni, C., Stella, G., Buffo, P., Vecchio, F., Onorati, P., Muratori, C., Miano, S., Gheller, F., Antonaci, L., Albertini, G., & Rossini, P. M. (2012). Cortical sources of resting state EEG rhythms are abnormal in dyslexic children. *Clinical Neurophysiology*, 123(12), 2384-2391. https://doi.org/10.1016/j.clinph.2012.05.002

Barbas, H., García-Cabezas, M. Á., & Zikopoulos, B. (2013). Frontal-thalamic circuits associated with language. *Brain and Language*, 126(1), 49-61. https://doi.org/10.1016/j.bandl.2012.10.001

Barta, P. E., Petty, R. G., McGilchrist, I., Lewis, R. W., Jerram, M., Casanova, M. F., Powers, R. E., Brill, L. B., & Pearlson, G. D. (1995). Asymmetry of the planum temporale: methodological considerations and clinical associations. *Psychiatry Research: Neuroimaging*, 61(3), 137-150. https://doi.org/10.1016/0925-4927(95)02650-M

Barth, A. E., Denton, C. A., Stuebing, K. K., Fletcher, J. M., Cirino, P. T., Francis, D. J., & Vaughn, S. (2010). A test of the cerebellar hypothesis of dyslexia in adequate and inadequate responders to reading intervention. *Journal of the International Neuropsychological Society*, 16(3), 526. https://doi.org/10.1017/S1355617710000135

Bartos, M., Vida, I., & Jonas, P. (2007). Synaptic mechanisms of synchronized gamma oscillations in inhibitory interneuron networks. In *Nature Reviews Neuroscience*, 8(1), 45-56. https://doi.org/10.1038/nrn2044

Başar, E., Başar-Eroglu, C., Karakaş, S., & Schürmann, M. (2000). Brain oscillations in perception and memory. *International Journal of Psychophysiology*, 35(2-3), 95-124. https://doi.org/10.1016/S0167-8760(99)00047-1

Bauer, E. P., Paz, R., & Paré, D. (2007). Gamma oscillations coordinate amygdalo-rhinal

interactions during learning. *Journal of Neuroscience*, 27(35), 9369-9379. https://doi.org/10.1523/JNEUROSCI.2153-07.2007

Baumeister, J., Reinecke, K., & Weiss, M. (2008). Changed cortical activity after anterior cruciate ligament reconstruction in a joint position paradigm: An EEG study. *Scandinavian Journal of Medicine and Science in Sports*, 18(4), 473-484. https://doi.org/10.1111/j.1600-0838.2007.00702.x

Becerra, J., Fernández, T., Harmony, T., Caballero, M. I., Garcia, F., Fernández-Bouzas, A., Santiago-Rodriguez, E., & Prado-Alcalá, R. A. (2006). Follow-Up Study of Learning-Disabled Children Treated with Neurofeedback or Placebo. *Clinical EEG and Neuroscience*, 37(3), 198-203. https://doi.org/10.1177/155005940603700307

Behrmann, M., & Bub, D. (1992). Surface dyslexia and dysgraphia: Dual routes, single lexicon. *Cognitive Neuropsychology*, 9(3), 209-251. https://doi.org/10.1080/02643299208252059

Bell, A. N., Moss, D., & Kallmeyer, R. J. (2019). Healing the neurophysiological roots of trauma: A controlled study examining loreta z-score neurofeedback and HRV biofeedback for chronic PTSD. *NeuroRegulation*, 6(2), 54-54. https://doi.org/10.15540/nr.6.2.54

Benfatto, M. N., Seimyr, G. Ö., Ygge, J., Pansell, T., Rydberg, A., & Jacobson, C. (2016). Screening for dyslexia using eye tracking during reading. *PLoS ONE*, 11(12), e0165508. https://doi.org/10.1371/journal.pone.0165508

Benwell, C. S. Y., London, R. E., Tagliabue, C. F., Veniero, D., Gross, J., Keitel, C., & Thut, G. (2019). Frequency and power of human alpha oscillations drift systematically with time-on-task. *NeuroImage*, 192, 101-114. https://doi.org/10.1016/j.neuroimage.2019.02.067

Berger, H. (1929). Über das Elektrenkephalogramm des Menschen. *Archiv Für Psychiatrie*

Und Nervenkrankheiten, https://doi.org/10.1007/BF01797193

Berger, H. (1937). Über das Elektrenkephalogramm des Menschen: XII. Mitteilung. *Archiv Für Psychiatrie Und Nervenkrankheiten*, https://doi.org/10.1007/BF01987704

Berkes, P., Orbán, G., Lengyel, M., & Fiser, J. (2011). Spontaneous cortical activity reveals hallmarks of an optimal internal model of the environment. *Science*, 331(6013), 83-87. https://doi.org/10.1126/science.1195870

Blachman, B. A., Tangel, D. M., Ball, E. W., Black, R., & McGraw, C. K. (1999). Developing phonological awareness and word recognition skills: A two-year intervention with low-income, inner-city children. *Reading and Writing*, 11(3), 239-273. https://doi.org/10.1023/A:1008050403932

Blau, V., Reithler, J., Van Atteveldt, N., Seitz, J., Gerretsen, P., Goebel, R., & Blomert, L. (2010). Deviant processing of letters and speech sounds as proximate cause of reading failure: A functional magnetic resonance imaging study of dyslexic children. *Brain*, 133(3), 868-879. https://doi.org/10.1093/brain/awp308

Boden, C., & Giaschi, D. (2007). M-stream deficits and reading-related visual processes in developmental dyslexia. In *Psychological Bulletin*, 133(2), 346. https://doi.org/10.1037/0033-2909.133.2.346

Boder, E. (1973). Developmental Dyslexia: a Diagnostic Approach Based on Three Atypical Reading-spelling Patterns. *Developmental Medicine & Child Neurology*, 15(5), 663-687. https://doi.org/10.1111/j.1469-8749.1973.tb05180.x

Boets, B., Vandermosten, M., Cornelissen, P., Wouters, J., & Ghesquière, P. (2011). Coherent Motion Sensitivity and Reading Development in the Transition From Prereading to Reading Stage. *Child Development*, 82(3), 854-869. https://doi.org/10.1111/j.1467-8624.2010.01527.x

Bohsali, A. A., Triplett, W., Sudhyadhom, A., Gullett, J. M., McGregor, K., FitzGerald, D.

B., Mareci, T., White, K., & Crosson, B. (2015). Broca's area - Thalamic connectivity. *Brain and Language*, 141, 80-88. https://doi.org/10.1016/j.bandl.2014.12.001

Bollimunta, A., Mo, J., Schroeder, C. E., & Ding, M. (2011). Neuronal mechanisms and attentional modulation of corticothalamic alpha oscillations. *Journal of Neuroscience*, 31(13), 4935-4943. https://doi.org/10.1523/JNEUROSCI.5580-10.2011

Bornkessel, I. D., Fiebach, C. J., & Friederici, A. D. (2004). On the cost of syntactic ambiguity in human language comprehension: An individual differences approach. *Cognitive Brain Research*, 21(1), 11-21. https://doi.org/10.1016/j.cogbrainres.2004.05.007

Bosse, M. L., Tainturier, M. J., & Valdois, S. (2007). Developmental dyslexia: The visual attention span deficit hypothesis. *Cognition*, 104(2), 198-230. https://doi.org/10.1016/j.cognition.2006.05.009

Bowyer-Crane, C., Snowling, M. J., Duff, F. J., Fieldsend, E., Carroll, J. M., Miles, J., Götz, K., & Hulme, C. (2008). Improving early language and literacy skills: Differential effects of an oral language versus a phonology with reading intervention. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 49(4), 422-432. https://doi.org/10.1111/j.1469-7610.2007.01849.x

Boytsova, Y. A., & Danko, S. G. (2010). EEG differences between resting states with eyes open and closed in darkness. *Human Physiology*, 36(3), 367-369. https://doi.org/10.1134/S0362119710030199

Brambati, S. M., Termine, C., Ruffino, M., Stella, G., Fazio, F., Cappa, S. F., & Perani, D. (2004). Regional reductions of gray matter volume in familial dyslexia. *Neurology*, 63(4), 742-745. https://doi.org/10.1212/01.WNL.0000134673.95020.EE

Brandt, J., & Rosen, J. J. (1980). Auditory phonemic perception in dyslexia: Categorical identification and discrimination of stop consonants. *Brain and Language*, 9(2), 324-337. https://doi.org/10.1016/0093-934X(80)90152-2

Breteler, M. H. M., Arns, M., Peters, S., Giepmans, I., & Verhoeven, L. (2010). Improvements in spelling after QEEG-based neurofeedback in dyslexia: A randomized controlled treatment study. *Applied Psychophysiology Biofeedback*, 35(1), 5-11. https://doi.org/10.1007/s10484-009-9105-2

Brovelli, A., Lachaux, J. P., Kahane, P., & Boussaoud, D. (2005). High gamma frequency oscillatory activity dissociates attention from intention in the human premotor cortex. *NeuroImage*, 28(1), 154-164. https://doi.org/10.1016/j.neuroimage.2005.05.045

Brown, W. E., Eliez, S., Menon, V., Rumsey, J. M., White, C. D., & Reiss, A. L. (2001). Preliminary evidence of widespread morphological variations of the brain in dyslexia. *Neurology*, 56(6), 781-783. https://doi.org/10.1212/WNL.56.6.781

Budzynski, T., Budzynski, H., Evans, J., & Abarbanel, A. (2009). Introduction to Quantitative EEG and Neurofeedback. In *Introduction to Quantitative EEG and Neurofeedback*, https://doi.org/10.1016/B978-0-12-374534-7.X0001-9

Burton, M. W., LoCasto, P. C., Krebs-Noble, D., & Gullapalli, R. P. (2005). A systematic investigation of the functional neuroanatomy of auditory and visual phonological processing. *NeuroImage*, 26(3), 647-661. https://doi.org/10.1016/j.neuroimage.2005.02.024

Busch, N. A., Dubois, J., & VanRullen, R. (2009). The phase of ongoing EEG oscillations predicts visual perception. *Journal of Neuroscience*, 29(24), 7869-7876. https://doi.org/10.1523/JNEUROSCI.0113-09.2009

Busch, N. A., Herrmann, C. S., Müller, M. M., Lenz, D., & Gruber, T. (2006). A cross-

laboratory study of event-related gamma activity in a standard object recognition paradigm. *NeuroImage*, 33(4), 1169-1177. https://doi.org/10.1016/j.neuroimage.2006.07.034

Buschman, T. J., Denovellis, E. L., Diogo, C., Bullock, D., & Miller, E. K. (2012). Synchronous Oscillatory Neural Ensembles for Rules in the Prefrontal Cortex. *Neuron*, 76(4), 838-846. https://doi.org/10.1016/j.neuron.2012.09.029

Buschman, T. J., & Miller, E. K. (2007). Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. *Science*, 315(5820), 1860-1862. https://doi.org/10.1126/science.1138071

Buzsáki, G., & Draguhn, A. (2004). Neuronal olscillations in cortical networks. In *Science*, 304(5679), 1926-1929. https://doi.org/10.1126/science.1099745

Buzsáki, G., & Schomburg, E. W. (2015). What does gamma coherence tell us about inter-regional neural communication?. *Nature neuroscience*, 18(4), 484-489.

Koberda, J. L., & Frey, L. C. (2015). Z-score LORETA neurofeedback as a potential therapy for patients with seizures and refractory epilepsy. *Neurol Neurobiol*, Volume1, 1. https://doi.org/10.16966/2379-7150.101

Cannon, R. L., Baldwin, D. R., Shaw, T. L., Diloreto, D. J., Phillips, S. M., Scruggs, A. M., & Riehl, T. C. (2012). Reliability of quantitative EEG (qEEG) measures and LORETA current source density at 30 days. *Neuroscience Letters*, 518(1), 27-31. https://doi.org/10.1016/j.neulet.2012.04.035

Cannon, R. L., Thatcher, R. W., Baldwin, D. R., & Lubar, J. F. (2009). EEG LORETA and the Default Mode of the Brain. *Transaction of the 1st Annual Human Behavior-Computational Modeling and Interoperability Conference*.

Cannon, R., Lubar, J., Gerke, A., Thornton, K., Hutchens, T. A., & McCammon, V. (2006). EEG spectral-power and coherence: LORETA neurofeedback training in the anterior

cingulate gyrus. *Journal of Neurotherapy*, 10(1), 5-31. https://doi.org/10.1300/J184v10n01_02

Cannon, R., Lubar, J., Sokhadze, E., & Baldwin, D. (2008). LORETA Neurofeedback for Addiction and the Possible Neurophysiology of Psychological Processes Influenced: A Case Study and Region of Interest Analysis of LORETA Neurofeedback in Right Anterior Cingulate Cortex. *Journal of Neurotherapy*, 12(4), 227-241. https://doi.org/10.1080/10874200802501948

Canolty, R. T., & Knight, R. T. (2010). The functional role of cross-frequency coupling. *Trends in cognitive sciences*, 14(11), 506-515.

Carroll, J. M., Snowling, M. J., Hulme, C., & Stevenson, J. (2003). The Development of Phonological Awareness in Preschool Children. *Developmental Psychology*, https://doi.org/10.1037/0012-1649.39.5.913

Castles, A., & Coltheart, M. (1993). Varieties of developmental dyslexia. *Cognition*, 39(5), 913. https://doi.org/10.1016/0010-0277(93)90003-E

Castro-Caldas, A., Petersson, K. M., Reis, A., Stone-Elander, S., & Ingvar, M. (1998). The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. *Brain*, 121(6), 1053-1063. https://doi.org/10.1093/brain/121.6.1053

Catani, M., & Mesulam, M. (2008). The arcuate fasciculus and the disconnection theme in language and aphasia: History and current state. *Cortex*, 44(8), 953-961. https://doi.org/10.1016/j.cortex.2008.04.002

Cavanagh, J. F., & Frank, M. J. (2014). Frontal theta as a mechanism for cognitive control. In *Trends in Cognitive Sciences*, https://doi.org/10.1016/j.tics.2014.04.012

Cecere, R., Rees, G., & Romei, V. (2015). Individual differences in alpha frequency drive crossmodal illusory perception. *Current Biology*, 25(2), 231-235.

https://doi.org/10.1016/j.cub.2014.11.034

Centanni, T. M., Norton, E. S., Ozernov-Palchik, O., Park, A., Beach, S. D., Halverson, K., Gaab, N., & Gabrieli, J. D. E. (2019). Disrupted left fusiform response to print in beginning kindergartners is associated with subsequent reading. *NeuroImage: Clinical*, 22, 101715. https://doi.org/10.1016/j.nicl.2019.101715

Charness, G., Gneezy, U., & Kuhn, M. A. (2012). Experimental methods: Between-subject and within-subject design. *Journal of Economic Behavior and Organization*, 81(1), 1-8. https://doi.org/10.1016/j.jebo.2011.08.009

Chen, A. C. N., Feng, W., Zhao, H., Yin, Y., & Wang, P. (2008). EEG default mode network in the human brain: Spectral regional field powers. *NeuroImage*, 41(2), 561-574. https://doi.org/10.1016/j.neuroimage.2007.12.064

Colenbrander, D., Nickels, L., & Kohnen, S. (2017). Similar but different: differences in comprehension diagnosis on the Neale Analysis of Reading Ability and the York Assessment of Reading for Comprehension. *Journal of Research in Reading*, 40(4), 403-419. https://doi.org/10.1111/1467-9817.12075

Collura, T. F. (2010). Conclusion: QEEG-guided neurofeedback in context and in practice. In *Applied Psychophysiology Biofeedback*, 35(1), 37. https://doi.org/10.1007/s10484-009-9108-z

Collura, T. F. (2014). Technical Foundations of Neurofeedback. In *Technical Foundations of Neurofeedback*, https://doi.org/10.4324/9780203795132

Collura, T. F., Guan, J., Tarrant, J., Bailey, J., & Starr, F. (2010). EEG biofeedback case studies using live Z-score training and a normative database. *Journal of Neurotherapy*, 14(1), 22-46. https://doi.org/10.1080/10874200903543963

Colon, E. J., Notermans, S. L. H., de Weerd, J. P. C., & Kap, J. (1979). The discriminating role of EEG power spectra in dyslexic children. *Journal of Neurology*, 221(4), 257-

262. https://doi.org/10.1007/BF00314642

Coltheart, M. (1978). Lexical access in simple reading tasks. In *Strategies of information processing,* 151-216.

