Executive Function (EF) in Dyslexia: Examining an EF Profile Associated with Dyslexia and Comorbid Dyslexia-ADHD and Exploring the Near and Far Transfer Effects of EF Training in Dyslexia Alone

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A thesis presented to Dublin City University for the Degree of Doctor of Philosophy

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December 2017

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Declaration

I hereby certify that this material, which I now submit for assessment on the programme of study leading to the award of Doctor in Philosophy is entirely my own work, and that I have exercised reasonable care to ensure that the work is original, and does not to the best of my knowledge breach any law of copyright, and has not been taken from the work of others save and to the extent that such work has been cited and acknowledged within the text of my work.

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Acknowledgements

Firstly, I would like to thank my supervisor Dr Lorraine Boran, I am so grateful for her continued time, support, encouragement and guidance over the years. Without her none of this would be possible, her wisdom over the years has helped me to grow into an independent researcher and she has instilled in me an invaluable passion for cognitive neuroscience. I would also like to thank the rest of my supervisory panel, Dr Richard Roche, Professor Alan Smeaton and Dr Geraldine Scanlon who have assisted me with recruitment and EEG training. I am incredibly grateful to our collaborators at WIT and UCD, Dr David Delany for developing and monitoring the training intervention, and Dr Jessica Bramham for her advice on clinical assessments. I would also like to thank Aoife, Shane, Laura, Terry, Julia, Gemma, Sarah and Katie for their support with data collection. I am so grateful to Dyslexia Ireland, especially the CEO Rosie Bissett, for her continued support with recruiting participants for this PhD project.

I would like to thank my mother and father, and their partners Tony and Anne, for encouraging me every step along the way. Thank you to my siblings Caragh, Conor and Ciaran for reminding me to laugh and enjoy life, and, to all my friends, in particular Sara McQuinn, Lisa McGarrigle, and Paul O'Hara for their incredible support over the years.

Most importantly, a massive thank you to Paolo D'Ettorre for his patience, kindness, encouragement, and cuddles especially over the last few months. Your support has been incredible and I am so lucky to have you!

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Abstract

Executive Function in Dyslexia: Examining Profile Associated with Dyslexia and Comorbid Dyslexia-ADHD and Exploring the Near and Far Transfer Effects of Executive Function Training in Dyslexia Alone

– Caoilainn Doyle

Although there are several competing theories to explain dyslexia, no clear causal pathway has been established. Current theories also fail to address associated socio-emotional difficulties and high co-occurrence of dyslexia with ADHD. Executive function (EF), an umbrella term for a triad of high-level cognitive processes associated with pre-frontal brain regions – response inhibition (RI), working memory updating and switching, is a candidate factor for explaining the overlap between dyslexia and ADHD and co-occurring socio-emotional issues. EF appears to be a modifiable trans-diagnostic factor differentially implicated in neurodevelopmental conditions and therefore may offer novel routes for targeted interventions. Yet, it is unclear if EF is an overlapping impairment associated with dyslexia and comorbid dyslexia-ADHD, and which aspects of EF are important for explaining severity of reading and socio-emotional outcomes. Addressing methodological issues from previous EF profiling studies, this PhD aimed to (a) examine EF in both dyslexia conditions using Miyake's 3-factor model (inhibition-common EF, updating and switching – specific EFs) (study 1), (b) explore the ability of EF to predict dyslexia diagnosis and severity of symptoms expressed in core reading and non-core socio-emotional domains (study 1), and (c) explore the near (EF, brain activity) and far (reading, self-regulation, socio-emotional problems) transfer effects of low and high doses of targeted common EF (inhibition) training in dyslexia (study 2). Study 1 established that response inhibition (RI) and updating are overlapping transdiagnostic impairments associated with dyslexia and comorbid dyslexia-ADHD. Logistic and linear regression analyses suggest that RI and updating impairments are predictive of dyslexia diagnosis and core reading outcomes (study 1). The predictive role of RI in dyslexia diagnosis and severity of reading outcomes was further confirmed in a secondary sample (study 2). A 6-week RI targeted training intervention led to pre-post changes across both doses in RI (cognitive and neural levels), other EF abilities (updating and switching), reading ability, socio-emotional problems and self-regulation in dyslexia alone (study 2). However, no interaction effects were observed, making it difficult to determine if RI training transfer was achieved in both cases. Overall findings suggest, for the first time, that RI is an overlapping impairment in dyslexia and comorbid dyslexia-ADHD that is implicated in reading and socio-emotional issues. Nevertheless, further research with passive and active placebo groups is needed to determine whether RI training can transfer to improvements in RI, other EFs and associated issues in children with dyslexia.

Chapter 1: Overview of Thesis

1.1 Background

This PhD project is funded by a Dublin City University School of Nursing and Human Sciences, Faculty of Science and Health Postdoctoral Research grant awarded to Dr. Lorraine Boran. The PhD research project aims: (1) to profile executive function in dyslexia and comorbid dyslexia-ADHD (study 1), and (2) to examine the near and far transfer effects of targeted executive function training in dyslexia (study 2). The framework adopted for the PhD research project represents a paradigm shift within psychiatry, where developmental disorders such as dyslexia are characterised by a brain based approach to cognitive profiling, routed in neuroscience and genetics, rather than a Diagnostic and Statistical Manual (DSM)-derived symptom based approach, which arguably represents the manifestation of a dysfunctional developmental trajectory (Insel, 2013). Categorical symptom based approaches to complex neurodevelopmental conditions are limited insofar as they do not address how overlapping conditions such as dyslexia and ADHD are linked at the underlying neuro-cognitive levels (Bishop, 2006; Frith, 1999; Insel, 2013), and, therefore, limit the development of new treatments targeted at addressing underlying neuro-cognitive impairments (Insel, 2013). The US National Institute for Mental Health (NIMH) suggests that a good starting point should be understanding dysfunctional neurocognitive processes and from there building symptom level explanations (Cuthbert & Insel, 2013). Cognitive processes play a fundamental role in linking neural dysfunction to the behavioural symptoms of complex neuro-developmental disorders, therefore explanations pitched at the cognitive level can help isolate dysfunctional neural systems and may explain the range of symptoms associated with a particular developmental condition (Frith, 1999).

High co-occurrence between behaviourally distinct conditions such as dyslexia and ADHD is often indicative of shared neuro-cognitive underpinnings (Bishop, 2006; Glahn et al., 2014; Miller & Rockstroh, 2013). Executive function is one particular candidate neuro-cognitive ability thought to explain the often noted overlap between dyslexia and ADHD,

as it is a cognitive process rooted in dysfunctional neural circuits which may explain behaviours associated with a wide range of disorders manifesting in attentional and reading problems (Kegel & Bus, 2013; Rommelse et al., 2009). EF also offers novel routes for targeted intervention as it appears to be modifiable at neural and cognitive levels (Berkman, Kahn, & Merchant, 2014; Johnstone et al., 2012).

1.2 PhD Research Program

This PhD consisted of two large scale studies (Study 1 and Study 2) which focused on profiling EF, exploring the predictive utility of EF, and training EF. The first overall aim of this PhD was to examine the involvement of EF in developmental dyslexia (independent of comorbid ADHD diagnosis) by comparing EF performance in dyslexia and control groups aged 10-12 years (Study 1). A second aim was to establish if EF impairments were more severe for children with a dual diagnosis of dyslexia and ADHD (Study 1). A third aim was to determine if EF abilities can predict both diagnosis and severity of symptoms associated with dyslexia (Study 1).

An extensive examination of previous literature demonstrated that although EF is considered an important neurocognitive aspect of dyslexia, there is little consensus on which key aspects of EF – response inhibition (common EF), updating and switching- are implicated in the aetiology and/or symptom expression of dyslexia. Several issues have been identified as impeding progress in understanding the exact EF profile associated with dyslexia and whether it is useful for predicting diagnosis and symptom severity. These issues include discrepancies in (a) clinical group classification: studies differ greatly regarding criteria for dyslexia and screening of potentially undiagnosed ADHD from dyslexia alone samples, (b) theoretical approach to profiling and measuring executive abilities, (c) exploring how profile differs with disorder-specific informational content (i.e. phoneme content), and (d) controlling for low-level processing speed confounds.

Using Miyake and Friedman's (2012) framework of executive function which focuses on 3 core abilities- inhibition, updating and switching- and addressing the above stated problems with previous research, the specific objectives associated with the first three aims of this PhD were to:

(1) establish the EF profile (strengths and impairments in common: response inhibition, and unique: updating and switching abilities) associated with dyslexia and examine whether EF performance manifests more severely in comorbid dyslexia-ADHD using Miyake and Friedman's (2012) framework while controlling for individual differences in processing speed (study 1).

(2) Determine whether executive processing of disorder specific versus disorder neutral information (phoneme task content) impacts on the EF profile (study 1).