Coltheart, M., Curtis, B., Atkins, P., & Haller, M. (1993). Models of Reading Aloud: Dual-Route and Parallel-Distributed-Processing Approaches. *Psychological Review*, 100(4), 589. https://doi.org/10.1037/0033-295X.100.4.589

Coltheart, M., Masterson, J., Byng, S., Prior, M., & Riddoch, J. (1983). Surface dyslexia. *The Quarterly Journal of Experimental Psychology Section A*, 35(3), 469-495.https://doi.org/10.1080/14640748308402483

Coltheart, M., Rastle, K., Perry, C., Langdon, R., & Ziegler, J. (2001). DRC: A dual route cascaded model of visual word recognition and reading aloud. *Psychological Review*, 108(1), 204. https://doi.org/10.1037/0033-295X.108.1.204

Conway, T., Heilman, K. M., Gopinath, K., Peck, K., Bauer, R., Briggs, R. W., Torgesen, J. K., & Crosson, B. (2008). Neural substrates related to auditory working memory comparisons in dyslexia: An fMRI study. *Journal of the International Neuropsychological Society*, 14(4), 629-639. https://doi.org/10.1017/S1355617708080867

Corina, D. P., Richards, T. L., Serafini, S., Richards, A. L., Steury, K., Abbott, R. D., Echelard, D. R., Maravilla, K. R., & Berninger, V. W. (2001). fMRI auditory language differences between dyslexic and able reading children. *NeuroReport*, 12(6), 1195-1201. https://doi.org/10.1097/00001756-200105080-00029

Cornelissen, P., Bradley, L., Fowler, S., & Stein, J. (1992). Covering one eye affects how some children read. *Developmental Medicine & Child Neurology*, 34(4), 296-304. https://doi.org/10.1111/j.1469-8749.1992.tb11433.x

Cornelissen, P. L., Kringelbach, M. L., Ellis, A. W., Whitney, C., Holliday, I. E., & Hansen,

P. C. (2009). Activation of the left inferior frontal gyrus in the first 200 ms of reading: Evidence from Magnetoencephalography (MEG). *PLoS ONE*, 4(4), e5359. https://doi.org/10.1371/journal.pone.0005359

Cosden, M., Patz, S., & Donahue, M. (2012). Psychosocial problems and psychotherapy for persons with dyslexia. In *Dyslexia and Mental Health: Investigations from Differing Perspectives*.

D'mello, A. M., & Gabrieli, J. D. E. (2018). Cognitive neuroscience of dyslexia. *Language, Speech, and Hearing Services in Schools*, 49(4), 798-809. https://doi.org/10.1044/2018_LSHSS-DYSLC-18-0020

De Santana, V. F., De Oliveira, R., Almeida, L. D. A., & Baranauskas, M. C. C. (2012). Web accessibility and people with dyslexia: A survey on techniques and guidelines. *W4A 2012 - International Cross-Disciplinary Conference on Web Accessibility*, 1-9. https://doi.org/10.1145/2207016.2207047

De Vos, A., Vanvooren, S., Vanderauwera, J., Ghesquière, P., & Wouters, J. (2017). Atypical neural synchronization to speech envelope modulations in dyslexia. *Brain and Language*, 164, 106-117. https://doi.org/10.1016/j.bandl.2016.10.002

Decker, S. L., Roberts, A. M., & Green, J. J. (2015). LORETA Neurofeedback in College Students with ADHD. In *Z Score Neurofeedback: Clinical Applications*, 333-352. https://doi.org/10.1016/B978-0-12-801291-8.00014-5

Dehaene-Lambertz, G., Montavont, A., Jobert, A., Allirol, L., Dubois, J., Hertz-Pannier, L., & Dehaene, S. (2010). Language or music, mother or Mozart? Structural and environmental influences on infants' language networks. *Brain and Language*, 114(2), 53-65. https://doi.org/10.1016/j.bandl.2009.09.003

Dehaene, S., & Cohen, L. (2011). The unique role of the visual word form area in reading. In *Trends in Cognitive Sciences*, 15(6), 254-262.

https://doi.org/10.1016/j.tics.2011.04.003

Delorme, A., Jung, T.-P., Sejnowski, T., & Makeig, S. (2007). Improved rejection of artifacts from EEG data using high-order statistics and independent component analysis. *NeuroImage*.

Delorme, A., & Makeig, S. (2004). EEGLAB: an open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, 134(1), 9-21. https://doi.org/10.1016/j.jneumeth.2003.10.009

Demb, J. B., Boynton, G. M., Best, M., & Heeger, D. J. (1998). Psychophysical evidence for a magnocellular pathway deficit in dyslexia. *Vision Research*, 38(11), 1555-1559. https://doi.org/10.1016/S0042-6989(98)00075-3

Demb, J. B., Boynton, G. M., & Heeger, D. J. (1998). Functional magnetic resonance imaging of early visual pathways in dyslexia. *Journal of Neuroscience*, 18(17), 6939-6951. https://doi.org/10.1523/jneurosci.18-17-06939.1998

Demir, A. (2006). Computing timing jitter from phase noise spectra for oscillators and phase-locked loops with white and 1/f noise. *IEEE Transactions on Circuits and Systems I: Regular Papers*, 53(9), 1869-1884. https://doi.org/10.1109/TCSI.2006.881184

de Pesters, A., Coon, W. G., Brunner, P., Gunduz, A., Ritaccio, A. L., Brunet, N. M., ... & Schalk, G. (2016). Alpha power indexes task-related networks on large and small scales: A multimodal ECoG study in humans and a non-human primate. *Neuroimage*, 134, 122-131.

Devlin, J. T., Jamison, H. L., Gonnerman, L. M., & Matthews, P. M. (2006). The role of the posterior fusiform gyrus in reading. *Journal of Cognitive Neuroscience*, 18(6), 911-922. https://doi.org/10.1162/jocn.2006.18.6.911

Dhar, M., Been, P. H., Minderaa, R. B., & Althaus, M. (2010). Information processing

differences and similarities in adults with dyslexia and adults with Attention Deficit Hyperactivity Disorder during a Continuous Performance Test: A study of cortical potentials. *Neuropsychologia*, 48(10), 3045-3056. https://doi.org/10.1016/j.neuropsychologia.2010.06.014

Díaz, B., Hintz, F., Kiebel, S. J., & Von Kriegstein, K. (2012). Dysfunction of the auditory thalamus in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 109(34), 13841-13846. https://doi.org/10.1073/pnas.1119828109

Dole, M., Meunier, F., & Hoen, M. (2013). Gray and White Matter Distribution in Dyslexia: A VBM Study of Superior Temporal Gyrus Asymmetry. *PLoS ONE*, 8(10), e76823. https://doi.org/10.1371/journal.pone.0076823

Donner, T. H., & Siegel, M. (2011). A framework for local cortical oscillation patterns. In *Trends in Cognitive Sciences*, 15(5), 191-199. https://doi.org/10.1016/j.tics.2011.03.007

Dougherty, R. F., Ben-Shachar, M., Deutsch, G. K., Hernandez, A., Fox, G. R., & Wandell, B. A. (2007). Temporal-callosal pathway diffusivity predicts phonological skills in children. *Proceedings of the National Academy of Sciences of the United States of America*, 104(20), 8556-8561. https://doi.org/10.1073/pnas.0608961104

Drewes, J., & VanRullen, R. (2011). This is the rhythm of your eyes: The phase of ongoing electroencephalogram oscillations modulates saccadic reaction time. *Journal of Neuroscience*, 31(12), 4698-4708. https://doi.org/10.1523/JNEUROSCI.4795-10.2011

Drijvers, L., Mulder, K., & Ernestus, M. (2016). Alpha and gamma band oscillations index differential processing of acoustically reduced and full forms. *Brain and Language*, 153, 27-37. https://doi.org/10.1016/j.bandl.2016.01.003

Du, J., Rolls, E. T., Cheng, W., Li, Y., Gong, W., Qiu, J., & Feng, J. (2020). Functional connectivity of the orbitofrontal cortex, anterior cingulate cortex, and inferior frontal gyrus in humans. *Cortex*, 123, 185-199. https://doi.org/10.1016/j.cortex.2019.10.012

Duffy, F. H., Denckla, M. B., Bartels, P. H., Sandini, G., & Kiessling, L. S. (1980). Dyslexia: Automated diagnosis by computerized classification of brain electrical activity. *Annals of Neurology*, 7(5), 421-428. https://doi.org/10.1002/ana.410070506

Durup, G., & Fessard, A. (1935). I. L'électrencéphalogramme de l'homme. Observations psycho-physiologiques relatives à l'action des stimuli visuels et auditifs. *L'année Psychologique*, 36(1), 1-32. https://doi.org/10.3406/psy.1935.30643

Eckert, M., Ebert, D. D., Lehr, D., Sieland, B., & Berking, M. (2016). Overcome procrastination: Enhancing emotion regulation skills reduce procrastination. *Learning and Individual Differences*, 52, 10-18. https://doi.org/10.1016/j.lindif.2016.10.001

Eden, G. F., Stein, J. F., Wood, H. M., & Wood, F. B. (1994). Differences in eye movements and reading problems in dyslexic and normal children. *Vision Research*, 34(10), 1345-1358. https://doi.org/10.1016/0042-6989(94)90209-7

Eden, G. F., VanMeter, J. W., Rumsey, J. M., Maisog, J. M., Woods, R. P., & Zeffiro, T. A. (1996). Abnormal processing of visual motion in dyslexia revealed by functional brain imaging. *Nature*, 382(6586), 66-69. https://doi.org/10.1038/382066a0

Eden, Guinevere F., Jones, K. M., Cappell, K., Gareau, L., Wood, F. B., Zeffiro, T. A., Dietz, N. A. E., Agnew, J. A., & Flowers, D. L. (2004). Neural changes following remediation in adult developmental dyslexia. *Neuron*, 44(3), 411-422. https://doi.org/10.1016/j.neuron.2004.10.019

Engel, A. K., & Singer, W. (2001). Temporal binding and the neural correlates of sensory awareness. In *Trends in Cognitive Sciences*, 5(1), 16-25.

https://doi.org/10.1016/S1364-6613(00)01568-0

Engelbregt, H. J., Keeser, D., van Eijk, L., Suiker, E. M., Eichhorn, D., Karch, S., Deijen, J. B., & Pogarell, O. (2016). Short and long-term effects of sham-controlled prefrontal EEG-neurofeedback training in healthy subjects. *Clinical Neurophysiology*, 127(4), 1931-1937. https://doi.org/10.1016/j.clinph.2016.01.004

Enriquez-Geppert, S., Huster, R. J., & Herrmann, C. S. (2017). EEG-neurofeedback as a tool to modulate cognition and behavior: A review tutorial. *Frontiers in Human Neuroscience*, 11, 51. https://doi.org/10.3389/fnhum.2017.00051

Enriquez-Geppert, S., Huster, R. J., Scharfenort, R., Mokom, Z. N., Zimmermann, J., & Herrmann, C. S. (2014). Modulation of frontal-midline theta by neurofeedback. *Biological Psychology*, 95, 59-69. https://doi.org/10.1016/j.biopsycho.2013.02.019

Enriquez-Geppert, S., Smit, D., Pimenta, M. G., & Arns, M. (2019). Neurofeedback as a Treatment Intervention in ADHD: Current Evidence and Practice. In *Current Psychiatry Reports*, 21(6), 46. https://doi.org/10.1007/s11920-019-1021-4

Fadzal, C. W. N. F. C. W., Mansor, W., Lee, K. Y., Mohamad, S., & Amirin, S. (2012). Frequency analysis of EEG signal generated from dyslexic children. *ISCAIE 2012 - 2012 IEEE Symposium on Computer Applications and Industrial Electronics*, 202-204. https://doi.org/10.1109/ISCAIE.2012.6482096

Fahle, M. (2005). Perceptual learning: Specificity versus generalization. In *Current Opinion in Neurobiology*, 15(2), 154-160. https://doi.org/10.1016/j.conb.2005.03.010

Fein, G., Galin, D., Yingling, C. D., Johnstone, J., Davenport, L., & Herron, J. (1986). EEG spectra in dyslexic and control boys during resting conditions. *Electroencephalography and Clinical Neurophysiology*, 63(2), 87-97. https://doi.org/10.1016/0013-4694(86)90001-5

Fernández, T., Herrera, W., Harmony, T., Díaz-Comas, L., Santiago, E., Sánchez, l., Bosch,

J., Fernández-Bouzas, A., Otero, G., Ricardo-Garcell, J., Barraza, C., Aubert, E., Galán, L., & Valdés, P. (2003). EEG and Behavioral Changes following Neurofeedback Treatment in Learning Disabled Children. *Clinical EEG and Neuroscience*, 34(3), 145-152. https://doi.org/10.1177/155005940303400308

Fiez, J. A., & Petersen, S. E. (1998). Neuroimaging studies of word reading. *Proceedings of the National Academy of Sciences of the United States of America*, 95(3), 914-921. https://doi.org/10.1073/pnas.95.3.914

Fletcher, J. M., Barth, A. E., & Stuebing, K. K. (2011). A response to intervention (RTI) Approach to SLD Identification. In *Essentials of Specific Learning Disability Identification*, 115-144.

Fletcher, J. M., Lyon, G. R., Fuchs, L. S., & Barnes, M. A. (2018). Learning Disabilities: From Identification to Intervention. Second Edition. In *Guilford Press*.

Flinker, A., Korzeniewska, A., Shestyuk, A. Y., Franaszczuk, P. J., Dronkers, N. F., Knight, R. T., & Crone, N. E. (2015). Redefining the role of broca's area in speech. *Proceedings of the National Academy of Sciences of the United States of America*, 112(9), 2871-2875. https://doi.org/10.1073/pnas.1414491112

Flowers, D. L., Wood, F. B., & Naylor, C. E. (1991). Regional Cerebral Blood Flow Correlates of Language Processes in Reading Disability. *Archives of Neurology*, 48(6), 637-643. https://doi.org/10.1001/archneur.1991.00530180095023

Floyd, R. G., Keith, T. Z., Taub, G. E., & McGrew, K. S. (2007). Cattell-Horn-Carroll cognitive abilities and their effects on reading decoding skills: g has indirect effects, more specific abilities have direct effects. *School Psychology Quarterly*, 22(2), 200. https://doi.org/10.1037/1045-3830.22.2.200

Flynn, J. M., Deering, W., Goldstein, M., & Rahbar, M. H. (1992). Electrophysiological correlates of dyslexic subtypes. *Journal of Learning Disabilities*, 25(2), 133-141.

https://doi.org/10.1177/002221949202500207

Fonseca, L. C., Tedrus, G. M. A. S., Chiodi, M. G., Cerqueira, J. N., & Tonelotto, J. M. F. (2006). Quantitative EEG in children with learning disabilities: Analysis of band power. *Arquivos de Neuro-Psiquiatria*, 64(2B), 376-381. https://doi.org/10.1590/S0004-282X2006000300005

Foster, D. S., & Thatcher, R. W. (2015). Surface and LORETA Neurofeedback in the Treatment of Post-Traumatic Stress Disorder and Mild Traumatic Brain Injury. In *Z Score Neurofeedback: Clinical Applications*, 59-92. https://doi.org/10.1016/B978-0-12-801291-8.00004-2

Foster, P. S., & Drago, V. (2009). Handbook of Neurofeedback: Dynamics and Clinical Applications. *Archives of Clinical Neuropsychology*, https://doi.org/10.1093/arclin/acp018

Foxe, J. J., & Snyder, A. C. (2011). The role of alpha-band brain oscillations as a sensory suppression mechanism during selective attention. *Frontiers in Psychology*, 2, 154. https://doi.org/10.3389/fpsyg.2011.00154

Fraga González, G., Žarić, G., Tijms, J., Bonte, M., Blomert, L., Leppänen, P., & van der Molen, M. W. (2016). Responsivity to dyslexia training indexed by the N170 amplitude of the brain potential elicited by word reading. *Brain and Cognition*, 106, 42-54. https://doi.org/10.1016/j.bandc.2016.05.001

Fraga González, Gorka, Smit, D. J. A., van der Molen, M. J. W., Tijms, J., Stam, C. J., de Geus, E. J. C., & van der Molen, M. W. (2018). EEG Resting State Functional Connectivity in Adult Dyslexics Using Phase Lag Index and Graph Analysis. *Frontiers in Human Neuroscience*, 12, 341. https://doi.org/10.3389/fnhum.2018.00341

Friend, A., Defries, J. C., & Olson, R. K. (2008). Parental education moderates genetic

influences on reading disability: Research article. *Psychological Science*, 19(11), 1124-1130. https://doi.org/10.1111/j.1467-9280.2008.02213.x

Gaab, N., Gabrieli, J. D. E., Deutsch, G. K., Tallal, P., & Temple, E. (2007). Neural correlates of rapid auditory processing are disrupted in children with developmental dyslexia and ameliorated with training: An fMRI study. *Restorative Neurology and Neuroscience*, 25(3-4), 295-310.

Gabrieli, J. D. E. (2009). Dyslexia: A new synergy between education and cognitive neuroscience. In *Science*. 325(5938), 280-283. https://doi.org/10.1126/science.1171999

Gasser, T., Bächer, P., & Steinberg, H. (1985). Test-retest reliability of spectral parameters of the EEG. *Electroencephalography and Clinical Neurophysiology*, 60(4), 312-319. https://doi.org/10.1016/0013-4694(85)90005-7

Geiger, G., & Lettvin, J. Y. (1987). Peripheral Vision in Persons with Dyslexia. *New England Journal of Medicine*, 316(20), 1238-1243. https://doi.org/10.1056/NEJM198705143162003

Gerez, M., Tello, A., & Franco, M. (2018). S177. A bird-eye view on EEG networks in relation to personality traits in healthy controls. *Clinical Neurophysiology*, 129, e208. https://doi.org/10.1016/j.clinph.2018.04.537

Gevensleben, H., Holl, B., Albrecht, B., Schlamp, D., Kratz, O., Studer, P., Rothenberger, A., Moll, G. H., & Heinrich, H. (2010). Neurofeedback training in children with ADHD: 6-month follow-up of a randomised controlled trial. *European Child and Adolescent Psychiatry*, 19(9), 715-724. https://doi.org/10.1007/s00787-010-0109-5

Giacino, J. T., Fins, J. J., Laureys, S., & Schiff, N. D. (2014). Disorders of consciousness after acquired brain injury: The state of the science. In *Nature Reviews Neurology*, 10(2), 99. https://doi.org/10.1038/nrneurol.2013.279

Giesbrecht, B., Woldorff, M. G., Song, A. W., & Mangun, G. R. (2003). Neural mechanisms of top-down control during spatial and feature attention. Neuroimage, 19(3), 496-512.

Giraldo-Chica, M., Hegarty, J. P., & Schneider, K. A. (2015). Morphological differences in the lateral geniculate nucleus associated with dyslexia. *NeuroImage: Clinical*, 7, 830-836. https://doi.org/10.1016/j.nicl.2015.03.011

Goddard, C. A., Sridharan, D., Huguenard, J. R., & Knudsen, E. I. (2012). Gamma oscillations are generated locally in an attention-related midbrain network. *Neuron*, 73(3), 567-580. https://doi.org/10.1016/j.neuron.2011.11.028

González, G. F., Žarić, G., Tijms, J., Bonte, M., Blomert, L., & Van Der Molen, M. W. (2015). A Randomized Controlled Trial on the Beneficial Effects of Training Letter-Speech Sound Integration on Reading Fluency in Children with Dyslexia. *PLoS ONE*, 10(12), e0143914. https://doi.org/10.1371/journal.pone.0143914

Gori, S., Cecchini, P., Bigoni, A., Molteni, M., & Facoetti, A. (2014). Magnocellular-dorsal pathway and sub-lexical route in developmental dyslexia. *Frontiers in Human Neuroscience*, 8, 460. https://doi.org/10.3389/fnhum.2014.00460

Gori, S., Seitz, A. R., Ronconi, L., Franceschini, S., & Facoetti, A. (2016). Multiple Causal Links between Magnocellular-Dorsal Pathway Deficit and Developmental Dyslexia. *Cerebral Cortex*, 26(11), 4356-4369. https://doi.org/10.1093/cercor/bhv206

Goswami, U. (2003). How to beat dyslexia. In *Psychologist*.

Goswami, U. (2011). A temporal sampling framework for developmental dyslexia. In *Trends in Cognitive Sciences*, 15(1), 3-10. https://doi.org/10.1016/j.tics.2010.10.001

Goswami, U., Fosker, T., Huss, M., Mead, N., & SzuCs, D. (2011). Rise time and formant transition duration in the discrimination of speech sounds: The Ba-Wa distinction in developmental dyslexia. *Developmental Science*, 14(1), 34-43.

https://doi.org/10.1111/j.1467-7687.2010.00955.x

Goucha, T., & Friederici, A. D. (2015). The language skeleton after dissecting meaning: A functional segregation within Broca's Area. *NeuroImage*, 114, 294-302. https://doi.org/10.1016/j.neuroimage.2015.04.011

Gould, I. C., Rushworth, M. F., & Nobre, A. C. (2011). Indexing the graded allocation of visuospatial attention using anticipatory alpha oscillations. *Journal of neurophysiology*, 105(3), 1318-1326.

Grandy, T. H., Werkle-Bergner, M., Chicherio, C., Lövdén, M., Schmiedek, F., & Lindenberger, U. (2013). Individual alpha peak frequency is related to latent factors of general cognitive abilities. *NeuroImage*, 79, 10-18. https://doi.org/10.1016/j.neuroimage.2013.04.059

Grandy, T. H., Werkle-Bergner, M., Chicherio, C., Schmiedek, F., Lövdén, M., & Lindenberger, U. (2013). Peak individual alpha frequency qualifies as a stable neurophysiological trait marker in healthy younger and older adults. *Psychophysiology*, 50(6), 570-582. https://doi.org/10.1111/psyp.12043

Groeneveld, K. M., Mennenga, A. M., Heidelberg, R. C., Martin, R. E., Tittle, R. K., Meeuwsen, K. D., Walker, L. A., & White, E. K. (2019). Z-Score Neurofeedback and Heart Rate Variability Training for Adults and Children with Symptoms of Attention-Deficit/Hyperactivity Disorder: A Retrospective Study. *Applied Psychophysiology Biofeedback*, 44(4), 291-308. https://doi.org/10.1007/s10484-019-09439-x

Gross-Glenn, K., Duara, R., Barker, W. W., Loewenstein, D., Chang, J. Y., Yoshii, F., Apicella, A. M., Pascal, S., Boothe, T., Sevush, S., Jallad, B. J., Lovoa, L., & Lubs, H. A. (1991). Positron-emission tomographic studies during serial word-reading by normal and dyslexic adults. *Journal of Clinical and Experimental Neuropsychology*,

13(4), 531-544. https://doi.org/10.1080/01688639108401069

Gruber, T., Tsivilis, D., Giabbiconi, C. M., & Müller, M. M. (2008). Induced electroencephalogram oscillations during source memory: Familiarity is reflected in the gamma band, recollection in the theta band. *Journal of Cognitive Neuroscience*, 20(6), 1043-1053. https://doi.org/10.1162/jocn.2008.20068

Guez, J., Rogel, A., Getter, N., Keha, E., Cohen, T., Amor, T., Gordon, S., Meiran, N., & Todder, D. (2015). Influence of electroencephalography neurofeedback training on episodic memory: A randomized, sham-controlled, double-blind study. *Memory*, 23(5), 683-694. https://doi.org/10.1080/09658211.2014.921713

Gvion, A., & Friedmann, N. (2010). Dyscravia: Voicing substitution dysgraphia. *Neuropsychologia*, 48(7), 1935-1947. https://doi.org/10.1016/j.neuropsychologia.2010.03.014

Habib, M. (2000). The neurological basis of developmental dyslexia: An overview and working hypothesis. *Brain*, 123(12), 2373-2399. https://doi.org/10.1093/brain/123.12.2373

Haegens, S., Cousijn, H., Wallis, G., Harrison, P. J., & Nobre, A. C. (2014). Inter- and intra-individual variability in alpha peak frequency. *NeuroImage*, 92, 46-55. https://doi.org/10.1016/j.neuroimage.2014.01.049

Haegens, S., Händel, B. F., & Jensen, O. (2011). Top-down controlled alpha band activity in somatosensory areas determines behavioral performance in a discrimination task. *Journal of Neuroscience*, 31(14), 5197-5204. https://doi.org/10.1523/JNEUROSCI.5199-10.2011

Hagoort, P., Indefrey, P., Brown, C., Herzog, H., Steinmetz, H., & Seitz, R. J. (1999). The neural circuitry involved in the reading of German words and pseudowords: A PET study. *Journal of Cognitive Neuroscience*, 11(4), 383-398.

https://doi.org/10.1162/089892999563490

HajiHosseini, A., Rodríguez-Fornells, A., & Marco-Pallarés, J. (2012). The role of beta-gamma oscillations in unexpected rewards processing. *NeuroImage*, 60(3), 1678-1685. https://doi.org/10.1016/j.neuroimage.2012.01.125

Hakvoort, B., van der Leij, A., van Setten, E., Maurits, N., Maassen, B., & van Zuijen, T. (2016). Dichotic listening as an index of lateralization of speech perception in familial risk children with and without dyslexia. *Brain and Cognition*, 109, 75-83. https://doi.org/10.1016/j.bandc.2016.09.004

Hampson, M., Tokoglu, F., Sun, Z., Schafer, R. J., Skudlarski, P., Gore, J. C., & Constable, R. T. (2006). Connectivity-behavior analysis reveals that functional connectivity between left BA39 and Broca's area varies with reading ability. *NeuroImage*, 31(2), 513-519. https://doi.org/10.1016/j.neuroimage.2005.12.040

Harmony, T., Hinojosa, G., Marosi, E., Becker, J., Rodriguez, M., Reyes, A., & Rocha, C. (1990). Correlation between eeg spectral parameters and an educational evaluation. *International Journal of Neuroscience*, 54(1-2), 147-155. https://doi.org/10.3109/00207459008986630

Hasson, U., Levy, I., Behrmann, M., Hendler, T., & Malach, R. (2002). Eccentricity bias as an organizing principle for human high-order object areas. *Neuron*, 34(3), 479-490.

Hashemian, P., & Hashemian, P. (2015). Effectiveness of neuro-feedback on mathematics disorder. *African Journal of Psychiatry (South Africa)*, 18(2). https://doi.org/10.4172/Psychiatry.1000243

He, S., Mostofi, A., Syed, E., Torrecillos, F., Tinkhauser, G., Fischer, P., Pogsyan, A., Hasegawa, H., Li, Y., Ashkan, K., Pereira, E., & Tan, H. (2019). Neurofeedback linked suppression of subthalamic beta oscillations speeds up movement initialisation in Parkinsonian Patients. *BioRxiv*, 687582.

https://doi.org/10.1101/687582

Heath, S. M., Bishop, D. V. M., Bloor, K. E., Boyle, G. L., Fletcher, J., Hogben, J. H., Wigley, C. A., & Yeong, S. H. M. (2014). A spotlight on preschool: The influence of family factors on children's early literacy skills. *PLoS ONE*, 9(4), e95255. https://doi.org/10.1371/journal.pone.0095255

Heinrich, H., Gevensleben, H., Freisleder, F. J., Moll, G. H., & Rothenberger, A. (2004). Training of slow cortical potentials in attention-deficit/hyperactivity disorder: Evidence for positive behavioral and neurophysiological effects. *Biological Psychiatry*, 55(7), 772-775. https://doi.org/10.1016/j.biopsych.2003.11.013

Hinshelwood, J. (1911). Two cases of hereditary congenital word-blindness. *British Medical Journal*, 1(2620), 608. https://doi.org/10.1136/bmj.1.2620.608

Hoeft, F., McCandliss, B. D., Black, J. M., Gantman, A., Zakerani, N., Hulme, C., Lyytinen, H., Whitfield-Gabrieli, S., Glover, G. H., Reiss, A. L., & Gabrieli, J. D. E. (2011). Neural systems predicting long-term outcome in dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 108(1), 361-366. https://doi.org/10.1073/pnas.1008950108

Hoeft, F., Meyler, A., Hernandez, A., Juel, C., Taylor-Hill, H., Martindale, J. L., McMillon, G., Kolchugina, G., Black, J. M., Faizi, A., Deutsch, G. K., Wai, T. S., Reiss, A. L., Whitfield-Gabrieli, S., & Gabrieli, J. D. E. (2007). Functional and morphometric brain dissociation between dyslexia and reading ability. *Proceedings of the National Academy of Sciences of the United States of America*, 104(10), 4234-4239. https://doi.org/10.1073/pnas.0609399104

Holtmann, M., Sonuga-Barke, E., Cortese, S., & Brandeis, D. (2014). Neurofeedback for ADHD: A Review of Current Evidence. In *Child and Adolescent Psychiatric Clinics of North America*, 23(4), 789-806. https://doi.org/10.1016/j.chc.2014.05.006

Horwitz, B., Rumsey, J. M., & Donohue, B. C. (1998). Functional connectivity of the angular gyrus in normal reading and dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 95(15), 8939-8944. https://doi.org/10.1073/pnas.95.15.8939

Horwitz, Barry, & Braun, A. R. (2004). Brain network interactions in auditory, visual and linguistic processing. *Brain and Language*, 89(2), 377-384. https://doi.org/10.1016/S0093-934X(03)00349-3

Hsueh, J. J., Chen, T. S., Chen, J. J., & Shaw, F. Z. (2016). Neurofeedback training of EEG alpha rhythm enhances episodic and working memory. *Human Brain Mapping*, 37(7), 2662-2675. https://doi.org/10.1002/hbm.23201

Hwang, K., Velanova, K., & Luna, B. (2010). Strengthening of top-down frontal cognitive control networks underlying the development of inhibitory control: A functional magnetic resonance imaging effective connectivity study. *Journal of Neuroscience*, 30(46), 15535-15545. https://doi.org/10.1523/JNEUROSCI.2825-10.2010

J Lucas, K. (2015). LORETA Z-score Neurofeedback-Effectiveness in Rehabilitation of Patients Suffering from Traumatic Brain Injury. *Journal of Neurology and Neurobiology*, 1(4), 1-9. https://doi.org/10.16966/2379-7150.113

Jasper, H. (1958). The ten twenty electrode system of the international federation. *Electroencephalography and Clinical Neurophysiology*, 10, 370-375.

Jasper, H., & Shagass, C. (1941). Conditioning of the occipital alpha rhythm in man. *Journal of Experimental Psychology*, 28(5), 373. https://doi.org/10.1037/h0056139

Jenkins, J. R., & O'Connor, R. E. (2002). Early identification and intervention for young children with reading/learning disabilities. *Identification of Learning Disabilities: Research to Practice*, 2, 99-149.

Jensen, O., Kaiser, J., & Lachaux, J. P. (2007). Human gamma-frequency oscillations

associated with attention and memory. In *Trends in Neurosciences*, 30(7), 317-324. https://doi.org/10.1016/j.tins.2007.05.001

Jensen, O., & Mazaheri, A. (2010). Shaping functional architecture by oscillatory alpha activity: Gating by inhibition. *Frontiers in Human Neuroscience*, 4, 186. https://doi.org/10.3389/fnhum.2010.00186

Jernigan, T. L., Trauner, D. A., Hesselink, J. R., & Tallal, P. A. (1991). Maturation of human cerebrum observed in vivo during adolescence. *Brain*, 114(5), 2037-2049. https://doi.org/10.1093/brain/114.5.2037

Jimsheleishvili, S., & Dididze, M. (2019). Neuroanatomy, Cerebellum. In *StatPearls*.