(3) Develop and validate EF predictive models of core and non-core symptoms associated with dyslexia alone while systemically screening for potentially undiagnosed ADHD, and, controlling for individual differences in processing speed (Study 1: development, and Study 2: validation)

The fourth aim of this PhD was to design and track the efficacy of an intervention to target EF implicated in core symptom expression in dyslexia, as identified in Study 1 and further confirmed in Study 2. This latter study also focused on exploring whether a computerised EF training intervention can improve the trained EF (RI), alter N2 and P3 response inhibition-related event related potentials (ERPs) (Study 2), and reduce symptom expression in children with dyslexia (Study 2). EF appears to be a modifiable cognitive factor with studies finding improvements in performance and brain activity after training (Benikos, Johnstone, & Roodenrys, 2013; Berkman et al., 2014; Manuel, Bernasconi, & Spierer, 2013); and training transfer effects to improved symptoms in some conditions such as ADHD (Johnstone et al., 2012). Previous research also suggests that common EF (response inhibition) is impaired in dyslexia and may be predictive of severity of symptoms expressed (Wang & Yang, 2014). Yet, no study to date has examined the efficacy of common EF (response inhibition) training for improving a range of outcomes in children with dyslexia. The specific objectives of the fourth aim of the PhD were to:

(4) Assess whether common EF training can directly improve common EF abilities and brain activity in dyslexia (study 2)

(5) Assess whether improvements in common EF as a function of training transfer to improvements in other EFs and symptom expression in dyslexia (study 2)

1.3 Summary of Research Thesis

The overall aims of the thesis were to develop and validate predictive models of EF for dyslexia and severity of symptoms, assess the modifiability of common EF training in dyslexia, and assess if common EF training translates to improvements at symptom level in dyslexia. These overall aims will be explored with two large scale studies (study 1 and study 2).

Chapter 2 reviews literature in relation to EF in dyslexia and outlines a range of issues which impede progress in understanding EF involvement in dyslexia and isolating which aspects of EF can be targeted in a training intervention for dyslexia. This chapter concludes with a summary of the specific objectives of the PhD.

Chapter 3 establishes the EF profile (response inhibition, updating and switching) associated with both dyslexia alone, and comorbid dyslexia-ADHD condition while systematically addressing issues within previous literature (Study 1).

Chapter 4 develops an EF predictive profile for dyslexia diagnosis, and severity of symptoms in core (reading) and non-core (socio-emotional) domains associated with dyslexia while systematically addressing issues within previous literature (Study 1).

Chapter 5 further confirms in a different sample (Study 2) an EF association and predictive role in dyslexia diagnosis, symptoms severity in core (reading) and non-core (socio-emotional) domains while systematically addressing issues within previous literature.

Chapter 6 addresses whether modifying dyslexia-related EF impairments, identified in Study 1 and confirmed in Study 2, can alter symptom expression. In Study 2 high and low-doses of a Go No-Go response inhibition training programme are compared in order to examine direct performance impact on response inhibition and its underlying neural processes.

Chapter 7 (Study 2) explores whether Go No-Go response inhibition training can also transfer to improvements in related EFs such as updating and switching, and reductions in symptoms such as reading ability, socio-emotional problems and self-regulatory problems in children with dyslexia.

Chapter 8 discusses the impact and importance of key findings from the PhD within the broader literature.

Chapter 2: Literature Review

2.0 Introduction

This thesis explores the role of executive function in dyslexia, its relationship with symptom expression and whether an executive function training intervention can improve executive function, brain activity, and symptom expression in children with dyslexia. This chapter will consider various categorical definitions of dyslexia (section 2.1), explore potential reasons for high co-occurrence of dyslexia with ADHD (section 2.2), critically evaluate major theories of dyslexia (section 2.2), and outline the argument for why EF should be viewed as a candidate explanatory factor of dyslexia (section 2.3- 2.4) that provides a framework for intervention solutions (section 2.5).

2.1 What is Dyslexia?

Dyslexia is a prevalent neurodevelopmental disorder observed in approximately 5-15% of school age children, and is characterised by significant difficulties achieving typical reading milestones through adequate instruction (American Psychiatric Association, 2013; American Psychiatric Association, 1994; World Health Organization, 1992). Reading difficulties are the core diagnostic feature of dyslexia, and are classified as such when intellectual ability, age, socio-economic status, and educational opportunities do not adequately explain the observed reading impairments (American Psychiatric Association, 2013; American Psychiatric Association, 1994; World Health Organization, 1992).

To receive a clinical diagnosis of dyslexia, reading accuracy (including omissions, substitutions, reversals), reading speed (slow, effortful), spelling and writing problems must persist for more than 6 months (despite intervention) and impact upon academic/occupational life (American Psychiatric Association, 2013; American Psychiatric Association, 1994; World Health Organization, 1992). These difficulties may also impact on social life, however this is not a core diagnostic criterion (American Psychiatric Association, 2013; American Psychiatric Association, 1994). Dyslexia assessments are typically conducted by a certified psychologist (clinical/educational) in line with the

Diagnostic and Statistical Manual or DSM (American Psychiatric Association, 2013; American Psychiatric Association, 1994) or the International Statistical Classification of Diseases and Related Health Problems or ICD diagnostic criteria (World Health Organization, 1992).

The DSM and ICD are criticised for adopting a categorical syndrome approach to diagnosis based on the presence of core disorder features alone (Cuthbert & Insel, 2013). A dimensional symptom based approach as proposed by the US National Institute for Mental Health (NIMH) may be more fruitful in understanding the causal mechanisms underpinning a broader range of behavioural features associated with a disorder (Cuthbert & Insel, 2013). Such an approach extends beyond core diagnostic features to non-core behavioural features, which although not required for a diagnosis of a disorder are frequently observed. Non-core behavioural features associated with dyslexia include social and emotional difficulties, which are frequently found in internalizing and externalizing behavioural domains (Dahle, Knivsberg, & Andreassen, 2011; Heiervang, Stevenson, Lund, & Hugdahl, 2001; Knivsberg & Andreassen, 2008; Mugnaini, Lassi, La Malfa, & Albertini, 2009). Although these non-core socio-emotional difficulties may be viewed as secondary to core reading problems, they may provide more insight into underlying dysfunctional mechanisms and novel pathways for targeted intervention (Cuthbert & Insel, 2013).

2.2 Co-Occurrence of Dyslexia with Attention Deficit Hyperactivity Disorder (ADHD)

Dyslexia co-occurs with Attention Deficit Hyperactivity Disorder (ADHD) at a greater than chance rate (American Psychiatric Association, 2013; Gilger, Pennington, & DeFries, 1992), with comorbidity estimated in 15-40% of cases (Willcutt & Pennington, 2000). After dyspraxia, ADHD is the highest co-occurring condition associated with a primary dyslexia diagnosis (Pauc, 2005). At the level of core symptoms, dyslexia and ADHD appear to be distinct neurodevelopmental disorders. Dyslexia is characterised by a difficulty in acquiring reading skills which significantly impacts social and academic functioning (American Psychiatric Association, 2013; American Psychiatric Association, 1994; World Health Organization, 1992), while ADHD is characterised by severe inattention and/or

hyperactivity which significantly impacts social and academic functioning (American Psychiatric Association, 2013; American Psychiatric Association Assoc, 1994; World Health Organization, 1992). However, high comorbidity rates between neurodevelopmental disorders is indicative of shared genetic, neural or cognitive underpinnings (Gottesman & Gould, 2003). Although both conditions are associated with distinct genetic, neural and cognitive underpinnings, commonality is also observed at each level (Germanò, Gagliano, & Curatolo, 2010). A pattern of more severe underlying cognitive impairments also manifests in the comorbid condition (Rucklidge & Tannock, 2002), which suggests that having a diagnosis of both conditions may enhance the severity of underlying impairments. Exploring underlying reasons for overlap, has the potential for enhancing the understanding of both distinct and shared risk factors at play.

Both dyslexia and ADHD are described and diagnosed at the symptom (behavioural phenotype) level. This categorical (behavioural) approach to diagnosis limits (a) the understanding of how both disorders are related at the neural, cognitive and genetic levels (Bishop, 2006; Frith, 1999; Insel, 2013), and (b) the development of new treatments to target neural and cognitive factors implicated in both disorders (Insel, 2013). The US NIMH has launched a new research criteria for enhancing the understanding of disorders by examining genetic, neural and cognitive factors implicated in symptoms associated with distinct and overlapping conditions (Cuthbert, 2014; Cuthbert & Insel, 2013; Insel, 2013). This research framework proposes multiple cognitive levels of examination rooted in dysfunctional neural circuits which can enhance the understanding of the range of behaviours associated with complex disorders (Cuthbert, 2014; Cuthbert & Insel, 2013; Insel, 2013). It is important to explore how these cognitive dimensions rooted in dysfunctional neural circuits relate to functional outcome at the behavioural level to progress in developing more precise avenues for diagnosis and treatment (Insel, 2013). The NIMH starting point for enquiry is exploring dysfunctional neurocognitive processes and from this building a symptom level explanation(Cuthbert & Insel, 2013).

Frith (1999) proposed a similar 3-level framework to enhance the understanding of causal underpinnings implicated in symptoms of dyslexia. The 3-level framework (*see Figure 1*) can be used to causally model biological, cognitive and environmental influences on

dyslexia, and also emphasised the importance of examining comorbidities (such as ADHD) to highlight the neural and cognitive factors which may be causally implicated. Frith (1999) explains how theories of dyslexia pitched at the biological level of explanation may have difficulty explaining distal behavioural signs as cognitive processes intervene. Cognitive processes play a fundamental role in linking neural dysfunction to the behavioural symptoms of a condition, therefore explanations pitched at the cognitive level can help pinpoint dysfunctional neural systems at the biological level and may explain the range of symptoms at the behavioural level (Frith, 1999). Although biological and cognitive factors may cause neurodevelopmental disorders, environmental influences may alter abilities at each level (Frith, 1999). Therefore, exploring intermediate cognitive processes rooted in dysfunctional neural systems has implications for refining causal explanations of disorders and pinpointing processes to target with interventions.

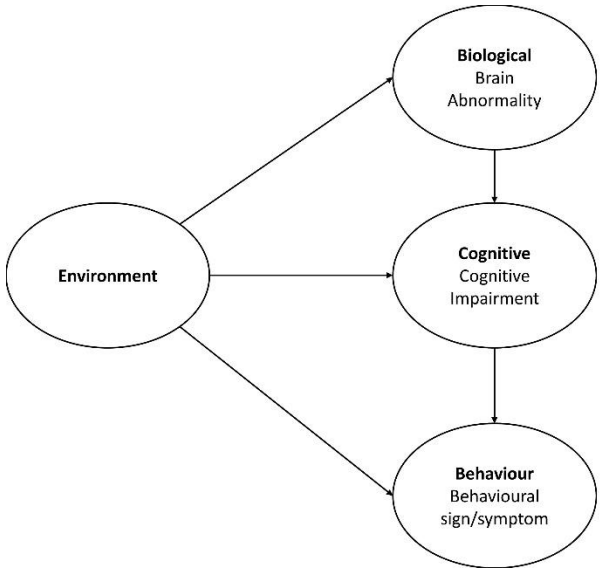


Figure 1 Frith's (1999) 3-level Causal Model for exploring the neurocognitive origins of Dyslexia

Examining candidate intermediate neuro-cognitive factors (also called endophenotypes) implicated in both neuro-developmental disorders may enhance the understanding of the gene-symptom pathway of dyslexia and ADHD and their cross-diagnostic relatedness (Bishop, 2006; Glahn et al., 2014; Miller & Rockstroh, 2013; Robbins, Gillan, Smith, de Wit, & Ersche, 2012). This highlights the need to move away from isolated behavioural level

explanations of dyslexia and ADHD, and an increased need to understand how cognitive processes rooted in shared dysfunctional neural systems may link both conditions. A move away from symptom level explanations of neuro-developmental disorders is necessary to make substantive progress in establishing etiological factors which may be targeted with intervention.

Both disorders are highly heritable, with higher rates of diagnosis in first degree relatives compared to the general population (American Psychiatric Association, 2013), suggesting potential genetic linkages. Indeed, comorbidity of dyslexia and ADHD has been linked at the genetic level via pleiotropic risk genes (related to multiple behavioural phenotypes) (Gayan et al., 2005) and genes crucial for the development of dopamine receptors in prefrontal brain areas necessary for the development of executive function (Kegel & Bus, 2013). However, understanding the gene-symptom relationship is quite complex as numerous factors can influence the phenotypic expression of a gene. To understand the gene-symptom relationship, researchers suggest looking at the intermediate factors – endophenotypes – which are also highly heritable and operate closer to the gene and phenotypic expression (Bishop, 2006; Gottesman & Gould, 2003). Endophenotypes can enhance the understanding of cross diagnostic categories e.g. comorbidity of dyslexia and ADHD, and aid in identifying potential risk factors for developing a psychological disorder (Bishop, 2006; Glahn et al., 2014; Miller & Rockstroh, 2013).

An important neuro-cognitive endophenotype for understanding comorbidity of dyslexia and ADHD is the EF brain system. EF is an umbrella term for a range of cognitive processes (including but not limited to) – response inhibition, updating and switching (Friedman & Miyake, 2016; Miyake et al., 2000; Miyake & Friedman, 2012) (see section 2.4 for a more comprehensive review of EF). EF abilities appear to be highly heritable (response inhibition- 96%, updating- 100%, switching-79%) and stable with similar heritability estimates manifesting across a 6-year period (Friedman et al., 2016). Given the strong genetic influence, EF has been proposed as a useful cognitive level endophenotype (intermediate in the gene-symptom pathway) for explaining a wide range of neuro-developmental and psychiatric disorders, for sensitively detecting prodromal phases and predicting severity of functional outcome (Glahn et al., 2014; Glahn, Knowles, & Pearlson,

2016; Miller & Rockstroh, 2013; Snyder, Miyake, & Hankin, 2015). EF is outlined in the NIMH research criteria as a cognitive level process rooted in dysfunctional neural circuits which may explain behaviours associated with a wide range of disorders (Cuthbert, 2014; Cuthbert & Insel, 2013). EF also appears to be implicated in ADHD at the endophenotype level (Castellanos & Tannock, 2002; Crosbie, Pérusse, Barr, & Schachar, 2008; Friedman et al., 2008; Rommelse et al., 2009), and may be a candidate endophenotype for understanding the high co-occurrence of attentional and reading problems (Kegel & Bus, 2013; Rommelse et al., 2009).

However, there is considerable disagreement within the literature as to whether EF is actually impaired in dyslexia, let alone if it is a cognitive endophenotype. There is a difficulty in understanding if and how EF is compromised in dyslexia, and how this impacts upon the manifestation of EF impairments in comorbid dyslexia-ADHD. Given the large degree of overlap between dyslexia and ADHD, a good theory of dyslexia should be able to explain high co-occurrence. An executive dysfunction framework may provide an explanation for why these disorders so frequently co-occur.

2.3 Theories of Dyslexia

The majority of theories of dyslexia explain the disorder as originating from low-level (balance, vision and auditory) as opposed to high-level (phonological) cognitive processes. Low-level cognitive processes refer to sensory mechanisms such as audition and vision, while high-level cognitive processes refer to more complex abilities such as intelligence, planning or language (Ktinig, Ktihnberger, & Kietzmann, 2013). Therefore, a theory of dyslexia can provide a low-level sensory explanation or a high-level cognitive explanation of core features of dyslexia.

Although there are several low-level competing theories to explain dyslexia, no clear causal pathway has been established and current theories fail to also address associated non-core problems in dyslexia (socio-emotional issues) and high co-occurrence of dyslexia with ADHD, which point to high-level cognitive processes such as EF playing a role.

The major low-level causal explanations of dyslexia include: (a) a cerebellar dysfunction which results in implicit learning and motor difficulties which impact the automatization of skills crucial for reading and spelling further upstream (Fawcett, Nicolson, & Dean, 1996; Nicolson & Fawcett, 1990; Nicolson, Fawcett, & Dean, 2001); (b) a magnocellular dysfunction which results in low-level sensory deficits which impact binocular control and phonological processing necessary for reading abilities further upstream (Livingstone, Rosen, Drislane, & Galaburda, 1991; Stein & Walsh, 1997; Stein, 2001); and (c) a temporal auditory processing deficit which impacts the development of phonological skills which are necessary for the development of reading abilities further upstream (Farmer & Klein, 1995; Tallal & Benasich, 2002; Tallal & Gaab, 2006). The major high-level cognitive causal explanation of dyslexia is a phonological deficit which manifests due to abnormalities in left hemisphere brain regions which impact reading abilities further upstream (Snowling, 1998; Snowling & Hulme, 1994; Snowling, 2001; Wagner & Torgesen, 1987). Although these theories of dyslexia propose exclusive causes, a hypothesis emerging from an attempt to understand overlap between dyslexia and ADHD suggests that each condition arises from multiple deficits which can be distinct and shared (Pennington, 2006).

Each single causal theory of dyslexia is faced with gaps in linking speculated cause to core symptoms of dyslexia (reading impairment), and different levels of evidence from each theory are confounded by high-level cognitive processes such as executive function, attention and working memory and pre-frontal implication in task performance (see Table 1). For instance, implicit learning and motor difficulties are a line of evidence supporting the cerebellar deficit theory, but we know that inattention modulates task performance (Jiang & Chun, 2001; Jiménez & Méndez, 1999), working memory brain networks may be implicated in implicit learning measures (Yang & Li, 2012) and EF may play a role in motor abilities such as balance (Reilly, van Donkelaar, Saavedra, & Woollacott, 2008; Yogev-Seligmann, Hausdorff, & Giladi, 2008). Similarly, low-level sensory processing and binocular fixation difficulties are a line of evidence to support the magnocellular theory, yet inattention can influence performance on low-level magnocellular measures (Stuart, McAnally, & Castles, 2001) and those with poor binocular fixation also demonstrate EF impairments (Daniel & Kapoula, 2016). In addition, phonological difficulties are a line of

evidence to support the phonological theory, yet these impairments appear to only manifest when measures tax working memory and EF systems (Ramus & Szenkovits, 2008) and neural studies suggest that top down attentional control areas are recruited during phonological measures (Richlan, 2012). Difficulties in detecting transients in rapidly changing auditory information is a line of evidence used to support the temporal auditory processing theory, yet again attention modulates task performance here (Brown, Schneider, & Lidsky, 1997) and measures tap the working memory system (Temple et al., 2003). In effect, EF abilities may modulate or account for evidence used to support the major causal explanations of dyslexia.