Jokisch, D., & Jensen, O. (2007). Modulation of gamma and alpha activity during a working memory task engaging the dorsal or ventral stream. *Journal of Neuroscience*, 27(12), 3244-3251. https://doi.org/10.1523/JNEUROSCI.5399-06.2007

Joliot, M., Ribary, U., & Llinás, R. (1994). Human oscillatory brain activity near 40 Hz coexists with cognitive temporal binding. *Proceedings of the National Academy of Sciences of the United States of America*, 91(24), 11748-11751. https://doi.org/10.1073/pnas.91.24.11748

Kadosh, K. C., & Staunton, G. (2019). A systematic review of the psychological factors that influence neurofeedback learning outcomes. *NeuroImage*, 185, 545-555. https://doi.org/10.1016/j.neuroimage.2018.10.021

Kamarajan, C., Porjesz, B., Jones, K. A., Choi, K., Chorlian, D. B., Padmanabhapillai, A., Rangaswamy, M., Stimus, A. T., & Begleiter, H. (2005). Alcoholism is a disinhibitory disorder: Neurophysiological evidence from a Go/No-Go task. *Biological Psychology*, 69(3), 353-373. https://doi.org/10.1016/j.biopsycho.2004.08.004

Karim, I., Abdul, W., & Kamaruddin, N. (2013). Classification of dyslexic and normal

children during resting condition using KDE and MLP. *2013 5th International Conference on Information and Communication Technology for the Muslim World, 1-5. ICT4M 2013*. https://doi.org/10.1109/ICT4M.2013.6518886

Kassubek, J., Schmidtke, K., Kimmig, H., Lücking, C. H., & Greenlee, M. W. (2001). Changes in cortical activation during mirror reading before and after training: An fMRI study of procedural learning. *Cognitive Brain Research*, 10(3), 207-217. https://doi.org/10.1016/S0926-6410(00)00037-9

Keil, A., Müller, M. M., Ray, W. J., Gruber, T., & Elbert, T. (1999). Human gamma band activity and perception of a gestalt. *Journal of Neuroscience*, 19(16), 7152-7161. https://doi.org/10.1523/jneurosci.19-16-07152.1999

Keitel, C., Keitel, A., Benwell, C. S. Y., Daube, C., Thut, G., & Gross, J. (2019). Stimulus-driven brain rhythms within the alpha band: The attentional-modulation conundrum. *Journal of Neuroscience*, 39(16), 3119-3129. https://doi.org/10.1523/JNEUROSCI.1633-18.2019

Kennison, S. M. (2017). Introduction to Language Development. In *Introduction to Language Development*. https://doi.org/10.4135/9781506374499

Kesler, M. L., Andersen, A. H., Smith, C. D., Avison, M. J., Davis, C. E., Kryscio, R. J., & Blonder, L. X. (2001). Neural substrates of facial emotion processing using fMRI. *Cognitive Brain Research*, 11(2), 213-226.

Ketz, N. A., Jensen, O., & O'Reilly, R. C. (2015). Thalamic pathways underlying prefrontal cortex-medial temporal lobe oscillatory interactions. In *Trends in Neurosciences*, 38(1), 3-12. https://doi.org/10.1016/j.tins.2014.09.007

Kilavik, B. E., Zaepffel, M., Brovelli, A., MacKay, W. A., & Riehle, A. (2013). The ups and downs of beta oscillations in sensorimotor cortex. In *Experimental Neurology*, 245, 15-26. https://doi.org/10.1016/j.expneurol.2012.09.014

Kim, J., Park, J., Park, Y. M., Jang, D. P., Namkoong, K., Jung, Y. C., & Kim, I. Y. (2019). Diminished Frontal Theta Activity During Gaming in Young Adults With Internet Gaming Disorder. *Frontiers in Neuroscience*, 13, 1183. https://doi.org/10.3389/fnins.2019.01183

Kim, Y. Y., Lee, B., Shin, Y. W., Kwon, J. S., & Kim, M. S. (2006). Activity of left inferior frontal gyrus related to word repetition effects: LORETA imaging with 128-channel EEG and individual MRI. *Neuroimage*, 29(3), 712-720.

Klein, P. D., & Shaywitz, S. (2005). Overcoming Dyslexia: A New and Complete Science-Based Program for Reading Problems at Any Level. *Canadian Journal of Education / Revue Canadienne de l'éducation*, 162(1), 197-197. https://doi.org/10.2307/4126492

Klimesch, W., Doppelmayr, M., Schimke, H., & Pachinger, T. (1996). Alpha frequency, reaction time, and the speed of processing information. *Journal of Clinical Neurophysiology*, 13(6), 511-518. https://doi.org/10.1097/00004691-199611000-00006

Klimesch, W., Doppelmayr, M., Yonelinas, A., Kroll, N. E. A., Lazzara, M., Röhm, D., & Gruber, W. (2001). Theta synchronization during episodic retrieval: Neural correlates of conscious awareness. *Cognitive Brain Research*, 12(1), 33-38. https://doi.org/10.1016/S0926-6410(01)00024-6

Klimesch, Wolfgang. (1996). Memory processes, brain oscillations and EEG synchronization. *International Journal of Psychophysiology*, 24(1-2), 61-100. https://doi.org/10.1016/S0167-8760(96)00057-8

Klimesch, Wolfgang. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: A review and analysis. In *Brain Research Reviews*, 29(2-3), 169-195. https://doi.org/10.1016/S0165-0173(98)00056-3

Klimesch, Wolfgang. (2012). Alpha-band oscillations, attention, and controlled access to stored information. In *Trends in Cognitive Sciences*, 16(12), 606-617. https://doi.org/10.1016/j.tics.2012.10.007

Klimesch, Wolfgang, Doppelmayr, M., & Hanslmayr, S. (2006). Event-Related Dynamics of Brain Oscillations. In *Progress in brain research*. https://doi.org/10.1016/S0079-6123(06)59010-7

Klimesch, Wolfgang, Sauseng, P., Hanslmayr, S., Gruber, W., & Freunberger, R. (2007). Event-related phase reorganization may explain evoked neural dynamics. In *Neuroscience and Biobehavioral Reviews*, 31(7), 1003-1016. https://doi.org/10.1016/j.neubiorev.2007.03.005

Knoop-van Campen, C. A. N., Segers, E., & Verhoeven, L. (2018). How phonological awareness mediates the relation between working memory and word reading efficiency in children with dyslexia. *Dyslexia*, 24(2), 156-169. https://doi.org/10.1002/dys.1583

Knott, J. R., & Henry, C. E. (1941). The conditioning of the blocking of the alpha rhythm of the human electroencephalogram. *Journal of Experimental Psychology*, 28(2), 134. https://doi.org/10.1037/h0063280

Knyazev, G. G., Slobodskoj-Plusnin, J. Y., & Bocharov, A. V. (2009). Event-related delta and theta synchronization during explicit and implicit emotion processing. *Neuroscience*, 164(4), 1588-1600. https://doi.org/10.1016/j.neuroscience.2009.09.057

Knyazev, Gennady G. (2007). Motivation, emotion, and their inhibitory control mirrored in brain oscillations. In *Neuroscience and Biobehavioral Reviews*, 31(3), 377-395. https://doi.org/10.1016/j.neubiorev.2006.10.004

Knyazev, Gennady G., Savostyanov, A. N., Volf, N. V., Liou, M., & Bocharov, A. V. (2012).

EEG correlates of spontaneous self-referential thoughts: A cross-cultural study. *International Journal of Psychophysiology*, 86(2), 173-181. https://doi.org/10.1016/j.ijpsycho.2012.09.002

Kobayashi, S., De Carvalho, O. P., & Schultz, W. (2010). Adaptation of reward sensitivity in orbitofrontal neurons. *Journal of Neuroscience*, 30(2), 534-544. https://doi.org/10.1523/JNEUROSCI.4009-09.2010

Koberda, J. L. (2014). Z-score LORETA Neurofeedback as a Potential Rehabilitation Modality in Patients with CVA. *Journal of Neurology & Stroke*, 1(5), 00029. https://doi.org/10.15406/jnsk.2014.01.00029

Koberda, J. L. (2015). Application of Z-score LORETA Neuro-feedback in Therapy of Epilepsy. *Journal of Neurology and Neurobiology*, 1. https://doi.org/10.16966/2379-7150.e001

Koberda, J. L., Hillier, D. S., Jones, B., Moses, A., & Koberda, L. (2012). Application of Neurofeedback in General Neurology Practice. *Journal of Neurotherapy*, 16(3), 231-234. https://doi.org/10.1080/10874208.2012.705770

Koberda J, L. (2014). Z-Score LORETA Neurofeedback as a Potential Therapy in Cognitive Dysfunction and Dementia. *Journal of Psychology & Clinical Psychiatry*, 1(6), 00037. https://doi.org/10.15406/jpcpy.2014.01.00037

Kondacs, A., & Szabó, M. (1999). Long-term intra-individual variability of the background EEG in normals. *Clinical Neurophysiology*, 110(10), 1708-1716. https://doi.org/10.1016/S1388-2457(99)00122-4

Kouijzer, M. E. J., de Moor, J. M. H., Gerrits, B. J. L., Buitelaar, J. K., & van Schie, H. T. (2009). Long-term effects of neurofeedback treatment in autism. *Research in Autism Spectrum Disorders*, 3(2), 496-501. https://doi.org/10.1016/j.rasd.2008.10.003

Kovelman, I., Norton, E. S., Christodoulou, J. A., Gaab, N., Lieberman, D. A., Triantafyllou, C., Wolf, M., Whitfield-Gabrieli, S., & Gabrieli, J. D. E. (2012). Brain basis of phonological awareness for spoken language in children and its disruption in dyslexia. *Cerebral Cortex*, 22(4), 754-764. https://doi.org/10.1093/cercor/bhr094

Krafnick, A. J., Lynn Flowers, D., Luetje, M. M., Napoliello, E. M., & Eden, G. F. (2014). An investigation into the origin of anatomical differences in dyslexia. *Journal of Neuroscience, 34(3), 901-908*. https://doi.org/10.1523/JNEUROSCI.2092-13.2013

Krigbaum, G., & Wigton, N. L. (2014). When discussing neurofeedback, does modality matter? *NeuroRegulation*, 1(1), 48-48. https://doi.org/10.15540/nr.1.1.48

Kronbichler, M., Wimmer, H., Staffen, W., Hutzier, F., Mair, A., & Ladurner, G. (2008). Developmental dyslexia: Gray matter abnormalities in the occipitotemporal cortex. *Human Brain Mapping*, 29(5), 613-625. https://doi.org/10.1002/hbm.20425

Kussmaul, A. (1877). Word deafness and word blindness. In *Clycopedia of the practice of medicine, 770-778.*

Lambos, W. A., & Williams, R. A. (2015a). Treating Anxiety Disorders Using Z-Scored EEG Neurofeedback. In *Z Score Neurofeedback: Clinical Applications*, 189-217 https://doi.org/10.1016/B978-0-12-801291-8.00009-1

Lambos, W. A., & Williams, R. A. (2015b). Treating Executive Functioning Disorders Using LORETA Z-Scored EEG Biofeedback. In *Z Score Neurofeedback: Clinical Applications*, 141-157. https://doi.org/10.1016/B978-0-12-801291-8.00007-8

Landerl, K., Freudenthaler, H. H., Heene, M., De Jong, P. F., Desrochers, A., Manolitsis, G., Parrila, R., & Georgiou, G. K. (2019). Phonological Awareness and Rapid Automatized Naming as Longitudinal Predictors of Reading in Five Alphabetic Orthographies with Varying Degrees of Consistency. *Scientific Studies of Reading*, 23(3), 220-234. https://doi.org/10.1080/10888438.2018.1510936

Lange, J., Oostenveld, R., & Fries, P. (2013). Reduced occipital alpha power indexes enhanced excitability rather than improved visual perception. *Journal of Neuroscience*, 33(7), 3212-3220. https://doi.org/10.1523/JNEUROSCI.3755-12.2013

Langer, N., Peysakhovich, B., Zuk, J., Drottar, M., Sliva, D. D., Smith, S., Becker, B. L. C., Grant, P. E., & Gaab, N. (2017). White Matter Alterations in Infants at Risk for Developmental Dyslexia. *Cerebral Cortex, 27(2), 1027-1036.* https://doi.org/10.1093/cercor/bhv281

Lansbergen, M. M., Van Dongen-Boomsma, M., Buitelaar, J. K., & Slaats-Willemse, D. (2011). ADHD and EEG-neurofeedback: A double-blind randomized placebo-controlled feasibility study. *Journal of Neural Transmission*, 118(2), 275-284. https://doi.org/10.1007/s00702-010-0524-2

Laycock, R., & Crewther, S. G. (2008). Towards an understanding of the role of the "magnocellular advantage" in fluent reading. In *Neuroscience and Biobehavioral Reviews*, 32(8), 1494-1506. https://doi.org/10.1016/j.neubiorev.2008.06.002

Lees, R. B., & Chomsky, N. (1957). Syntactic Structures. *Language*. https://doi.org/10.2307/411160

Lehongre, K., Morillon, B., Giraud, A. L., & Ramus, F. (2013). Impaired auditory sampling in dyslexia: Further evidence from combined fMRI and EEG. *Frontiers in Human Neuroscience*, 7, 454. https://doi.org/10.3389/fnhum.2013.00454

Lehongre, K., Ramus, F., Villiermet, N., Schwartz, D., & Giraud, A. L. (2011). Altered low-gamma sampling in auditory cortex accounts for the three main facets of dyslexia. *Neuron*, 72(6), 1080-1090. https://doi.org/10.1016/j.neuron.2011.11.002

Leins, U., Goth, G., Hinterberger, T., Klinger, C., Rumpf, N., & Strehl, U. (2007). Neurofeedback for children with ADHD: A comparison of SCP and Theta/Beta

protocols. *Applied Psychophysiology Biofeedback, 32(2), 73-88.* https://doi.org/10.1007/s10484-007-9031-0

Leonard, C. M., Lombardino, L. J., Walsh, K., Eckert, M. A., Mockler, J. L., Rowe, L. A., Williams, S., & DeBose, C. B. (2002). Anatomical risk factors that distinguish dyslexia from SLI predict reading skill in normal children. *Journal of Communication Disorders*, 35(6), 501-531. https://doi.org/10.1016/S0021-9924(02)00120-X

Leppänen, P. H. T., Richardson, U., Pihko, E., Eklund, K. M., Guttorm, T. K., Aro, M., & Lyytinen, H. (2002). Brain responses to changes in speech sound durations differ between infants with and without familial risk for dyslexia. *Developmental Neuropsychology*, 22(1), 407-422. https://doi.org/10.1207/S15326942dn2201_4

Lewis, A. G., Schoffelen, J. M., Schriefers, H., & Bastlaansen, M. (2016). A predictive coding perspective on beta oscillations during sentence-level language comprehension. *Frontiers in Human Neuroscience*, 10, 85. https://doi.org/10.3389/fnhum.2016.00085

Li, S., & Chen, Z. (2017). Effects of neurofeedback training on dyslexic students' aggression: An experimental study. *NeuroQuantology*, 15(2). https://doi.org/10.14704/nq.2017.15.2.1072

Liberman, A. M., Cooper, F. S., Shankweiler, D. P., & Studdert-Kennedy, M. (1967). Perception of the speech code. *Psychological Review*, 74(6), 431. https://doi.org/10.1037/h0020279

Liberman, Alvin M., Harris, K. S., Hoffman, H. S., & Griffith, B. C. (1957). The discrimination of speech sounds within and across phoneme boundaries. *Journal of Experimental Psychology*, 54(5), 358. https://doi.org/10.1037/h0044417

Livingston, E. M., Siegel, L. S., & Ribary, U. (2018). Developmental dyslexia: emotional

impact and consequences. In *Australian Journal of Learning Difficulties*, 23(2), 107-135. https://doi.org/10.1080/19404158.2018.1479975

Livingstone, M. S., Rosen, G. D., Drislane, F. W., & Galaburda, A. M. (1991). Physiological and anatomical evidence for a magnocellular defect in developmental dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 88(18), 7943-7947. https://doi.org/10.1073/pnas.88.18.7943

Loomis, A. L., Harvey, E. N., & Hobart, G. (1936). Electrical potentials of the human brain. *Journal of Experimental Psychology*, 19(3), 249. https://doi.org/10.1037/h0062089

Lovegrove, S., Patron-Perez, A., & Sibley, G. (2013). Spline fusion: A continuous-time representation for visual-inertial fusion with application to rolling shutter cameras. *BMVC 2013 - Electronic Proceedings of the British Machine Vision Conference 2013*, 5, 8. https://doi.org/10.5244/C.27.93

Lubar, J. F., Bianchini, K. J., Calhoun, W. H., Lambert, E. W., Brody, Z. H., & Shabsin, H. S. (1985). Spectral analysis of EEG differences between children with and without learning disabilities. *Journal of Learning Disabilities*, 18(7), 403-408. https://doi.org/10.1177/002221948501800708

Lubar, R. S. (1997). Unmasking Pablo's gertrude: Queer desire and the subject of portraiture. *Art Bulletin*, 79(1), 56-84. https://doi.org/10.1080/00043079.1997.10786723

Luck, S.J. & Kappenman, E. S. (2011). *The Oxford Handbook of Event-Related Potential Components.*

Luck, S. J. (2005). An Introduction to Event-Related Potentials and Their Neural Origins. *An Introduction to the Event-Related Potential Technique*, 2–50. https://doi.org/10.1007/s10409-008-0217-3

Mahé, G., Bonnefond, A., Gavens, N., Dufour, A., & Doignon-Camus, N. (2012). Impaired visual expertise for print in French adults with dyslexia as shown by N170 tuning.

Neuropsychologia, 50(14), 3200-3206. https://doi.org/10.1016/j.neuropsychologia.2012.10.013

Mann, V. A., & Liberman, A. M. (1983). Some differences between phonetic and auditory modes of perception. *Cognition*, 14(2), 211-235. https://doi.org/10.1016/0010-0277(83)90030-6

Marco-Pallares, J., Cucurell, D., Cunillera, T., García, R., Andrés-Pueyo, A., Münte, T. F., & Rodríguez-Fornells, A. (2008). Human oscillatory activity associated to reward processing in a gambling task. *Neuropsychologia*, 46(1), 241-248. https://doi.org/10.1016/j.neuropsychologia.2007.07.016

Markovska-Simoska, S., & Pop-Jordanova, N. (2011). Quantitative EEG Spectrum-weighted Frequency (Brain Rate) Distribution in Adults with ADHD. *CNS Spectrums*, 16(5), 111-119. https://doi.org/10.1017/s1092852912000272

Marshall, C. M., Snowling, M. J., & Bailey, P. J. (2001). Rapid Auditory Processing and Phonological Ability in Normal Readers and Readers with Dyslexia. *Journal of Speech, Language, and Hearing Research*.

Marshall, J. C., & Newcombe, F. (1973). Patterns of paralexia: A psycholinguistic approach. *Journal of Psycholinguistic Research*, 2(3), 175-199. https://doi.org/10.1007/BF01067101

Martin, C. (2011). York Assessment of Reading for Comprehension (YARC). *Educational Psychology in Practice*. https://doi.org/10.1080/02667363.2011.629456

Marzbani, H., Marateb, H. R., & Mansourian, M. (2016). Methodological note: Neurofeedback: A comprehensive review on system design, methodology and clinical applications. *Basic and Clinical Neuroscience*, 7 (2): 143–58. https://doi.org/10.15412/j.bcn.03070208

Mathes, P. G., Denton, C. A., Fletcher, J. M., Anthony, J. L., Francis, D. J., &

Schatschneider, C. (2005). The effects of theoretically different instruction and student characteristics on the skills of struggling readers. *Reading Research Quarterly*, 40(2), 148-182. https://doi.org/10.1598/rrq.40.2.2

Mathewson, K. E., Lleras, A., Beck, D. M., Fabiani, M., Ro, T., & Gratton, G. (2011). Pulsed out of awareness: EEG alpha oscillations represent a pulsed-inhibition of ongoing cortical processing. In *Frontiers in Psychology*, 2, 99. https://doi.org/10.3389/fpsyg.2011.00099

Maunsell, J. (1987). Visual Processing In Monkey Extrastriate Cortex. *Annual Review of Neuroscience*. https://doi.org/10.1146/annurev.neuro.10.1.363

Mazuka, R., Jincho, N., & Oishi, H. (2009). Development of executive control and language processing. *Linguistics and Language Compass*, 3(1), 59-89. https://doi.org/10.1111/j.1749-818X.2008.00102.x

McAnally, K. I., & Stein, J. F. (1996). Auditory temporal coding in dyslexia. *Proceedings of the Royal Society B: Biological Sciences*, 263(1373), 961-965. https://doi.org/10.1098/rspb.1996.0142

McCandliss, B. D., Cohen, L., & Dehaene, S. (2003). The visual word form area: Expertise for reading in the fusiform gyrus. *Trends in Cognitive Sciences*, 7(7), 293-299. https://doi.org/10.1016/S1364-6613(03)00134-7

McDermott, B., Porter, E., Hughes, D., McGinley, B., Lang, M., O'Halloran, M., & Jones, M. (2018). Gamma Band Neural Stimulation in Humans and the Promise of a New Modality to Prevent and Treat Alzheimer's Disease. *Journal of Alzheimer's Disease : JAD*, 65(2), 363-392. https://doi.org/10.3233/JAD-180391

McGrew, K. S., & Woodcock, R. W. (2001). Technical Manual. *Woodcock-Johnson ® III Tests of Achievement*.

Mechelli, A., Gorno-Tempini, M. L., & Price, C. J. (2003). Neuroimaging studies of word

and pseudoword reading: Consistencies, inconsistencies, and limitations. *Journal of Cognitive Neuroscience*, 15(2), 260-271. https://doi.org/10.1162/089892903321208196

Menghini, D., Finzi, A., Benassi, M., Bolzani, R., Facoetti, A., Giovagnoli, S., Ruffino, M., & Vicari, S. (2010). Different underlying neurocognitive deficits in developmental dyslexia: A comparative study. *Neuropsychologia*, 48(4), 863-872. https://doi.org/10.1016/j.neuropsychologia.2009.11.003

Menolascino, S. M., Belgin, M., Izzo, G. N., & Fisher, L. E. (2017). Proceedings #19. Maintenance tDCS: A Case of Full and Durable Recovery from Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). *Brain Stimulation*, 10(4), e69-e71. https://doi.org/10.1016/j.brs.2017.04.112

Merigan, W. H., & Maunsell, J. H. R. (1993). How Parallel are the Primate Visual Pathways? *Annual Review of Neuroscience*, 16(1), 369-402. https://doi.org/10.1146/annurev.ne.16.030193.002101

Misselhorn, J., Friese, U., & Engel, A. K. (2019). Frontal and parietal alpha oscillations reflect attentional modulation of cross-modal matching. *Scientific Reports*, 9(1), 1-11. https://doi.org/10.1038/s41598-019-41636-w

Mockler, J. L. (2004). Predicting reading achievement in children: The significance of naming speed, phonological awareness, cognitive ability, processing speed, and neuroanatomy. *Dissertation Abstracts International Section A: Humanities and Social Sciences*.

Mody, M., Studdert-Kennedy, M., & Brady, S. (1997). Speech Perception Deficits in Poor Readers: Auditory Processing or Phonological Coding? *Journal of Experimental Child Psychology*, 64(2), 199-231. https://doi.org/10.1006/jecp.1996.2343

Mohammadi, M. R., Malmir, N., & Khaleghi, A. (2015). Comparison of Sensorimotor

Rhythm (SMR) and beta training on selective attention and symptoms in children with Attention Deficit/Hyperactivity Disorder (ADHD): A Trend Report. *Iranian Journal of Psychiatry*, 10(3), 165.

Molfese, D. L. (2000). Predicting dyslexia at 8 years of age using neonatal brain responses. *Brain and Language*, 72(3), 238-245. https://doi.org/10.1006/brln.2000.2287

Molinaro, N., Lizarazu, M., Lallier, M., Bourguignon, M., & Carreiras, M. (2016). Out-of-synchrony speech entrainment in developmental dyslexia. *Human Brain Mapping*, 37(8), 2767-2783. https://doi.org/10.1002/hbm.23206

Monzalvo, K., Fluss, J., Billard, C., Dehaene, S., & Dehaene-Lambertz, G. (2012). Cortical networks for vision and language in dyslexic and normal children of variable socio-economic status. *NeuroImage*, 61(1), 258-274. https://doi.org/10.1016/j.neuroimage.2012.02.035

Mortel, T. Van de. (2008). Faking it: social desirability response bias in self-report research. *Australian Journal of Advanced Nursing*, 25(4), 40.

Müller-Axt, C., Anwander, A., & von Kriegstein, K. (2017). Altered Structural Connectivity of the Left Visual Thalamus in Developmental Dyslexia. *Current Biology*, 27(23), 3692-3698. https://doi.org/10.1016/j.cub.2017.10.034

Muthukumaraswamy, S. (2013). High-frequency brain activity and muscle artifacts in MEG/EEG: a review and recommendations. *Frontiers in human neuroscience*, 7, 138.

Myers, C. A., Vandermosten, M., Farris, E. A., Hancock, R., Gimenez, P., Black, J. M., Casto, B., Drahos, M., Tumber, M., Hendren, R. L., Hulme, C., & Hoeft, F. (2014). White Matter Morphometric Changes Uniquely Predict Children's Reading Acquisition. *Psychological Science*, 25(10), 1870-1883. https://doi.org/10.1177/0956797614544511

Nagarajan, S., Mahncke, H., Salz, T., Tallal, P., Roberts, T., & Merzenich, M. M. (1999). Cortical auditory signal processing in poor readers. *Proceedings of the National Academy of Sciences of the United States of America*, 96(11), 6483-6488. https://doi.org/10.1073/pnas.96.11.6483

Nakada, T., Fujii, Y., Yoneoka, Y., & Kwee, I. L. (2001). Planum temporale: Where spoken and written language meet. *European Neurology*, 46(3), 121-125. https://doi.org/10.1159/000050784

Nardone, R., De Blasi, P., Bergmann, J., Caleri, F., Tezzon, F., Ladurner, G., Golaszewski, S., & Trinka, E. (2011). Theta burst stimulation of dorsolateral prefrontal cortex modulates pathological language switching: A case report. *Neuroscience Letters*, 487(3), 378-382. https://doi.org/10.1016/j.neulet.2010.10.060

Nathaniel-James, D. A., & Frith, C. D. (2002). The role of the dorsolateral prefrontal cortex: Evidence from the effects of contextual constraint in a sentence completion task. *NeuroImage*, 16(4), 1094-1102. https://doi.org/10.1006/nimg.2002.1167

Nazari, M. A., Mosanezhad, E., Hashemi, T., & Jahan, A. (2012). The effectiveness of neurofeedback training on EEG coherence and neuropsychological functions in children with reading disability. *Clinical EEG and Neuroscience*, 43(4), 315-322. https://doi.org/10.1177/1550059412451880

Nicolson, R. I., & Fawcett, A. J. (2005). Developmental dyslexia, learning and the cerebellum. In *Journal of Neural Transmission, Supplement*, 19-36. https://doi.org/10.1007/3-211-31222-6_2

Nicolson, Roderick I., Fawcett, A. J., & Dean, P. (2001). Developmental dyslexia: The cerebellar deficit hypothesis. In *Trends in Neurosciences*, 24(9), 508-511. https://doi.org/10.1016/S0166-2236(00)01896-8

Nixon, P., Lazarova, J., Hodinott-Hill, I., Gough, P., & Passingham, R. (2004). The Inferior

Frontal Gyrus and Phonological Processing: An Investigation using rTMS. *Journal of Cognitive Neuroscience*, 16(2), 289-300. https://doi.org/10.1162/089892904322984571

Norton, E. S., & Wolf, M. (2012). Rapid Automatized Naming (RAN) and Reading Fluency: Implications for Understanding and Treatment of Reading Disabilities. *Annual Review of Psychology, 63, 427-452.* https://doi.org/10.1146/annurev-psych-120710-100431

O'Brien, G. E., McCloy, D. R., Kubota, E. C., & Yeatman, J. D. (2018). Reading ability and phoneme categorization. *Scientific Reports*, 8(1), 1-17. https://doi.org/10.1038/s41598-018-34823-8

O'Brien, G. E., McCloy, D. R., & Yeatman, J. D. (2019). Categorical phoneme labeling in children with dyslexia does not depend on stimulus duration. *The Journal of the Acoustical Society of America*, 146(1), 245-255. https://doi.org/10.1121/1.5116568

O'Connor, R. E., Fulmer, D., Harty, K. R., & Bell, K. M. (2005). Layers of Reading Intervention in Kindergarten Through Third Grade. *Journal of Learning Disabilities*, 38(5), 440-455. https://doi.org/10.1177/00222194050380050701

O'Keefe, J., & Burgess, N. (1999). Theta activity, virtual navigation and the human hippocampus. In *Trends in Cognitive Sciences*, 3(11), 403-406. https://doi.org/10.1016/S1364-6613(99)01396-0

Odegard, T. N., Ring, J., Smith, S., Biggan, J., & Black, J. (2008). Differentiating the neural response to intervention in children with developmental dyslexia. *Annals of Dyslexia*, 58(1), 1. https://doi.org/10.1007/s11881-008-0014-5

Ogrim, G., Kropotov, J., & Hestad, K. (2012). The quantitative EEG theta/beta ratio in attention deficit/hyperactivity disorder and normal controls: Sensitivity, specificity, and behavioral correlates. *Psychiatry Research*, 198(3), 482-488.

https://doi.org/10.1016/j.psychres.2011.12.041

Olulade, O. A., Koo, D. S., Lasasso, C. J., & Eden, G. F. (2014). Neuroanatomical profiles of deafness in the context of native language experience. *Journal of Neuroscience*, 34(16), 5613-5620. https://doi.org/10.1523/JNEUROSCI.3700-13.2014

Olulade, O. A., Napoliello, E. M., & Eden, G. F. (2013). Abnormal Visual Motion Processing Is Not a Cause of Dyslexia. *Neuron*, 79(1), 180-190. https://doi.org/10.1016/j.neuron.2013.05.002

Omejc, N., Rojc, B., Battaglini, P. P., & Marusic, U. (2019). Review of the therapeutic neurofeedback method using electroencephalography: EEG neurofeedback. In *Bosnian Journal of Basic Medical Sciences*, 19(3), 213. https://doi.org/10.17305/bjbms.2018.3785

Orton, S. T. (1925). "Word-blindness" in school children. *Archives of Neurology And Psychiatry*, 14(5), 581-615. https://doi.org/10.1001/archneurpsyc.1925.02200170002001

Palva, S., & Palva, J. M. (2007). New vistas for α-frequency band oscillations. *Trends in Neurosciences*, 30(4), 150-158. https://doi.org/10.1016/j.tins.2007.02.001

Pammer, K., & Wheatley, C. (2001). Isolating the M(y)-cell response in dyslexia using the spatial frequency doubling illusion. *Vision Research*, 41(16), 2139-2147. https://doi.org/10.1016/S0042-6989(01)00092-X

Papagiannopoulou, E. A., & Lagopoulos, J. (2016). Resting state EEG hemispheric power asymmetry in children with dyslexia. *Frontiers in Pediatrics*, 4, 11. https://doi.org/10.3389/fped.2016.00011

Pape-Neumann, J., Van Ermingen-Marbach, M., Grande, M., Willmes, K., & Heim, S. (2015). The role of phonological awareness in treatments of dyslexic primary school children. *Acta Neurobiologiae Experimentalis*, 75, 80-106.

Park, S., Ryu, H., Lee, J. Y., Choi, A., Kim, D. J., Kim, S. N., & Choi, J. S. (2018). Longitudinal changes in neural connectivity in patients with internet gaming disorder: A resting-state EEG coherence study. *Frontiers in Psychiatry*, 9, 252. https://doi.org/10.3389/fpsyt.2018.00252

Pascual-Marqui, R. D., Michel, C. M., & Lehmann, D. (1994). Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *International Journal of Psychophysiology*, 18(1), 49-65. https://doi.org/10.1016/0167-8760(84)90014-X

Pascual-Marqui, Roberto D., Esslen, M., Kochi, K., & Lehmann, D. (2002). Functional imaging with low-resolution brain electromagnetic tomography (LORETA): A review. *Methods and Findings in Experimental and Clinical Pharmacology*, 24, 91-95.