Overall, cerebellar, magnocellular, phonological and temporal auditory processing explanations of dyslexia are limited, insofar as they cannot account for the influence of high-level cognitive processes (such as attention, working memory and EF) on task performance. These explanations also cannot effectively explain why dyslexia is so highly comorbid with ADHD – a disorder characterised by attention, working memory and EF – (Barkley, 1997). Moreover, these low-level explanations cannot explain non-core impairments (socio-emotional) associated with dyslexia. Yet, EF appears to be a necessary pre-requisite for socio-emotional wellbeing (Diamond, 2013). A difficulty in looking at complex neurodevelopmental disorders such as dyslexia in isolation, is that rarely are disruptions in complex human behaviours such as reading ability observed in isolation as they typically co-occur with disruptions to other complex behaviours. High comorbidity rates between behaviourally distinct disorders is often indicative of shared underlying neural, cognitive and genetic risk factors (Gottesman & Gould, 2003; Rommelse et al., 2009). Yet the major theories of dyslexia fail to highlight why dyslexia frequently co-occurs with ADHD.

Examining candidate endophenotypes - such as EF- can enhance the understanding of causal and risk factors associated with the disorder in question, including cross-diagnostic categories e.g. comorbidity with dyslexia and ADHD and functional outcome (Glahn et al., 2014, 2016; Miller & Rockstroh, 2013). This type of profiling or early detection approach also may have implications for the development of new targeted treatments. EF is a candidate endophenotype for ADHD (Castellanos & Tannock, 2002), and for self-

regulatory and socio-emotional behaviours (Friedman et al., 2008; Snyder et al., 2015) which may be non-core problems in dyslexia (Dahle et al., 2011; Heiervang et al., 2001; Knivsberg & Andreassen, 2008; Mugnaini et al., 2009). Although no study to date has explored EF as an endophenotype for dyslexia, Rommelse et al. (2009) found that EF is a candidate endophenotype for explaining overlap between ADHD and reading problems.

Indeed, executive function (EF) is a neuro-cognitive factor worthy of further investigation in relation to dyslexia and its co-occurrence with ADHD. Independent of ADHD, dyslexia alone is associated with EF impairments (Beneventi, Tønnessen, Ersland, & Hugdahl, 2010(b); Brosnan et al., 2002; Helland & Asbjørnsen, 2000; Poljac et al., 2010; Reiter, Tucha, & Lange, 2005; Rucklidge & Tannock, 2002), and, under-activation of frontal brain areas during EF tasks (Beneventi et al., 2010(a); Horowitz-Kraus, 2014; Liotti, Pliszka, Higgins, Perez, & Semrud-Clikeman, 2010; Van De Voorde, Roeyers, & Wiersema, 2010). EF is also predictive of core reading and non-core socio-emotional outcomes in dyslexia (Moura, Simões, & Pereira, 2015; Thompson & Schumann, 1987; Wang & Yang, 2014). EF appears to be a modifiable factor, with targeted interventions transferring to improvements in reading ability, ADHD symptoms and underlying brain activation (Berkman et al., 2014; Johnstone, Roodenrys, Phillips, Watt, & Mantz, 2010; Loosli, Buschkuehl, Perrig, & Jaeggi, 2012; Manuel et al., 2013). Therefore, EF may provide new avenues for targeted intervention in dyslexia.

Each of the four major theories of dyslexia introduced at the start of this section, and their limitations are outlined in sections 2.3.1 – 2.1.4.

2.3.1 The Cerebellar Deficit Theory

The cerebellar deficit theory argues that dyslexia is caused by abnormalities in the cerebellar lobes, particularly in the function of skill automatization (Nicolson et al., 2001). Here, the causal chain begins with structural abnormalities in the cerebellar lobes which result in implicit learning (the process by which skills become automatized) and motor ability impairments. Implicit learning impairment causes failures in automatizing skills such as grapheme-phoneme conversions which result in failures further upstream in reading and spelling ability; while motor impairments cause difficulty with fine motor

control such as required for writing (Nicolson et al., 2001) (*See Figure 2 for causal chain*).

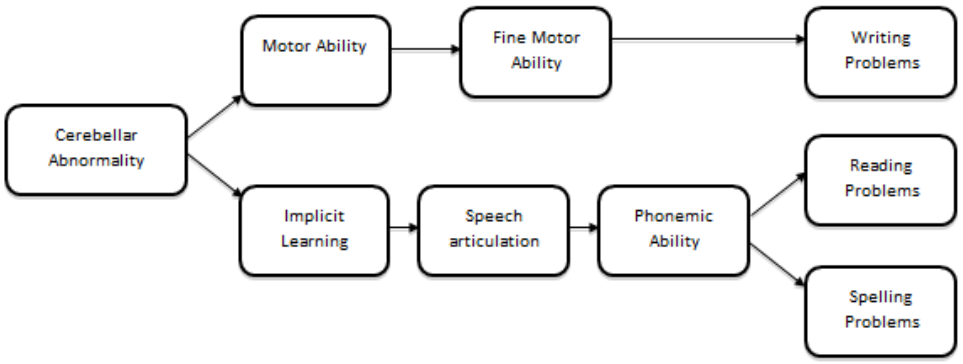


Figure 2 Nicolson et al.'s (2001) Causal cerebellar deficit theory of dyslexia

Behavioural Evidence for the Cerebellar Deficit theory

At the behavioural level, evidence of motor impairments in dyslexia are interpreted as support for the cerebellar deficit theory. A number of studies report motor impairments in dyslexia similar to those found in cerebellar lesion patients (Fawcett & Nicolson, 1999; Fawcett et al., 1996), and find reading impairments in cerebellar lesion patients similar to those found in dyslexia (Fabbro, Moretti, & Bava, 2000; Moretti, Bava, Torre, Antonello, & Cazzato, 2002)- suggesting cerebellar abnormalities may be central to dyslexia.

However, studies finding motor impairments in dyslexia do not demonstrate how motor impairments are causally linked to core reading impairments characteristic of dyslexia. There are also difficulties interpreting studies due to inherent methodological issues such as: (1) biased sample selection (motor impairments confirmed prior to participation) (Fawcett et al., 1996), (2) use of subjective motor impairment measures (Fawcett et al., 1996), (3) comparison groups recruited from distinctively heterogeneous groups (Fawcett & Nicolson, 1999), and, (4) not accounting for presence of comorbidities in the sample e.g. ADHD.

Studies employing more objective measures of motor abilities (Irannejad & Savage, 2012; Wimmer, Mayringer, & Landerl, 1998), screening for ADHD in the sample (Wimmer et al., 1998), and employing a homogenous sample (Irannejad & Savage, 2012), fail to find motor impairments in dyslexia. Additional cognitive factors (e.g. attention and executive function) also play a role in motor abilities such as gait, balance and posture stability (Reilly et al., 2008; Yogev-Seligmann et al., 2008). Given that participants with dyslexia also demonstrate executive function impairments (Reiter et al., 2005), it is difficult to isolate cerebellar abnormalities as the sole cause of motor problems if any are present.

Another behavioural level line of research used to support the cerebellar deficit theory is evidence of implicit learning impairments in dyslexia. Implicit learning impairments are associated with dyslexia (Stoodley, Harrison, & Stein, 2006; Vicari et al., 2005), and performance on implicit learning tasks is linked to language acquisition (grammar and vocabulary) (Conway, Bauernschmidt, Huang, & Pisoni, 2010; Conway, Karpicke, & Pisoni, 2007)- suggesting that the implicit learning function of the cerebellum may be implicated in language abilities (Conway et al., 2010, 2007).

However, inconsistent findings and issues within this research paradigm limit the interpretations and conclusions drawn. There is conflict as to whether implicit learning is impaired in dyslexia with both evidence for (Bennett, Romano, Howard Jr, & Howard, 2008; Howard, Howard, Japikse, & Eden, 2006; Stoodley et al., 2006; Vicari et al., 2005) and against implicit learning impairments (Rüsseler, Gerth, & Münte, 2006; Waber et al., 2003). Such inconsistent findings could be related to issues such as: (1) type of task employed and (2) underlying task demands tapping high-level cognitive factors.

Across the implicit learning literature a range of different tasks are employed and inferred to measure the same underlying construct, for example, serial reaction time tasks (higher order sequence learning), spatial contextual cueing tasks (spatial context learning) and artificial grammar learning tasks (statistical learning) are used to measure implicit sequence learning in dyslexia despite these tasks requiring different underlying brain areas to complete(Howard et al., 2006; Perruchet & Pacton, 2006). One study found that children with dyslexia are impaired on higher order sequence learning and not on spatial

context learning tasks (Howard et al., 2006), suggesting that these tasks are not tapping the same underlying construct. Indeed, higher order sequence tasks focus on the formation of chunks, while statistical learning tasks focus on statistical computations (Perruchet & Pacton, 2006).

Neural Evidence for the Cerebellar Deficit theory

At the neural level, there is evidence of cerebellar abnormalities in dyslexia, such as abnormalities in the right cerebellar lobe (Eckert et al., 2003) and biochemical differences indicative of lower cell density (Rae et al., 1998). Dyslexia also appears to be characterised by abnormal asymmetry of the cerebellar lobes (demonstrate reversed asymmetry or symmetry) (Kibby, Fancher, Markanen, & Hynd, 2008), however some individuals with dyslexia demonstrate normal asymmetry of the cerebellum and do not express symptoms associated with the cerebellar theory, indicating that this theory may not account for all instances of dyslexia.