Patterson, K. E. (1995). The relation between reading and phonological coding: further neuropsychological observations. *Neurocase*, 1(3), 251-257. https://doi.org/10.1093/neucas/1.3.251-i

Paulesu, E., Danelli, L., & Berlingeri, M. (2014). Reading the dyslexic brain: Multiple dysfunctional routes revealed by a new meta-analysis of PET and fMRI activation studies. In *Frontiers in Human Neuroscience*, 8, 830. https://doi.org/10.3389/fnhum.2014.00830

Paulesu, E., Frith, U., Snowling, M., Gallagher, A., Morton, J., Frackowiak, R. S. J., & Frith, C. D. (1996). Is developmental dyslexia a disconnection syndrome? Evidence from PET scanning. *Brain*, 119(1), 143-157. https://doi.org/10.1093/brain/119.1.143

Penolazzi, B., Spironelli, C., & Angrilli, A. (2008). Delta EEG activity as a marker of dysfunctional linguistic processing in developmental dyslexia. *Psychophysiology*, 45(6), 1025-1033. https://doi.org/10.1111/j.1469-8986.2008.00709.x

Pesaran, B., Pezaris, J. S., Sahani, M., Mitra, P. P., & Andersen, R. A. (2002). Temporal structure in neuronal activity during working memory in macaque parietal cortex. *Nature Neuroscience*, 5(8), 805-811. https://doi.org/10.1038/nn890

Peterson, R. L., Pennington, B. F., & Olson, R. K. (2013). Subtypes of developmental dyslexia: Testing the predictions of the dual-route and connectionist frameworks. *Cognition*, 126(1), 20-38. https://doi.org/10.1016/j.cognition.2012.08.007

Pfost, M. (2015). Children's phonological awareness as a predictor of reading and spelling: A systematic review of longitudinal research in German-speaking countries. In *Zeitschrift fur Entwicklungspsychologie und Padagogische Psychologie*. https://doi.org/10.1026/0049-8637/a000141

Pfurtscheller, G., & Lopes Da Silva, F. H. (1999). Event-related EEG/MEG synchronization and desynchronization: Basic principles. In *Clinical Neurophysiology*, 110(11), 1842-1857. https://doi.org/10.1016/S1388-2457(99)00141-8

Pineda, J. A., Brang, D., Hecht, E., Edwards, L., Carey, S., Bacon, M., Futagaki, C., Suk, D., Tom, J., Birnbaum, C., & Rork, A. (2008). Positive behavioral and electrophysiological changes following neurofeedback training in children with autism. *Research in Autism Spectrum Disorders*, 2(3), 557-581. https://doi.org/10.1016/j.rasd.2007.12.003

Plaut, D. C. (1999). A connectionist approach to word reading and acquired dyslexia: Extension to sequential processing. *Cognitive Science*, 23(4), 543-568.

Pop-Jordanova, N., Markovska-Simoska, S., Milovanovic, M., & Lecic-Tosevski, D. (2020). Analysis of EEG Characteristics and Coherence in Patients Diagnosed as Borderline Personality. *PRILOZI*, 40(3), 57-68. https://doi.org/10.2478/prilozi-2020-0005

Price, C. J. (2012). A review and synthesis of the first 20years of PET and fMRI studies of heard speech, spoken language and reading. In *NeuroImage*, 62(2), 816-847.

https://doi.org/10.1016/j.neuroimage.2012.04.062

Price, C. J., & Devlin, J. T. (2011). The Interactive Account of ventral occipitotemporal contributions to reading. In *Trends in Cognitive Sciences*, 15(6), 246-253. https://doi.org/10.1016/j.tics.2011.04.001

Pscherer, C., Mückschel, M., Summerer, L., Bluschke, A., & Beste, C. (2019). On the relevance of EEG resting theta activity for the neurophysiological dynamics underlying motor inhibitory control. *Human Brain Mapping*, 40(14), 4253-4265. https://doi.org/10.1002/hbm.24699

Pugh, K. R., Mencl, W. E., Jenner, A. R., Katz, L., Frost, S. J., Lee, J. R., Shaywitz, S. E., & Shaywitz, B. A. (2001). Neurobiological studies of reading and reading disability. *Journal of Communication Disorders*, 34(6), 479-492. https://doi.org/10.1016/S0021-9924(01)00060-0

Pugh, K. R., Mencl, W. E., Shaywitz, B. A., Shaywitz, S. E., Fulbright, R. K., Constable, R. T., ... & Gore, J. C. (2000). The angular gyrus in developmental dyslexia: task-specific differences in functional connectivity within posterior cortex. *Psychological science*, 11(1), 51-56.

Putman, P. (2011). Resting state EEG delta-beta coherence in relation to anxiety, behavioral inhibition, and selective attentional processing of threatening stimuli. *International Journal of Psychophysiology*, 80(1), 63-68. https://doi.org/10.1016/j.ijpsycho.2011.01.011

Raesi, S., Dadgar, H., Soleymani, Z., & Hajjeforoush, V. (2016). Efficacy of Neurofeedback Training on Reading and Spelling Skills of 8 to 12 Years Old Children With Dyslexia. *Journal of Modern Rehabilitation*, 177-184. https://doi.org/10.18869/nirp.jmr.10.4.177

Ramus, F. (2004). Neurobiology of dyslexia: A reinterpretation of the data. *Trends in*

Neurosciences, 27(12), 720-726. https://doi.org/10.1016/j.tins.2004.10.004

Ramus, F., Altarelli, I., Jednoróg, K., Zhao, J., & Scotto di Covella, L. (2018). Neuroanatomy of developmental dyslexia: Pitfalls and promise. In *Neuroscience and Biobehavioral Reviews*, 84, 434-452. https://doi.org/10.1016/j.neubiorev.2017.08.001

Ramus, F., Rosen, S., Dakin, S. C., Day, B. L., Castellote, J. M., White, S., & Frith, U. (2003). Theories of developmental dyslexia: Insights from a multiple case study of dyslexic adults. *Brain*, 126(4), 841-865. https://doi.org/10.1093/brain/awg076

Raschle, N. M., Chang, M., & Gaab, N. (2011). Structural brain alterations associated with dyslexia predate reading onset. *NeuroImage*, 57(3), 742-749. https://doi.org/10.1016/j.neuroimage.2010.09.055

Ravens-Sieberer, U., Wille, N., Erhart, M., Bettge, S., Wittchen, H.-U., Rothenberger, A., Herpertz-Dahlmann, B., Resch, F., Hölling, H., Bullinger, M., Barkmann, C., Schulte-Markwort, M., & Döpfner, M. (2008). Prevalence of Mental Health Problems among Children and Adolescents in Germany. *European Child Adolescent Psychiatry*.

Renvall, H., Lehtonen, R., & Hari, R. (2005). Abnormal response recovery in the right somatosensory cortex of dyslexic adults. *Cerebral Cortex*, 15(5), 507-513. https://doi.org/10.1093/cercor/bhh150

Richardson, U., Thomson, J. M., Scott, S. K., & Goswami, U. (2004). Auditory processing skills and phonological representation in dyslexic children. *Dyslexia*, 10(3), 215-233. https://doi.org/10.1002/dys.276

Richlan, F. (2020). The Functional Neuroanatomy of Developmental Dyslexia Across Languages and Writing Systems. In *Frontiers in Psychology*, 11, 155. https://doi.org/10.3389/fpsyg.2020.00155

Richlan, F., Kronbichler, M., & Wimmer, H. (2009). Functional abnormalities in the dyslexic

brain: A quantitative meta-analysis of neuroimaging studies. *Human Brain Mapping*, 30(10), 3299-3308. https://doi.org/10.1002/hbm.20752

Richlan, F., Kronbichler, M., & Wimmer, H. (2011). Meta-analyzing brain dysfunctions in dyslexic children and adults. *NeuroImage*, 56(3), 1735-1742. https://doi.org/10.1016/j.neuroimage.2011.02.040

Richlan, F., Kronbichler, M., & Wimmer, H. (2013). Structural abnormalities in the dyslexic brain: A meta-analysis of voxel-based morphometry studies. *Human Brain Mapping*, 34(11), 3055-3065. https://doi.org/10.1002/hbm.22127

Richlan, F., Sturm, D., Schurz, M., Kronbichler, M., Ladurner, G., & Wimmer, H. (2010). A common left occipito-temporal dysfunction in developmental dyslexia and acquired letter-by-letter reading? *PLoS ONE*, 5(8), e12073. https://doi.org/10.1371/journal.pone.0012073

Rilling, J. K., & Sanfey, A. G. (2011). The Neuroscience of Social Decision-Making. *Annual Review of Psychology*, 62, 23-48. https://doi.org/10.1146/annurev.psych.121208.131647

Rippon, G., & Brunswick, N. (2000). Trait and state EEG indices of information processing in developmental dyslexia. *International Journal of Psychophysiology*, 36(3), 251-265. https://doi.org/10.1016/S0167-8760(00)00075-1

Robichon, F., & Habib, M. (1998). Abnormal callosal morphology in male adult dyslexics: Relationships to handedness and phonological abilities. *Brain and Language*, 62(1), 127-146. https://doi.org/10.1006/brln.1997.1891

Rogala, J., Jurewicz, K., Paluch, K., Kublik, E., Cetnarski, R., & Wróbel, A. (2016). The do's and don'ts of neurofeedback training: A review of the controlled studies using healthy adults. In *Frontiers in Human Neuroscience*, 10, 301. https://doi.org/10.3389/fnhum.2016.00301

Ros, T., Michela, A., Bellman, A., Vuadens, P., Saj, A., & Vuilleumier, P. (2017). Increased Alpha-Rhythm Dynamic Range Promotes Recovery from Visuospatial Neglect: A Neurofeedback Study. *Neural Plasticity*. https://doi.org/10.1155/2017/7407241

Rossion, B., Joyce, C. A., Cottrell, G. W., & Tarr, M. J. (2003). Early lateralization and orientation tuning for face, word, and object processing in the visual cortex. *NeuroImage*, 20(3), 1609-1624. https://doi.org/10.1016/j.neuroimage.2003.07.010

Rumsey, J. M., Horwitz, B., Donohue, B. C., Nace, K., Maisog, J. M., & Andreason, P. (1997). Phonological and orthographic components of word recognition. A PET-rCBF study. *Brain*, 120(5), 739-759. https://doi.org/10.1093/brain/120.5.739

Rumsey, Judith M., Aquino, T., King, A. C., Hamburger, S. D., Rapoport, J. L., Andreason, P., Zametkin, A. J., Cohen, R. M., & Pikus, A. (1992). Failure to Activate the Left Temporoparietal Cortex in Dyslexia: An Oxygen 15 Positron Emission Tomographic Study. *Archives of Neurology*, 49(5), 527-534. https://doi.org/10.1001/archneur.1992.00530290115020

Rumsey, Judith M., Coppola, R., Denckla, M. B., Hamburger, S. D., & Kruesi, M. J. P. (1989). EEG spectra in severely dyslexic men: rest and word and design recognition. *Electroencephalography and Clinical Neurophysiology*, 73(1), 30-40. https://doi.org/10.1016/0013-4694(89)90017-5

Rumsey, Judith M., Hanahan, A. P., Hamburger, S. D., Aquino, T., King, A. C., Zametkin, A. J., Andreason, P., Cohen, R. M., & Pikus, A. (1994). Normal activation of frontotemporal language cortex in dyslexia, as measured with oxygen 15 positron emission tomography. *Archives of Neurology*, 51(1), 27-38. https://doi.org/10.1001/archneur.1994.00540130037011

Sadaghiani, S., Hesselmann, G., Friston, K. J., & Kleinschmidt, A. (2010). The relation of ongoing brain activity, evoked neural responses, and cognition. In *Frontiers in*

Systems Neuroscience, 4, 20. https://doi.org/10.3389/fnsys.2010.00020

Sahari, S. H., & Johari, A. (2012). Improvising Reading Classes and Classroom Environment for Children with Reading Difficulties and Dyslexia Symptoms. *Procedia - Social and Behavioral Sciences*, 38, 100-107. https://doi.org/10.1016/j.sbspro.2012.03.329

Salmelin, R., & Hari, R. (1994). Spatiotemporal characteristics of sensorimotor neuromagnetic rhythms related to thumb movement. *Neuroscience*, 60(2), 537-550. https://doi.org/10.1016/0306-4522(94)90263-1

Salmelin, Riitta, Schnitzler, A., Schmitz, F., & Freund, H. J. (2000). Single word reading in developmental stutterers and fluent speakers. *Brain*, 123(6), 1184-1202. https://doi.org/10.1093/brain/123.6.1184

Samaha, J., Iemi, L., & Postle, B. R. (2017). Prestimulus alpha-band power biases visual discrimination confidence, but not accuracy. *Consciousness and Cognition*, 54, 47-55. https://doi.org/10.1016/j.concog.2017.02.005

Samaha, J., & Postle, B. R. (2015). The Speed of Alpha-Band Oscillations Predicts the Temporal Resolution of Visual Perception. *Current Biology*, 25(22), 2985-2990. https://doi.org/10.1016/j.cub.2015.10.007

Santa, C. M., & Høien, T. (1999). An Assessment of Early Steps: A Program for Early Intervention of Reading Problems. *Reading Research Quarterly*, 34(1), 54-79. https://doi.org/10.1598/rrq.34.1.4

Saralegui, I., Ontañón, J. M., Fernandez-Ruanova, B., Garcia-Zapirain, B., Basterra, A., & Sanz-Arigita, E. J. (2014). Reading networks in children with dyslexia compared to children with ocular motility disturbances revealed by fMRI. *Frontiers in Human Neuroscience*, 8, 936. https://doi.org/10.3389/fnhum.2014.00936

Sauvé, K. (1999). Gamma-Band Synchronous Oscillations: Recent Evidence Regarding Their Functional Significance. *Consciousness and Cognition*, 8(2), 213-224.

https://doi.org/10.1006/ccog.1999.0383

Sauseng, P., Klimesch, W., Stadler, W., Schabus, M., Doppelmayr, M., Hanslmayr, S., ... & Birbaumer, N. (2005). A shift of visual spatial attention is selectively associated with human EEG alpha activity. *European Journal of Neuroscience*, 22(11), 2917-2926.

Scammaca, N., Roberts, G., Vaughn, S., Edmonds, M., Wexler, J., Reutebuch, C. K., & Torgesen, J. K. (2007). Interventions for adolescent struggling readers: A meta-analysis with implications for practice. *Center on Instruction*.

Schiller, P. H., & Lee, K. (1994). The effects of lateral geniculate nucleus, area V4, and middle temporal (MT) lesions on visually guided eye movements. *Visual Neuroscience*, 11(2), 229-241. https://doi.org/10.1017/S0952523800001590

Schmid, R. G., Sadowsky, K., Weinmann, H. M., Tirsch, W. S., & Pöppl, S. J. (1985). Z-transformed EEG power spectra of children with Down syndrome vs a control group. *Neuropediatrics*, 16(04), 218-224. https://doi.org/10.1055/s-2008-1059540

Schmidt, R., Herrojo Ruiz, M., Kilavik, B. E., Lundqvist, M., Starr, P. A., & Aron, A. R. (2019). Beta Oscillations in Working Memory, Executive Control of Movement and Thought, and Sensorimotor Function. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 39(42), 8231-8238. https://doi.org/10.1523/JNEUROSCI.1163-19.2019

Schrank, F. A., Mather, N., & McGrew, K. S. (2015). Test review: Woodcock-Johnson IV Tests of Achievement. *Journal of Psychoeducational Assessment*, 33(4), 391-398. https://doi.org/10.1177/0734282915569447

Schurz, M., Wimmer, H., Richlan, F., Ludersdorfer, P., Klackl, J., & Kronbichler, M. (2015). Resting-state and task-based functional brain connectivity in developmental dyslexia. *Cerebral Cortex*, 25(10), 3502-3514.

https://doi.org/10.1093/cercor/bhu184

Schwabedal, J. T. C., Riedl, M., Penzel, T., & Wessel, N. (2016). Alpha-wave frequency characteristics in health and insomnia during sleep. *Journal of Sleep Research*, 25(3), 278-286. https://doi.org/10.1111/jsr.12372

Seitz, A. R., & Dinse, H. R. (2007). A common framework for perceptual learning. In *Current Opinion in Neurobiology*, 17(2), 148-153. https://doi.org/10.1016/j.conb.2007.02.004

Sejnowski, T. J., & Paulsen, O. (2006). Network oscillations: Emerging computational principles. In *Journal of Neuroscience*, 26(6), 1673-1676. https://doi.org/10.1523/JNEUROSCI.3737-05d.2006

Serniclaes, W., Van Heghe, S., Mousty, P., Carré, R., & Sprenger-Charolles, L. (2004). Allophonic mode of speech perception in dyslexia. *Journal of Experimental Child Psychology*, 87(4), 336-361. https://doi.org/10.1016/j.jecp.2004.02.001

Shamaeva, T. F., Pronina, M. V., Polyakova, G. Y., Polyakov, Y. I., & Klimenko, V. M. (2018). Electrophysiological Correlates of Major Depression Disorder with Anxious Distress in Patients of Different Age Groups. *Human Physiology*, 44(1), 1-6. https://doi.org/10.1134/S0362119718010152

Shapleske, J., Rossell, S. L., Woodruff, P. W. R., & David, A. S. (1999). The planum temporale: A systematic, quantitative review of its structural, functional and clinical significance. In *Brain Research Reviews*, 29(1), 26-49. https://doi.org/10.1016/S0165-0173(98)00047-2

Shaw, J. C. (1981). An introduction to the coherence function and its use in EEG signal analysis. *Journal of Medical Engineering and Technology*, 5(6), 279-288. https://doi.org/10.3109/03091908109009362

Shaywitz, B. A., Shaywitz, S. E., Pugh, K. R., Mencl, W. E., Fulbright, R. K., Skudlarski, P.,

Constable, R. T., Marchione, K. E., Fletcher, J. M., Lyon, G. R., & Gore, J. C. (2002). Disruption of posterior brain systems for reading in children with developmental dyslexia. *Biological Psychiatry*, 52(2), 101-110. https://doi.org/10.1016/S0006-3223(02)01365-3

Shaywitz, S. E., & Shaywitz, B. A. (2005). Dyslexia (specific reading disability). In *Biological Psychiatry*, 57(11), 1301-1309. https://doi.org/10.1016/j.biopsych.2005.01.043

Shaywitz, S. E., Shaywitz, B. A., Pugh, K. R., Fulbright, R. K., Constable, R. T., Mencl, W. E., Shankweiler, D. P., Liberman, A. M., Skudlarski, P., Fletcher, J. M., Katz, L., Marchione, K. E., Lacadie, C., Gatenby, C., & Gore, J. C. (1998). Functional disruption in the organization of the brain for reading in dyslexia. *Proceedings of the National Academy of Sciences of the United States of America*, 95(5), 2636-2641. https://doi.org/10.1073/pnas.95.5.2636

Sherlin, L. H., Arns, M., Lubar, J., Heinrich, H., Kerson, C., Strehl, U., & Sterman, M. B. (2011). Neurofeedback and Basic Learning Theory: Implications for Research and Practice. In *Journal of Neurotherapy*, 15(4), 292-304. https://doi.org/10.1080/10874208.2011.623089

Simkin, D. R., Thatcher, R. W., & Lubar, J. (2014). Quantitative EEG and Neurofeedback in Children and Adolescents. Anxiety Disorders, Depressive Disorders, Comorbid Addiction and Attention-deficit/Hyperactivity Disorder, and Brain Injury. In *Child and Adolescent Psychiatric Clinics of North America*, 23(3), 427-464. https://doi.org/10.1016/j.chc.2014.03.001

Simon, J. R., & Rudell, A. P. (1967). Auditory S-R Compatibility - Effect of an Irrelevant Cue on Information Processing. *Journal of Applied Psychology*, *51*(3), 300-. https://doi.org/DOI 10.1037/h0020586

Singer, W. (2013). Cortical dynamics revisited. In *Trends in Cognitive Sciences*, 17(12), 616-626. https://doi.org/10.1016/j.tics.2013.09.006

Sitaram, R., Ros, T., Stoeckel, L., Haller, S., Scharnowski, F., Lewis-Peacock, J., Weiskopf, N., Blefari, M. L., Rana, M., Oblak, E., Birbaumer, N., & Sulzer, J. (2017). Closed-loop brain training: The science of neurofeedback. In *Nature Reviews Neuroscience*, 18(2), 86-100. https://doi.org/10.1038/nrn.2016.164

Skinner, B. F. (1948). "Superstition" in the pigeon. *Journal of Experimental Psychology*, 38(2), 168. https://doi.org/10.1037/h0055873

Sklar, B., Hanley, J., & Simmons, W. W. (1972). An EEG experiment aimed toward identifying dyslexic children. *Nature*, 240(5381), 414-416. https://doi.org/10.1038/240414a0

Slaghuis, W. L., Lovegrove, W. J., & Davidson, J. A. (1993). Visual and Language Processing Deficits are Concurrent in Dyslexia. *Cortex*, 29(4), 601-615. https://doi.org/10.1016/S0010-9452(13)80284-5

Snow, C. E., Burns, S., Griffin, P., & Washington, D. C. (1998). Preventing reading difficulties in young children. *National Academy Press*.

Sokolov, A., Pavlova, M., Lutzenberger, W., & Birbaumer, N. (2004). Reciprocal modulation of neuromagnetic induced gamma activity by attention in the human visual and auditory cortex. *NeuroImage*, 22(2), 521-529. https://doi.org/10.1016/j.neuroimage.2004.01.045

Spinelli, D., De Luca, M., Judica, A., & Zoccolotti, P. (2002). Crowding effects on word identification in developmental dyslexia. *Cortex*, 38(2), 179-200. https://doi.org/10.1016/S0010-9452(08)70649-X

Staddon, J. E. R., & Cerutti, D. T. (2003). Operant Conditioning. In *Annual Review of Psychology*, 54(1), 115-144.

https://doi.org/10.1146/annurev.psych.54.101601.145124

Stam, C. J., Montez, T., Jones, B. F., Rombouts, S. A. R. B., Van Der Made, Y., Pijnenburg, Y. A. L., & Scheltens, P. (2005). Disturbed fluctuations of resting state EEG synchronization in Alzheimer's disease. *Clinical Neurophysiology*, 116(3), 708-715. https://doi.org/10.1016/j.clinph.2004.09.022

Stancák, A., & Pfurtscheller, G. (1995). Desynchronization and recovery of β rhythms during brisk and slow self-paced finger movements in man. *Neuroscience Letters*, 196(1-2), 21-24. https://doi.org/10.1016/0304-3940(95)11827-J

Stein, J. (2001). The Magnocellular Theory of Developmental Dyslexia. *Dyslexia*, 7(1), 12-36. https://doi.org/10.1002/dys.186

Stein, J. (2018). What is developmental dyslexia? In *Brain Sciences*, 8(2), 26. https://doi.org/10.3390/brainsci8020026

Stein, J., & Walsh, V. (1997). To see but not to read; the magnocellular theory of dyslexia. *Trends in Neurosciences*, 20(4), 147-152. https://doi.org/10.1016/S0166-2236(96)01005-3

Sterman, M. B., & Egner, T. (2006). Foundation and practice of neurofeedback for the treatment of epilepsy. In *Applied Psychophysiology Biofeedback*, 31(1), 21. https://doi.org/10.1007/s10484-006-9002-x

Stoodley, C. J., Valera, E. M., & Schmahmann, J. D. (2012). Functional topography of the cerebellum for motor and cognitive tasks: An fMRI study. *NeuroImage*, 59(2), 1560-1570. https://doi.org/10.1016/j.neuroimage.2011.08.065

Strehl, U., Leins, U., Goth, G., Klinger, C., Hinterberger, T., & Birbaumer, N. (2006). Self-regulation of slow cortical potentials: A new treatment for children with attention-deficit/hyperactivity disorder. *Pediatrics*, 118(5), e1530-e1540. https://doi.org/10.1542/peds.2005-2478

Surwillo, W. W. (1961). Frequency of the “alpha” rhythm, reaction time and age. *Nature*, 191(4790), 823-824. https://doi.org/10.1038/191823a0

Tallal, P. (1980). Auditory temporal perception, phonics, and reading disabilities in children. *Brain and Language*, *9*(2), 182-198. https://doi.org/10.1016/0093-934X(80)90139-X

Tallal, P. (2004). Improving language and literacy is a matter of time. In *Nature Reviews Neuroscience*, 5(9), 721-728. https://doi.org/10.1038/nrn1499

Tallon-Baudry, C., Bertrand, O., Peronnet, F., & Pernier, J. (1998). Induced γ-band activity during the delay of a visual short-term memory task in humans. *Journal of Neuroscience*, 18(11), 4244-4254. https://doi.org/10.1523/jneurosci.18-11-04244.1998

Tam, I. O. L., & Leung, C. (2019). Evaluation of the effectiveness of a literacy intervention programme on enhancing learning outcomes for secondary students with dyslexia in Hong Kong. *Dyslexia*, 25(3), 296-317. https://doi.org/10.1002/dys.1626

Tan, L. H., Liu, H. L., Perfetti, C. A., Spinks, J. A., Fox, P. T., & Gao, J. H. (2001). The neural system underlying Chinese logograph reading. *NeuroImage*, 13(5), 836-846. https://doi.org/10.1006/nimg.2001.0749

Tarar, J. M., Meisinger, E. B., & Dickens, R. H. (2015). Test Review: Test of Word Reading Efficiency–Second Edition (TOWRE-2) by Torgesen, J. K., Wagner, R. K., & Rashotte, C. A. . *Canadian Journal of School Psychology*. https://doi.org/10.1177/0829573515594334

Temple, E., Deutsch, G. K., Poldrack, R. A., Miller, S. L., Tallal, P., Merzenich, M. M., & Gabrieli, J. D. E. (2003). Neural deficits in children with dyslexia ameliorated by behavioral remediation: Evidence from functional MRI. *Proceedings of the National Academy of Sciences of the United States of America, 100(5), 2860-2865.*

https://doi.org/10.1073/pnas.0030098100

Temple, E., Poldrack, R. A., Salidis, J., Deutsch, G. K., Tallal, P., Merzenich, M. M., & Gabrieli, J. D. E. (2001). Disrupted neural responses to phonological and orthographic processing in dyslexic children: An fMRI study. *NeuroReport*, 12(2), 299-307. https://doi.org/10.1097/00001756-200102120-00024

Thatcher, R. W., North, D., & Biver, C. (2005). Evaluation and Validity of a LORETA Normative EEG Database. *Clinical EEG and Neuroscience*, 36(2), 116-122. https://doi.org/10.1177/155005940503600211

Thatcher, Robert W. (2010). Validity and reliability of quantitative electroencephalography. *Journal of Neurotherapy*, 14(2), 122-152. https://doi.org/10.1080/10874201003773500

Thatcher, Robert W., Biver, C. J., & North, D. M. (2015). Brainsurfer and Brain Computer Interface Z-Score Biofeedback. In *Z Score Neurofeedback: Clinical Applications*, 325-331. https://doi.org/10.1016/B978-0-12-801291-8.00013-3

Thatcher, Robert W., Walker, R. A., Biver, C. J., North, D. N., & Curtin, R. (2003). Quantitative EEG normative databases: Validation and clinical correlation. *Journal of Neurotherapy, 7(3-4), 87-121.* https://doi.org/10.1300/J184v07n03_05

Thut, G., Nietzel, A., Brandt, S. A., & Pascual-Leone, A. (2006). α-Band electroencephalographic activity over occipital cortex indexes visuospatial attention bias and predicts visual target detection. *Journal of Neuroscience, 26(37), 9494-9502.* https://doi.org/10.1523/JNEUROSCI.0875-06.2006

Toga, A. W., & Thompson, P. M. (2003). Mapping brain asymmetry. *Nature Reviews Neuroscience*, 4(1), 37-48. https://doi.org/10.1038/nrn1009

Torgesen, J. K., Wagner, R., & Rashotte, C. (2011). TOWRE 2: Test of word reading efficiency. In *Test of word reading efficiency*.

Torppa, M., Lyytinen, P., Erskine, J., Eklund, K., & Lyytinen, H. (2010). Language development, literacy skills, and predictive connections to reading in finnish children with and without familial risk for dyslexia. *Journal of Learning Disabilities*, 43(4), 308-321. https://doi.org/10.1177/0022219410369096

Treisman, A. M., & Gelade, G. (1980). A feature-integration theory of attention. *Cognitive Psychology*, 12(1), 97-136. https://doi.org/10.1016/0010-0285(80)90005-5

Vahabzadeh, A., & McDougle, C. J. (2014). Obsessive-Compulsive Disorder. In *Pathobiology of Human Disease: A Dynamic Encyclopedia of Disease Mechanisms*. https://doi.org/10.1016/B978-0-12-386456-7.05213-8

Van Atteveldt, N., Formisano, E., Goebel, R., & Blomert, L. (2004). Integration of letters and speech sounds in the human brain. *Neuron, 43(2), 271-282.* https://doi.org/10.1016/j.neuron.2004.06.025

Van de Vijver, I., Cohen, M. X., & Ridderinkhof, K. R. (2014). Aging affects medial but not anterior frontal learning-related theta oscillations. *Neurobiology of Aging, 35(3), 692-704.* https://doi.org/10.1016/j.neurobiolaging.2013.09.006

van der Kleij, S. W., Groen, M. A., Segers, E., & Verhoeven, L. (2019). Sequential Implicit Learning Ability Predicts Growth in Reading Skills in Typical Readers and Children with Dyslexia. *Scientific Studies of Reading*, 23(1), 77-88. https://doi.org/10.1080/10888438.2018.1491582

Van Doren, J., Arns, M., Heinrich, H., Vollebregt, M. A., Strehl, U., & K. Loo, S. (2019). Sustained effects of neurofeedback in ADHD: a systematic review and meta-analysis. In *European Child and Adolescent Psychiatry*, 28(3), 293-305. https://doi.org/10.1007/s00787-018-1121-4

Van Ermingen-Marbach, M., Grande, M., Pape-Neumann, J., Sass, K., & Heim, S. (2013). Distinct neural signatures of cognitive subtypes of dyslexia with and without

phonological deficits. *NeuroImage: Clinical*, 2, 477-490. https://doi.org/10.1016/j.nicl.2013.03.010

van Oers, C. A. M. M., Goldberg, N., Fiorin, G., van den Heuvel, M. P., Kappelle, L. J., & Wijnen, F. N. K. (2018). No evidence for cerebellar abnormality in adults with developmental dyslexia. *Experimental Brain Research*, 236(11), 2991-3001. https://doi.org/10.1007/s00221-018-5351-y

van Viersen, S., de Bree, E. H., Verdam, M., Krikhaar, E., Maassen, B., van der Leij, A., & de Jong, P. F. (2017). Delayed early vocabulary development in children at family risk of Dyslexia. *Journal of Speech, Language, and Hearing Research*, 60(4), 937-949. https://doi.org/10.1044/2016_JSLHR-L-16-0031

Vandermosten, M., Boets, B., Poelmans, H., Sunaert, S., Wouters, J., & Ghesquière, P. (2012). A tractography study in dyslexia: Neuroanatomic correlates of orthographic, phonological and speech processing. *Brain, 135(3), 935-948.* https://doi.org/10.1093/brain/awr363

Varvara, P., Varuzza, C., Sorrentino, A. C. P., Vicari, S., & Menghini, D. (2014). Executive functions in developmental dyslexia. *Frontiers in Human Neuroscience*, 8, 120. https://doi.org/10.3389/fnhum.2014.00120

Vaughn, S., & Fletcher, J. M. (2010). Thoughts on rethinking response to intervention with secondary students. In *School Psychology Review*, 39(2), 296-299.

Vellutino, F. R., Fletcher, J. M., Snowling, M. J., & Scanlon, D. M. (2004). Specific reading disability (dyslexia): What have we learned in the past four decades? In *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 45(1), 2-40. https://doi.org/10.1046/j.0021-9630.2003.00305.x

Vellutino, F. R., Scanlon, D. M., Small, S., & Fanuele, D. P. (2006). Response to intervention as a vehicle for distinguishing between children with and without reading

disabilities: Evidence for the role of kindergarten and first-grade interventions. In *Journal of Learning Disabilities*, 39(2), 157-169. https://doi.org/10.1177/00222194060390020401

Vidyasagar, T. R., & Pammer, K. (2010). Letter-order encoding is both bottom-up and top-down: Response to Whitney. In *Trends in Cognitive Sciences*, 6(14), 238-239. https://doi.org/10.1016/j.tics.2010.03.008

Vijayan, S., Ching, S. N., Purdon, P. L., Brown, E. N., & Kopell, N. J. (2013). Thalamocortical mechanisms for the anteriorization of alpha rhythms during propofol-induced unconsciousness. *Journal of Neuroscience*, 33(27), 11070-11075. https://doi.org/10.1523/JNEUROSCI.5670-12.2013

Vinckier, F., Dehaene, S., Jobert, A., Dubus, J. P., Sigman, M., & Cohen, L. (2007). Hierarchical Coding of Letter Strings in the Ventral Stream: Dissecting the Inner Organization of the Visual Word-Form System. *Neuron*, 55(1), 143-156. https://doi.org/10.1016/j.neuron.2007.05.031

Vingerhoets, G., de Lange, F. P., Vandemaele, P., & Deblaere, A. E. (2002). Motor imagery in mental rotation: an FMRI study. *Neuroimage*, 17.

Vuilleumier, P., Armony, J. L., Driver, J., & Dolan, R. J. (2001). Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. *Neuron*, 30(3), 829-841.