At the functional neural level, it is difficult to understand the role of the cerebellar lobes in core reading impairments in dyslexia. During reading tasks, there is no activation differences in the cerebellar lobes in participants with dyslexia compared to those without (Maisog, Einbinder, Flowers, Turkeltaub, & Eden, 2008; Simos et al., 2000). Instead, reading ability in dyslexia is underpinned by reduced activation in posterior regions of the superior temporal gyrus, angular gyrus and supramarginal gyrus of the left hemisphere (Simos et al., 2000). A large scale meta-analysis of brain activity during reading in dyslexia suggests that reading impairments are underpinned by reduced activation in left hemisphere (precuneus, inferior temporal gyrus, fusiform gyrus, inferior parietal lobule, superior temporal gyrus, thalamus, inferior frontal gyrus) and right hemisphere (fusiform gyrus, post central gyrus and superior temporal gyrus) (Maisog et al., 2008). In participants without dyslexia a network of left hemisphere (supplementary motor area, fusiform gyrus, inferior temporal gyrus, inferior frontal gyrus, middle temporal gyrus, precentral gyrus, thalamus, inferior occipital gyrus, inferior and superior parietal gyrus) and right hemisphere (insula) areas are activated during reading tasks (Houdé, Rossi, Lubin, & Joliot, 2010). Although, there is evidence of structural anomalies in the cerebellum of individuals

with dyslexia, it is difficult to understand how cerebellar impairments are related to reading impairments in dyslexia.

High-level Cognitive Confounds of Evidence Supporting the Cerebellar Deficit Theory

A central assumption of the cerebellar deficit theory is that motor impairments should manifest in dyslexia, although there is inconsistent evidence of this; and high-level cognitive factors such as attention and EF also play a role in motor abilities such as gait, balance and postural stability (Reilly et al., 2008; Yogev-Seligmann et al., 2008). This makes it difficult to determine that motor impairments (if any present) in dyslexia are caused by cerebellar abnormality. Performance on implicit learning tasks is also modulated by high-level cognitive processes (e.g. attention) (Jiang & Chun, 2001; Jiménez & Méndez, 1999), which limits the ability to infer that impaired implicit learning in dyslexia is caused by cerebellar abnormalities. Performance on implicit learning tasks are predicted by sustained attention abilities (Waber et al., 2003), and DLPFC activity during implicit learning tasks suggestive that the working memory system is implicated in efficient performance (Yang & Li, 2012). Given that EF impairments have been found in dyslexia (Reiter et al., 2005), it is difficult to isolate cerebellar abnormalities as the underlying cause of motor or implicit learning difficulties in dyslexia.

Conclusion

Overall, there is insufficient evidence to confirm that a cerebellar impairment is central to dyslexia. When accounting for limitations in motor ability studies, there is no evidence or only partial evidence for motor problems in dyslexia and interpretation is further complicated by the role of high-level cognitive processes (executive function and attention) in motor abilities. It is also difficult to interpret the source of implicit learning impairments due to inconsistent evidence and task performance being modulated by high-level cognitive processes (e.g. attention). At the neural level, there is evidence for abnormal cerebellar lobes in dyslexia: However, the cerebellar lobes are not activated during reading tasks in dyslexia. This theory also fails to explain the influence of high-level cognitive abilities on the manifestation of dyslexia, and the reason for such high co-occurrences between dyslexia and ADHD.

2.3.2 The Magnocellular Deficit Theory

The magnocellular deficit theory argues that dyslexia is caused by low-level sensory processing impairments (Stein, 2001) due to abnormal magnocells in the brain (Livingstone et al., 1991). Magnocellular abnormalities cause problems detecting rapid transients in visual and auditory stimuli; and result in problems further upstream in visuo-motor control and binocular fixation (a difficulty in convergence/coordinating both eyes) through the rich connections between the magnocells in the lateral geniculate nucleus and the posterior parietal cortex (Stein & Walsh, 1997; Stein, 2001). Problems with visuo-motor control and binocular fixation are argued to cause reading impairments due to unsteady letter perception (smearing, movement of letters) (Stein, 2001). Abnormal magnocells are also thought to cause phonological impairments in dyslexia due to problems detecting transients in auditory stimuli which result in a difficulty acquiring the phonological skills necessary for reading (Stein, 2001) (*See Figure 3 for causal chain).*

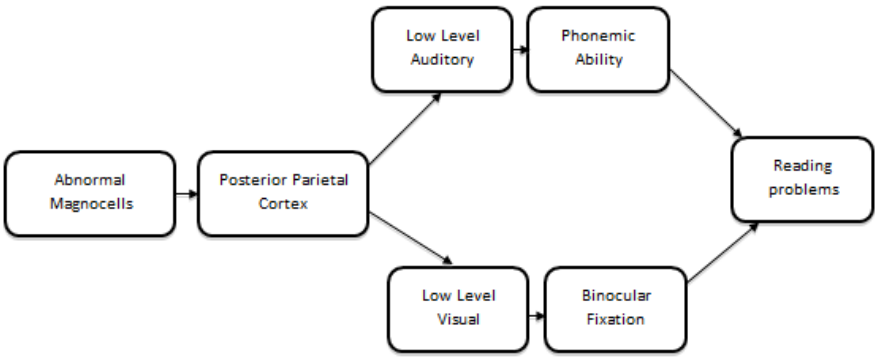


Figure 3 Stein's (2001) Causal magnocellular deficit theory of dyslexia

Behavioural Evidence for the Magnocellular Deficit Theory

At the behavioural level, the magnocellular visual system can be examined psychophysically due to its distinctive characteristics (low contrast, high frequency, low spatial resolution and low luminance) compared to the parvocellular visual system (high contrast, low frequency, high spatial resolution and high luminance) (Stein & Walsh,

1997). Psychophysical studies exploring magnocellular function in dyslexia find an impairment (Livingstone et al., 1991; Lovegrove, Bowling, Badcock, & Blackwood, 1980). Magnocellular impairments are also found to be associated with visuo-motor control and binocular fixation difficulties (Iles, Walsh, & Richardson, 2000).

However, there is difficulty in confirming a causal link between magnocellular impairments and dyslexia at a behavioural level due to: (1) phonological and reading problems occurring in the absence of magnocellular impairments, (2) magnocellular interventions improving reading yet not improving underlying magnocellular function, (3) magnocellular impairments occurring in other developmental disorders not characterised by reading problems, and (4) tasks demands tapping additional high-level cognitive abilities.

The magnocellular theory of dyslexia states that the high-level reading and phonological impairments in dyslexia are a result of low-level abnormalities in magnocellular function, yet a number of research studies find reading and phonological impairments in the absence of abnormal magnocellular function in dyslexia (Amitay, Ben-Yehudah, Banai, & Ahissar, 2002; Johannes, Kussmaul, Münte, & Mangun, 1996; Kronbichler, Hutzler, & Wimmer, 2002). Kronbichler et al. (2002) found phonological impairments in dyslexia but no underlying magnocellular deficit; while other studies have found reading, spelling and phonological impairments in dyslexia in the absence of magnocellular deficits (Amitay et al., 2002; Johannes et al., 1996), suggesting that magnocellular deficits are not at the core of dyslexia.

Interventions targeted at magnocellular impairments improve reading yet do not improve magnocellular function, again indicating that magnocellular impairments are not at the core of dyslexia. Tinted lens therapy improves reading speed by enhancing the magnocellular visual system and reducing associated visual stress (Wilkins et al., 1992), yet when comparing a tinted lens therapy group with a control group, no differences were found on magnocellular tasks (contrast sensitivity and flickering motion detection) (Simmers, Bex, Smith, & Wilkins, 2001).

Magnocellular impairments found in dyslexia appear to be present in several

developmental disorders which are not characterised by reading problems, suggesting that magnocellular impairments may be a non-specific biomarker of developmental disorders. Both dyslexia and autism are found to be impaired on magnocellular and sensorimotor tasks compared to controls (White et al., 2006a). This study also found that neither magnocellular or sensorimotor performance predicted reading ability within dyslexia and autism, or across the whole sample (White et al., 2006a). Another study found no differences between control and dyslexic participants on magnocellular tasks; and sensorimotor impairments found in a subgroup of dyslexia could not explain the phonological and reading impairments (White et al., 2006b). If a magnocellular deficit causes core reading impairments in dyslexia, then it should be predictive of reading problems in dyslexia. Furthermore, other groups with magnocellular impairments should express reading problems (White et al., 2006a). However, these studies have failed to find a predictive relationship between magnocellular impairments and reading difficulty and this suggests that these impairments are not a sufficient cause of core reading problems; instead, they suggest that sensorimotor impairments are not central to core issues in dyslexia and may be secondary in some but not all cases of dyslexia (White et al., 2006a). Consistent with this view, Dehaene et al. (2010) found that learning to read may contribute to the development of early stage visual processes, therefore sensory impairments may become associated with dyslexia as a secondary consequence of failing to acquire fluent reading skills.