Wagner, R. F. (1973). 5. Rudolf berlin: Originator of the term dyslexia. *Bulletin of the Orton Society*, 23(1), 57-63. https://doi.org/10.1007/BF02653841

Walker, J. E., & Norman, C. A. (2006). The neurophysiology of dyslexia: A selective review with implications for neurofeedback remediation and results of treatment in twelve consecutive patients. In *Journal of Neurotherapy*, 10(1), 45-55. https://doi.org/10.1300/J184v10n01_04

Wang, L. C. (2017). Effects of phonological training on the reading and reading-related abilities of Hong Kong children with dyslexia. *Frontiers in Psychology*, 8, 1904. https://doi.org/10.3389/fpsyg.2017.01904

Wang, Y., Mauer, M. V., Raney, T., Peysakhovich, B., Becker, B. L. C., Sliva, D. D., & Gaab, N. (2017). Development of tract-specific white matter pathways during early reading development in at-risk children and typical controls. *Cerebral Cortex*, 27(4), 2469-2485. https://doi.org/10.1093/cercor/bhw095

Wanzek, J., & Vaughn, S. (2007). Research-based implications from extensive early reading interventions. *School Psychology Review*.

Warrington, E. K., & Shallice, T. (1980). Word-form dyslexia. *Brain*, 103(1), 99-112. https://doi.org/10.1093/brain/103.1.99

Weiner, K. S., & Zilles, K. (2016). The anatomical and functional specialization of the fusiform gyrus. *Neuropsychologia*, 83, 48-62. https://doi.org/10.1016/j.neuropsychologia.2015.06.033

Welch, P. D. (1967). The Use of Fast Fourier Transform for the Estimation of Power Spectra: A Method Based on Time Averaging Over Short, Modified Periodograms. *IEEE Transactions on Audio and Electroacoustics*, 15(2), 70-73. https://doi.org/10.1109/TAU.1967.1161901

Welsh, M. C., Pennington, B. F., & Groisser, D. B. (1991). A Normative-Developmental Study of Executive Function: A Window on Prefrontal Function in Children. *Developmental Neuropsychology*, 7(2), 131-149. https://doi.org/10.1080/87565649109540483

Wheldall, K., & Arakelian, S. (2016). Comparing the performance of older low-progress readers on the York Assessment of Reading for Comprehension with performance on the Neale Analysis of Reading Ability and other measures of reading and related

skills. *Australian Journal of Learning Difficulties*, 21(2), 157-166. https://doi.org/10.1080/19404158.2017.1322993

Wilson, A. M., Deri Armstrong, C., Furrie, A., & Walcot, E. (2009). The mental health of canadians with self-reported learning disabilities. *Journal of Learning Disabilities*, 42(1), 24-40. https://doi.org/10.1177/0022219408326216

Wimmer, H., Schurz, M., Sturm, D., Richlan, F., Klackl, J., Kronbichler, M., & Ladurner, G. (2010). A dual-route perspective on poor reading in a regular orthography: An fMRI study. *Cortex*, 46(10), 1284-1298. https://doi.org/10.1016/j.cortex.2010.06.004

Worden, M. S., Foxe, J. J., Wang, N., & Simpson, G. V. (2000). Anticipatory biasing of visuospatial attention indexed by retinotopically specific alpha-band electroencephalography increases over occipital cortex. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 20(6), RC63-RC63. https://doi.org/10.1523/JNEUROSCI.20-06-j0002.2000

Wöstmann, M., Waschke, L., & Obleser, J. (2019). Prestimulus neural alpha power predicts confidence in discriminating identical auditory stimuli. *European Journal of Neuroscience*, 49(1), 94-105.

Wu, Y.J., Yang, W.H., Wang, Q.X., Yang, S., Hu, X.Y., Jing, J., Li, X.H. (2018). Eye-movement Patterns of Chinese Children with Developmental Dyslexia during the Stroop Test. *Biomed Environ Sci*., 31(9):677–85. doi:10.3967/bes2018.092.

Xia, Z., Hoeft, F., Zhang, L., & Shu, H. (2016). Neuroanatomical anomalies of dyslexia: Disambiguating the effects of disorder, performance, and maturation. *Neuropsychologia*, 81, 68-78. https://doi.org/10.1016/j.neuropsychologia.2015.12.003

Xu, B. (2001). Conjoint and Extended Neural Networks for the Computation of Speech Codes: The Neural Basis of Selective Impairment in Reading Words and

Pseudowords. *Cerebral Cortex*, 11(3), 267-277. https://doi.org/10.1093/cercor/11.3.267

Xu, W., Kolozsvari, O. B., Monto, S. P., & Hämäläinen, J. A. (2018). Brain Responses to Letters and Speech Sounds and Their Correlations With Cognitive Skills Related to Reading in Children. *Frontiers in Human Neuroscience*, 12, 304. https://doi.org/10.3389/fnhum.2018.00304

Yampolsky, S., & Waters, G. (2002). Treatment of single word oral reading in an individual with deep dyslexia. *Aphasiology*, 16(4-6), 455-471. https://doi.org/10.1080/02687030244000068

Yaple, Z., Martinez-Saito, M., Novikov, N., Altukhov, D., Shestakova, A., & Klucharev, V. (2018). Power of Feedback-Induced Beta Oscillations Reflect Omission of Rewards: Evidence From an EEG Gambling Study. *Frontiers in Neuroscience*, 12, 776. https://doi.org/10.3389/fnins.2018.00776

Ye, Z., & Zhou, X. (2009). Executive control in language processing. In *Neuroscience and Biobehavioral Reviews*, 33(8), 1168-1177. https://doi.org/10.1016/j.neubiorev.2009.03.003

Zakharov, I., Tabueva, A., Adamovich, T., Kovas, Y., & Malykh, S. (2020). Alpha Band Resting-State EEG Connectivity Is Associated With Non-verbal Intelligence. *Frontiers in Human Neuroscience*, 14, 10. https://doi.org/10.3389/fnhum.2020.00010

Zhang, Yajing, Zhang, L., Shu, H., Xi, J., Wu, H., Zhang, Y., & Li, P. (2012). Universality of categorical perception deficit in developmental dyslexia: An investigation of Mandarin Chinese tones. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, 53(8), 874-882. https://doi.org/10.1111/j.1469-7610.2012.02528.x

Zhang, Ying, Whitfield-Gabrieli, S., Christodoulou, J. A., & Gabrieli, J. D. E. (2013).

Atypical Balance between Occipital and Fronto-Parietal Activation for Visual Shape Extraction in Dyslexia. *PLoS ONE, 8(6), e67331.* https://doi.org/10.1371/journal.pone.0067331

Zhou, W., Xia, Z., Bi, Y., & Shu, H. (2015). Altered connectivity of the dorsal and ventral visual regions in dyslexic children: A resting-state fMRI study. *Frontiers in Human Neuroscience*, 9, 495. https://doi.org/10.3389/fnhum.2015.00495

Ziegler, J. C., & Goswami, U. (2005a). Reading acquisition, developmental dyslexia, and skilled reading across languages: A psycholinguistic grain size theory. In *Psychological Bulletin*, 131(1), 3. https://doi.org/10.1037/0033-2909.131.1.3

Ziegler, J. C., & Goswami, U. (2005b). Reading acquisition, developmental dyslexia, and skilled reading across languages: A psycholinguistic grain size theory. In *Psychological Bulletin*, 131(1), 3. https://doi.org/10.1037/0033-2909.131.1.3

Zinchenko, A., Conci, M., Taylor, P. C. J., Müller, H. J., & Geyer, T. (2018). Taking attention out of context: Frontopolar transcranial magnetic stimulation abolishes the formation of new context memories in visual search. *Journal of Cognitive Neuroscience*, 31(3), 442-452. https://doi.org/10.1162/jocn_a_01358

Appendix A

Email title: Seeking volunteers to trial a new treatment approach for Dyslexia

Dear SPELD member,

Brain Health Clinics, in conjunction with Flinders University of South Australia, is seeking 60 volunteers to participate in an open label study that will be testing the effectiveness of Neurotherapy as a treatment for Dyslexia.

A series of treatment sessions (up to 45 minutes per session) will be conducted at Brain Health Clinics over a 3-4 month period. Treatment will be individualized to each patient based on an assessment of brain function. Information sessions will be held at the Specific Learning Difficulties Association of South Australia (SPELD) in September 2012.

The study is open to individuals (aged 7 - 15 years) who have received a primary diagnosis of Dyslexia and who pass a number of related screening criteria. The study has been approved by Southern Adelaide Clinical Human Research Ethics Committee.

If you would like to express interest in this study, please contact Robbie, Practice Manager at Brain Health Clinics on **8410 6500** (Mon, Tues & Fri. 8am – 6pm). Alternatively, you can express your interest via email: admin@brainhealth.com.au, and Robbie will be in touch regarding an information session.

Thank you for your time and consideration.

Yours sincerely,

Prof. Richard Clark & Dr. Tim Hill
Brain Health Clinics
86-87 South Terrace, Adelaide, SA 5000

Appendix B

SCREENING QUESTIONNAIRE

Investigating the Efficacy of Neurotherapy as a Treatment for Dyslexia.

PARTICIPANT NAME:_____ *(Last, First)*	☐ M ☐ F	**DOB:** _ /___ /__	**School Grade:**_____
COUNTRY OF BIRTH: _____			

MEDICAL HISTORY

MEDICAL CONDITIONS (Please tick all boxes that apply)	☐ Epilepsy ☐ Traumatic Brain Injury ☐ Chronic Ill Health ☐ Mood disorder (e.g. Major Depression, Anxiety) ☐ Vision impairment ☐ Hearing impairment ☐ Childhood Schizophrenia ☐ Motor-coordination difficulties ☐ Family history of genetic disorder ☐ Family history of Mood Disorders ☐ Other serious medical condition Please specify _____	
	How many sick days on average does your child has off school each school year? _____ (please estimate)	
FORMAL DIAGNOSIS	Dyslexia (also known as Specific Reading Disability) Yes ☐ No ☐	
IS DYSLEXIA THE PRIMARY DIAGNOSIS?	Yes ☐ No ☐	
SOURCE OF DIAGNOSIS (please tick all boxes that apply)	General Practitioner (GP) Educational Psychologist Classroom Teacher SPELD Tutor Other	Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Please detail: _____

OTHER DIAGNOSES	Autistic Spectrum Disorders Language Disorder Dysphasia/Aphasia ADHD Dyspraxia Dysgraphia Other	Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐ Please detail: _____

TREATMENT FOR DYSLEXIA		
CURRENT TREATMENT (please tick all boxes that apply)	**1) Phonic-Based Intervention (such as "Jolly Phonics")** Hours per week: _____ **2) Extra tuition at school** Hours per week: _____ **3) Extra tuition at home** Hours per week:_____ **4) Other** Please detail: _____	Yes ☐ No ☐ Yes ☐ No ☐ Yes ☐ No ☐
PREVIOUS TREATMENT for dyslexia	Please detail (type, duration, and outcome):_____ _____ _____	
CURRENT MEDICATIONS (please list)	_____ _____ _____ _____	

Form completed by:_____ Date:_____
(Parent/Guardian)

Form reviewed by: _____ Date:_____

Appendix C

CONSENT BY A THIRD PARTY TO PARTICIPATION IN RESEARCH

I,.....give consent to .....
(first or given names) (last name)
.....'s involvement in the research project:
(first or given names)(last name)

"Investigating the Efficacy of Neurotherapy as a Treatment for Dyslexia."

I acknowledge the nature, purpose and contemplated effects of the research project, especially as far as they affect .....
(first or given names) (last name)

have been fully explained to my satisfaction by .....
(first or given names) (last name)

and my consent is given voluntarily.

I acknowledge that the details of the following have been explained to me, including indications of risks; any discomfort involved; anticipation of length of time; and the frequency with which they will be performed:

1. Psychological assessment procedures
2. Brain function assessment procedures
3. Treatment procedures
4. Locations at which procedures will take place
5. Aims of the project

I have understood and am satisfied with the explanations that I have been given.

I have been provided with a written information sheet.

I understand that .....'s involvement in this research
(first or given names) (last name)

project may not be of any direct benefit to him/her and that I may withdraw my consent at any stage without affecting his/her rights or the responsibilities of the researchers in any respect.

I declare that I am over the age of 18 years.

I acknowledge that I have been informed that should he/she receive an injury as a result of taking part in this study, legal action may need to be taken to determine whether he/she should be paid.

Signature of parent, legal guardian or authorised person: ..... Date: .....

Relationship to subject: .....

I assent to taking part in this study

Signature of participant: ..... Date: .....

I, ... have described to .....
the research project and nature and effects of procedure(s) involved. In my opinion he/she understands the explanation and has freely given his/her consent.

Signature: ..... Date: .....

Status in Project:.....

Appendix D

PREPARATION INSTRUCTIONS

There are a number of preparations you must make for the day of your Neuropsychological Assessment. It is imperative that these instructions are followed in order for us to successfully record your brain function on the day.

HAIR
Please wash your hair and scalp with **shampoo** (but not conditioner) once the day before and **at least twice** on the morning of the appointment.
Allow sufficient time for your hair to fully dry, or dry using a hair-dryer
Please DO NOT use hair conditioner, gel, hair cream, hair spray, or foam mousse on the morning of the appointment. These substances can make brainwave recordings difficult.

CLOTHING
Please wear comfortable clothing, especially a top with a loose fitting neck (please do not wear polo neck sweaters or similar high-neck garments).

CAFFEINE
Please refrain from any caffeine containing products (e.g., coke, chocolate milk etc.) for **2 hours before** the assessment.

Appendix E

Brain Health CLINICS

Flinders UNIVERSITY

Clinic address: 86-87 South Tce, Adelaide, SA 5000
Postal address: PO Box 6121 Halifax St, Adelaide SA 5000
Phone: (08) 8410 6500 *Fax*: (08) 8410 6511
Email enquiries: admin@brainhealth.com.au

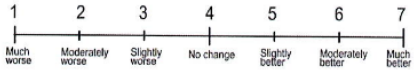
PARENT FEEDBACK

Please select one option for each area that best describes any changes to literacy skills and behaviour since receiving treatment at Brain Health Clinics. Please feel free to write any comments specific to your child to explain any changes you may have noticed. All responses will be treated confidentially. **Please circle the number that best represents your response.**

1. **Overall enjoyment for reading** - Has the amount that your child appears to enjoy reading changed at all compared to before they began the study?

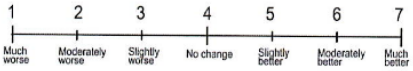
Comment:

2. **Willingness to practise reading** - Has your child's willingness to read, practise reading, practise spelling, etc. changed at all compared to before they began the study?



Comment:

3. **Choosing to read spontaneously** – Has your child's choice to read spontaneously (including reading signs out loud, or things presented on tv, or deciding to pick up a book or magazine) changed compared to before they began the study?



Comment:

4. **Self-esteem in relation to literacy tasks** – Has your child's confidence or belief in their capabilities in regards to their literacy skills (e.g spelling, reading comprehension, reading to themselves or out loud) changed compared to before they began the study?

Comment:

PLEASE TURN OVER 1

BrainHealth CLINICS
Clinic address: 86-87 South Tce, Adelaide, SA 5000
Postal address: PO Box 6121 Halifax St, Adelaide SA 5000
Phone: (08) 8410 6500 **Fax**: (08) 8410 6511
Email enquiries: admin@brainhealth.com.au

Flinders UNIVERSITY

PARENT FEEDBACK (continued)

5. **Expressive language skills –** Has your child's spontaneous use of words in speech changed at all since they began the study? For example using new vocabulary words in sentences etc .

Comment:

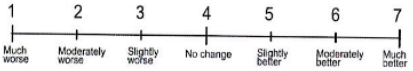
6. **Understanding verbal instructions** – Does your child appear to understand verbal instructions better since they began the study?

Comment:

7. **Pace of learning –** Do you find that your child is learning at a different rate than when they began the study? They may show this by needing to study words less or are becoming faster at completing homework etc.

Comment:

8. **Focus and attention for schoolwork –** Does your child find it easier to concentrate on their work? Do they appear to be finishing their homework faster or are better at staying on task?



Comment:

Thank you, please return this completed form back to us at PO BOX 6121 Halifax St Adelaide

*** A SELF ADRESSED, STAMPED ENVELOPE IS ENCLOSED ***

Name of Child: _____ **Name of Parent:** _____