Neural Evidence for the Magnocellular Deficit Theory

At the neural level, there is evidence of magnocellular abnormalities in dyslexia, with post-mortem examinations revealing abnormal symmetry of the planum temporale (related to auditory processing) (Galaburda, Sherman, Rosen, Aboitiz, & Geschwind, 1985) and smaller more disorganised magnocellular layers of the lateral geniculate nucleus (Livingstone et al., 1991) in the dyslexic brain. Abnormalities are not found in the parvo-cellular layers, suggesting that dyslexia is associated with abnormalities in low-level visual processing in visual area V1 only (Livingstone et al., 1991). Findings of abnormal magnocells in the planum temporale and lateral geniculate nucleus in dyslexia provide strong anatomical support for low-level sensory (auditory and visual) impairments

(Galaburda et al., 1985; Livingstone et al., 1991).

However, it is difficult to causally link magnocellular abnormalities to core reading impairments in dyslexia due to: (1) methodological issues relating to post-mortem examinations of the brain, and (2) magnocellular abnormalities being a consequence rather than a cause of poor reading ability.

Several confounding factors can lead to findings of symmetry in the planum temporale such as handedness (more common with left handedness), IQ (low IQ independent of dyslexia), and method of measurement (measuring planum temporale and/or the ramus) (Eckert & Leonard, 2000).Best and Demb (1999) examined the planum temporale in participants with dyslexia using a range of measurement methods and found leftward asymmetry inconsistent with the magnocellular theory.

Magnocellular impairments may also be a consequence rather than a cause of poor reading ability. Magnocellular activity correlates with reading ability, however the relationship may not be causal as illiterate participants demonstrate pre-post differences in the magnocellular layers after learning to read (Olulade, Napoliello, & Eden, 2013). Learning to read is also found to develop early stage visual processes and enhance the role of the planum temporale in phonological coding (Dehaene et al., 2010). Thus, it may be the acquisition of reading skills that enhances early visual skills, increases reliance on left hemisphere language networks and refines language processing in the planum temporale and not vice versa (Dehaene et al., 2010). These studies suggest a contrarian view that top down influence associated with learning to read results in enhanced development of the low-level visual system and the planum temporale.

High-level Cognitive Confounds of Evidence Supporting the Magnocellular Deficit Theory

A central assumption of the magnocellular deficit theory is that low-level visual/auditory processing impairments should manifest in dyslexia, although there is inconsistent evidence of this, the multiple task demands of magnocellular function tasks further complicate the role of the magnocellular system in dyslexia. High-level cognitive factors such as attention can influence performance on measures such as contrast sensitivity (e.g.

Stuart et al., 2001). The domain of tasks measuring magnocellular function such as alternative forced choice tasks require sufficient attentional capacities to detect contrast changes (Stuart et al., 2001). Magnocellular task performance is also correlated with performance on other temporal forced choice tasks (e.g. block design, digit symbol) suggesting that poor performance may also reflect working memory or sustained attention problems (Amitay et al., 2002). Binocular fixation difficulties have also been linked to poor executive abilities as measured with a Stroop task (task that varies colour word font and semantics for congruency e.g. the word RED in red ink, in order to tap into the ability to inhibit cognitive and behavioural impulses to read the word rather than focus on the font colour) , with the authors arguing that convergence should be viewed as a cognitive/attentional problem as opposed to a low-level visual problem (Daniel & Kapoula, 2016). Given that EF impairments have been found in dyslexia (Reiter et al., 2005), it is difficult to isolate magnocellular abnormalities as an underlying cause.

Conclusion

Overall it appears that magnocellular abnormalities are not causally related to dyslexia. Although magnocellular impairments are found in some cases of dyslexia, it would appear that phonological and reading impairments are often found in the absence of magnocellular impairments. Although interventions targeted at magnocellular impairments can improve reading ability, improvement appears to be supported by cognitive mechanisms and not directly by change in magnocellular function. Magnocellular impairments found in dyslexia are also found in autism in the absence of reading impairments suggesting that in general the magnocellular system does not facilitate reading ability. High-level cognitive factors may also play a role in the performance of tasks used to assess magnocellular function which complicates interpretation of results. Although there is structural evidence for magnocellular abnormalities, findings differ depending on measurement technique. Recent research also suggests that reading acquisition may enhance early visual processes, these findings are in contrast with the magnocellular theory which suggests that abnormal early visual processes cause reading impairment. The theory also does not propose any explanation for why dyslexia and ADHD so frequently co-occur. Considering this critical analysis, it

appears that magnocellular impairments may not be the central cause of dyslexia.

2.3.3 The Phonological Deficit Theory

The phonological deficit theory states that dyslexia is caused by a high-level phonological processing impairment (Snowling, 1998). This impairment can manifest as problems with: (1) phonological awareness (knowledge of the sound structure of language), (2) phonological recoding (converting letters into speech sounds), (3) holding speech sounds in working memory, (4) blending and segmenting different phonemes to sound out unfamiliar words, and (5) phonological representations in long term memory (Snowling, 1998; Snowling & Hulme, 1994; Snowling, 2001; Wagner & Torgesen, 1987). Such problems are argued to cause inefficient reading and spelling strategies (Wagner & Torgesen, 1987), and this is how a general phonological impairment is argued to cause the reading and spelling problems characteristic of dyslexia (*see Figure 4 for causal chain*).

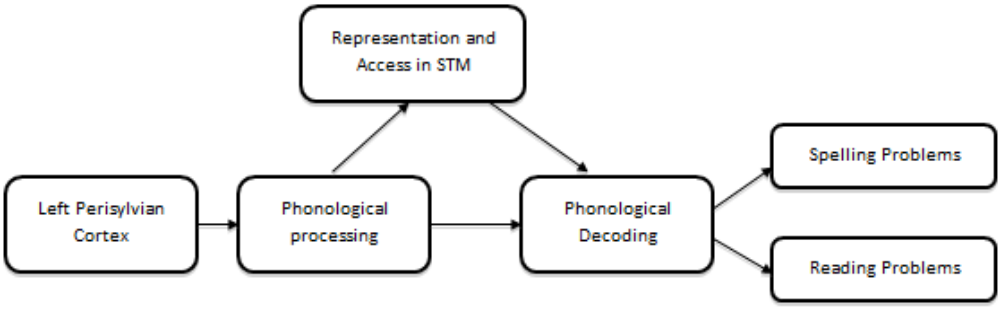


Figure 4 Snowling's (1998) Causal phonological deficit theory of dyslexia

Behavioural Evidence for the Phonological Deficit Theory

At the behavioural-level there is strong support for the phonological deficit theory due to: (1) phonological impairments observed in dyslexia, (2) phonological ability predicting future reading ability, and (3) phonological training improving reading ability.

Phonological impairments are consistently found in dyslexia (Katz, 1986; Swan & Goswami, 1997; Wimmer et al., 1998), and phonological awareness is found to be

predictive of future reading ability (Mann, 1984, 1993; Mann & Liberman, 1984); suggesting the phonological impairments may be at the core of dyslexia. Good readers demonstrate difficulties with phonetically confusable words compared to phonetically non-confusable words, whereas poor readers demonstrate no differences suggesting that poor readers do not employ phonological representations to aid in reading like non-impaired readers do (Mann, 1984). Phonological impairments also seem to be causally related to reading, as phoneme-based interventions result in reading and phonological improvements in children with and without dyslexia (Kozminsky & Kozminsky, 1995; Lovett et al., 1994).

Although there is strong evidence that phonological impairments are central to dyslexia, careful consideration is needed as: (1) the phonological theory is not able to account for different descriptive (i.e. not part of DSM diagnostic criteria) expressions of dyslexia (surface V phonological) while attentional abilities can, (2) lower level auditory processing appear to predict reading ability, and (3) other high-level cognitive processes (executive function) interfere with performance on phonological tasks.

One problem with the phonological deficit theory is that it cannot account for different expressions of dyslexia (surface and phonological dyslexia), whereas attentional impairments can (Facoetti et al., 2006; Valdois, Bosse, & Tainturier, 2004). Phonological dyslexia is characterised by phonological impairments, whereas surface dyslexia is not. When compared with surface dyslexia and a control group, phonological dyslexia is associated with a lack of attentional inhibition in the right visual field when instructed to attend to left (Facoetti et al., 2006), suggesting that attention may play a role in phonological reading. Both phonological and attentional impairments demonstrate independent predictive ability for reading impairments in dyslexia (Valdois et al., 2004). Attentional abilities better explain surface-phonological dyslexia distinction, indicating that the phonological theory is limited as it does not account for the influence of other high-level factors (attention) on the reading impairments found in dyslexia.

Although there is strong evidence for phonological impairments predicting reading ability, there is also evidence that auditory processing impairments are predictive of reading

ability. A longitudinal study of reading development examined dyslexia and non-dyslexia (with and without a genetic risk for dyslexia) and found that those who later developed dyslexia had auditory processing impairments (frequency modulation, speech perception) as well as phonological impairments (Boets et al., 2011). Both phonological abilities and lower level auditory processing abilities predicted different stages of development in reading: kindergarten to first grade reading was predicted by auditory processing, whereas third grade reading ability was predicted by phonological awareness (Boets et al., 2011). This suggests that non-phonological auditory processing impairments may also play a role in dyslexia.

Neural Evidence for the Phonological Deficit Theory

At the neural level, there is evidence of a disruption to the phonological brain system in dyslexia, with under-activation of Broca's area and the insula found in dyslexia during phonological tasks (Paulesu et al., 1996). Phonological deficits in dyslexia may be caused by malfunctioning of the insula which results in disconnection to other phonological sites in the brain (Paulesu et al., 1996). Disruption of the left perisylvian cortex is also found in dyslexia and is argued to cause problems with phonological representations (Ramus, 2004).

However, higher level cognitive factors implicated in task performance complicate the interpretation of such findings. Several meta-analyses exploring the neural underpinnings of phonological impairments in dyslexia indicate that the phonological brain system may not be implicated until adulthood and more importantly that attentional problems may cause phonological impairments in childhood (Richlan, 2012; Richlan et al., 2010; Richlan, Kronbichler, & Wimmer, 2009, 2011). For instance, Richlan et al. (2009) found abnormal activation in left temporo-parietal and occipito-temporal regions supporting the phonological deficit theory, however, when this analysis was split by age (child v adult dyslexia), left temporo-parietal and occipital-parietal abnormalities were observed in adult dyslexia, while children demonstrated a network of under activation in the inferior parietal lobule and only limited under activation in occipito-temporal regions. This suggests that abnormalities in the phonological brain system may only be associated with

adult dyslexia and not childhood dyslexia, making it difficult to understand how phonological impairments are causally implicated. Another meta-analysis, found under-activation in the left occipito-temporal region, inferior frontal gyrus and inferior parietal lobule in dyslexia during reading (Richlan et al., 2010). Richlan (2012) suggests that dyslexia could be caused by top down attentional mechanisms (due to the role of the inferior parietal lobule in attention) which influence the output of phonological representations in the inferior frontal gyrus and phonological decoding in the occipito-temporal region. Indeed, other high-level cognitive factors have also been argued to be implicated in phonological measures due to multiple task demands tapping executive function and working memory systems (Ramus & Szenkovits, 2008), suggesting that phonological impairments may manifest also as a consequence of other higher level cognitive problems (e.g. executive function, attention).

High-level Cognitive Confounds of Evidence Supporting the Phonological Deficit Theory

A central assumption of the phonological deficit theory is that phonological impairments manifest in dyslexia. Of interest is the observation that these impairments manifest more so with other higher level task demands (EF, working memory) (Ramus & Szenkovits, 2008). Those with dyslexia are not impaired on all tasks that measure phonological processing, and impairments are found only in tasks that have executive demands such as storage, speedy retrieval, detection and manipulation of phonemes (Ramus & Szenkovits, 2008). This suggests that impairments on these measures may be more reflective of a disorder specific EF impairment in processing phoneme information. At the neural level, there is also evidence to suggests that impairments in the top down attentional control network may be implicated in poor phonological decoding (Richlan, 2012). Given that EF impairments are found in dyslexia (Brosnan et al., 2002), and, also that EF processing contributes to reading ability independently of phonological processing (Swanson, 1999), a disorder specific EF impairment in processing phoneme content may explain why those with dyslexia are impaired on some but not all phonological tasks (Ramus & Ahissar, 2012), and potentially why dyslexia and ADHD so frequently co-occur.

Conclusion

Although there is strong evidence for the phonological deficit theory of dyslexia, interpretation of this research is complicated due to: (1) phonological theory not adequately explaining the difference between surface dyslexia and phonological dyslexia, (2) auditory processing also being predictive of dyslexia, (3) the role of high-level cognitive factors in task performance, and (4) top down control of the phonological brain system by the attentional brain system. The theory also provides no explanation for why dyslexia and ADHD so frequently co-occur.

2.3.4 The Temporal Auditory Processing Theory

The temporal auditory processing theory of dyslexia argues that the phonological and reading impairments in dyslexia are caused by an underlying deficit in perceiving brief and rapidly changing auditory information (Farmer & Klein, 1995; Tallal & Benasich, 2002; Tallal & Gaab, 2006). This auditory processing impairment can manifest as difficulties remembering, producing, discriminating between and sequencing brief and rapidly changing acoustic information (Tallal & Gaab, 2006). Such deficits in temporal auditory processing are argued to cause phonological deficits because the perception of different phonemes within words requires an ability to perceive brief and rapidly changing acoustic information (Tallal & Benasich, 2002; Tallal & Gaab, 2006). Phonological deficits result in reading problems by making it difficult to learn the grapheme-phoneme mappings crucial for developing an efficient reading strategy (*See Figure 5 for causal chain*).

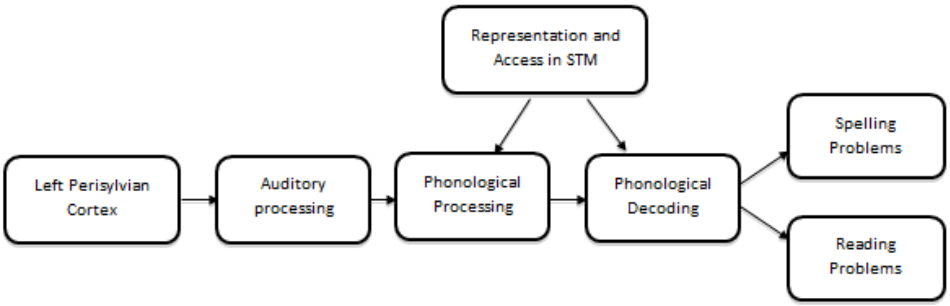


Figure 5 Tallal and Gaab's (2006) Causal temporal auditory processing theory of dyslexia

Behavioural Evidence for the Temporal Auditory Processing Theory

At the behavioural level, there is evidence for a temporal auditory processing impairment in dyslexia, with studies finding impaired judgements about temporal order of rapid auditory information (Rey, De Martino, Espesser, & Habib, 2002; Tallal, 1984) and amplitude modulation detection (Menell, McAnally, & Stein, 1999). A meta-analysis of auditory processing deficits in dyslexia found impairments in duration discrimination, detection of changes in frequency, amplitude and rise time which correlated with impaired phonological representations (Hämäläinen, Salminen, & Leppänen, 2013; Rey et al., 2002; Witton et al., 1998). High correlations are also found between temporal auditory processing and phonological abilities in those with and without dyslexia (Rey et al., 2002; Witton et al., 1998), suggesting an associative relationship between auditory processing and phonological impairments in dyslexia.

However, it is difficult to infer a causal relationship between auditory processing and phonological and reading impairments in dyslexia due to: (1) phonological impairments occurring in the absence of temporal auditory processing impairments; (2) temporal auditory processing interventions not improving phonological abilities; (3) the role of higher level cognitive processes in temporal auditory processing task performance; and (3) temporal auditory processing impairments occurring in other developmental disorders not characterised by phonological and reading impairments.

A wealth of research indicates that a temporal auditory processing deficit is not the central cause of phonological and reading impairments in dyslexia. Findings of phonological impairments in the absence of the proposed causal temporal auditory processing deficit (Marshall, Snowling, & Bailey, 2001), and low correlations between temporal auditory processing and reading abilities (Heiervang, Stevenson, & Hugdahl, 2002) indicate a lack of causality. Longitudinal studies also fail to demonstrate a predictive relationship between temporal auditory processing and high-level phonological and reading abilities (Boets, Wouters, Van Wieringen, & Ghesquiere, 2007; Share, Jorm, Maclean, & Matthews, 2002). Both studies found only a subgroup of dyslexia to demonstrate a temporal auditory processing deficit (Boets et al., 2007; Share et al., 2002),

yet this subgroup did not demonstrate more severe reading and phonological impairments than dyslexic participants without a temporal auditory processing deficit (Share et al., 2002). Auditory processing deficits were also found in participants without dyslexia and this group had intact reading abilities (Boets et al., 2007). Interventions targeted at temporal auditory processing impairments also fail to demonstrate pre-post improvements in phonological abilities (Agnew, Dorn, & Eden, 2004). This demonstrates that a temporal auditory processing deficit is not at the core of reading and phonological impairments in dyslexia.

Another challenge faced by the temporal auditory processing theory is that temporal auditory processing deficits are found in other developmental disorders which are not characterised by impaired reading ability (Goswami, 2015). Temporal auditory processing deficits are found both in autism (Kwakye, Foss-Feig, Cascio, Stone, & Wallace, 2010) and ADHD (Toplak, Dockstader, & Tannock, 2006), yet neither of these disorders are associated with phonological or reading impairments. This suggests that temporal auditory processing deficits may be a nonspecific marker of developmental disorders and not be specifically related to core (reading) issues in dyslexia (Goswami, 2015). However, some studies insufficiently screen for potentially undiagnosed comorbid ADHD in dyslexia alone samples when exploring temporal auditory processing impairments. This is problematic as it limits the ability to conclude a temporal auditory processing deficit to dyslexia alone. A recent study explored impairments in temporal auditory processing, working memory and processing speed in dyslexia while controlling for elevated ADHD features, and found only processing speed was impaired (Moll, Göbel, Gooch, Landerl, & Snowling, 2016), suggesting that evidence for temporal auditory processing deficit may be due to not systematically screening the sample for other comorbidities.

Neural Evidence for the Temporal Auditory Processing Theory

At the neural level, there is evidence for a temporal auditory processing deficit in dyslexia, with studies finding structural abnormalities in brain areas important for auditory processing such as the planum temporale (Hugdahl et al., 1998) and left medial geniculate nucleus (Galaburda, Menard, & Rosen, 1994). Dyslexia is also found to be characterised by

delayed mismatch negativity during temporal auditory processing tasks (Baldeweg, Richardson, Watkins, Foale, & Gruzelier, 1999; Hugdahl et al., 1998; Sharma et al., 2006). Mismatch negativity is an auditory evented related brain potential (ERP) which automatically occurs in response to a change in perceived auditory information (such as amplitude, intensity or frequency changes) (Näätänen, Paavilainen, Rinne, & Alho, 2007). The auditory mismatch negativity is calculated by subtracting ERP to regular auditory stimuli from ERP to changed auditory stimuli, and, typically occurs between 150-250ms ((Näätänen et al., 2007). Abnormal mismatch negativity ERPs also correlate with phonological impairments in dyslexia (Baldeweg et al., 1999), suggesting that abnormal neural activations to temporal auditory information are related to phonological impairments in dyslexia.

However, not all of those with dyslexia are found to demonstrate abnormal mismatch negativity (Hakvoort, van der Leij, Maurits, Maassen, & van Zuijen, 2015); and findings of mismatch negativity are difficult to interpret due to inherent methodological issues and approaches mainly measuring the detection of change as opposed to discrimination between stimuli, the latter thought to be impaired according to the theory (Bishop, 2007). Bishop (2007) conducted a large scale review of mismatch negativity in dyslexia and identified the following issues: (1) low statistical power across studies due to small samples, (2) inconsistent measurement of mismatch negativity- some studies use peak amplitude even though mean amplitude is a more reliable measure, (3) inconsistent definition of time frame capture- some use t-tests whereas others determine time frame visually which causes difficulty identifying individual variation, and (4) results differ depending on approach used. This makes it difficult draw conclusions on the meaning of findings of abnormal mismatch negativity in dyslexia.

There is also difficulty in understanding how temporal auditory processing deficits are functionally related to reading and phonological impairments, as activity during reading and phonological tasks appear to be localised in phonological and frontal networks. Pre-post intervention improvements in phoneme and morpheme mapping are underpinned by activation changes in frontal (right superior frontal gyrus, left middle frontal gyrus, inferior frontal gyrus) and parietal (bilateral superior parietal) regions (Aylward et al., 2003), while

reading improvements are correlated with improved activation in the left prefrontal cortex (Gaab, Gabrieli, Deutsch, Tallal, & Temple, 2007; Temple et al., 2003). Correlation studies also demonstrate reading impairments in dyslexia to be characterised by under activation of the left precentral gyrus, left temporal gyrus, inferior frontal gyrus, middle frontal gyrus, and left orbital frontal gyrus (Turkeltaub, Eden, Jones, & Zeffiro, 2002). When examining the neural underpinnings of reading and phonological tasks it is difficult to see how a temporal auditory processing deficit is causing dyslexia.

High-level Cognitive Confounds of Evidence Supporting the Temporal Auditory Processing Theory

A central assumption of the temporal auditory processing deficit theory is that a deficit in detecting rapid transients in auditory information are associated with dyslexia. Although there is inconsistent evidence of this in dyslexia, another challenge faced by the temporal auditory processing theory is the influence of higher level cognitive factors in successful task performance due to multiple task demands, making it difficult to determine if poor performance is due to auditory processing or high-level cognitive problems. Attention abilities are found to modulate task performance (Brown et al., 1997), and deficits manifest differently with different measures (Banai & Ahissar, 2006). Tasks requiring same-different distinctions in speech and non-speech information (function of auditory cortex) fail to find a deficit in dyslexia, whereas tasks taxing working memory such as those requiring short-long/high-low discrimination and ordinal position detection (function of frontal cortex) elicit poor performance in dyslexia (Banai & Ahissar, 2006). This suggests that an impairment found on these tasks could be more reflective of a higher-level working memory deficit as opposed to a lower level auditory deficit. Indeed, this may be the case as a similar temporal auditory processing training intervention found to effectively improve reading ability was correlated with improved activation in pre-frontal brain areas (Temple et al., 2003).

Conclusion

At the behavioural level, the evidence for temporal auditory processing deficits being at

the core of dyslexia is weak. Although some studies typically find temporal auditory processing deficits to be associated with dyslexia, a causal relationship cannot be established because phonological impairments are found in the absence of temporal auditory impairments; temporal auditory interventions do not improve phonological abilities; and temporal auditory impairments are also found in the other developmental disorders that are not characterised by reading and phonological impairments. Although this may be interpreted as support for a transdiagnostic factor, studies systematically controlling for undiagnosed ADHD in dyslexia samples do not find evidence of an impairment. At a neural level, the evidence for the temporal auditory processing theory is also lacking. This is because mismatch negativity evoked potentials are not properly or accurately measured, and brain activity during reading and phonological tasks in dyslexia is characterised by under-activation of frontal and phonological networks as opposed to abnormal activation of the auditory cortex. Indeed, it may be the case that temporal auditory processing impairments may occur in some cases of dyslexia, but generally they do not appear to play a role in the higher-level reading and phonological problems found in dyslexia. The theory also provides no explanation for why dyslexia and ADHD so frequently co-occur.

2.3.5 Summary

Cerebellar, magnocellular, and temporal auditory processing deficit theories of dyslexia are limited as they are low-level explanations that cannot explain the influence of higher cognitive processes (EF, working memory and attention) on performance measures (*see Table 1 for summary*). Although the phonological deficit theory is a high-level cognitive explanation of dyslexia, it too cannot explain the influence of the same high-level cognitive processes (EF, working memory and attention) on performance measures. These theories also cannot explain the presence of EF impairments in dyslexia (Beneventi et al., 2010(a); Brosnan et al., 2002; Helland & Asbjørnsen, 2000; Poljac et al., 2010; Reiter et al., 2005; Rucklidge & Tannock, 2002), why dyslexia is so highly comorbid with ADHD- a disorder characterised by EF impairments-, or the presence of non-core socio-emotional issues in dyslexia.

High comorbidity rates are often indicative of shared risk factors. EF is worthy of further exploration in dyslexia as previous research indicates that EF is compromised in dyslexia (Beneventi et al., 2010(a); Brosnan et al., 2002; Helland & Asbjørnsen, 2000; Poljac et al., 2010; Reiter et al., 2005; Rucklidge & Tannock, 2002), and also is a candidate endophenotype for explaining comorbidity with dyslexia and ADHD (Rommelse et al., 2009). Moreover, EF is often predictive of both core reading and non-core socio-emotional outcomes in dyslexia (Moura et al., 2015; Thompson et al., 2015; Wang & Yang, 2014), and it appears to be modifiable via targeted interventions transferring to improvements in reading, inattention and underlying brain activity (Berkman et al., 2014; Johnstone et al., 2010; Loosli et al., 2012; Manuel et al., 2013). Therefore, EF may be a useful framework for understanding core and non-core issues in dyslexia, why dyslexia frequently co-occurs with ADHD, and for targeted intervention.

EF may also be a useful framework for identifying those at risk for developing dyslexia and ADHD early on, as EF abilities appear to be highly heritable (Friedman & Miyake, 2016). In such a manner, children of parents with low EF abilities could be tested prior to reading acquisition and potential impairments could be ameliorated with EF training. EF is also an intermediate cognitive factor mediating the gene symptom pathway of a wide range of neurodevelopmental and psychiatric disorders, relates to severity of functional outcome and is capable of detecting disorder prodromes (Glahn et al., 2016, 2016; Goschke, 2014; Miller & Rockstroh, 2013; Snyder et al., 2015). This suggests that if implicated in the core and non-core features of dyslexia, EF impairments may emerge prior to reading impairment and thus could be a useful early risk indicator that can be addressed prior to reading instruction.

Table 1 Summary of behavioural and neural evidence for theories of dyslexia and high-level (EF/WM/Attentional) confounds complicating interpretation

Theory	Behavioural Evidence	Neural Evidence	EF/Attentional Confound
Cerebellar	- Motor impairments - Implicit learning impairments	- Cerebellar abnormalities	- EF implicated in motor abilities - High-level attention modulates implicit learning performance - PFC activity during implicit learning suggests WM is taxed
Magnocellular	- Low-level visual/auditory impairments - Binocular fixation problems - Phonological impairments	- Magnocellular abnormalities	- High-level attention implicated in measures - EF impairment associated with binocular fixation - EF and WM implicated in phonological measures
Phonological	- Phonological impairments	- Under-activation of phonological processing areas	- EF and WM implicated in phonological measures - Frontal areas also underactive during phonological tasks suggesting top down attentional control implication
Temporal Auditory	- Temporal auditory processing impairments - Phonological impairments	- Abnormalities in auditory processing areas - Delayed ERPs for rapidly changing auditory information	- WM and Attention implicated in temporal auditory processing measures - EF and WM implicated in phonological measures

Note. EF=executive function, PFC=prefrontal cortex, WM= working memory, ERPs=event related potentials, PFC = Pre-Frontal Cortex

2.5 Executive Function (High-level Cognitive Processes)

Executive function (EF) is an umbrella term for a triad of high-level cognitive processes-response inhibition, working memory updating and switching – associated with frontal regions of the brain (Collette et al., 2005; Friedman et al., 2006, 2007, 2008; Huizinga, Dolan, & van der Molen, 2006; Lehto, Juujarvi, Kooistra, & Pulkkinen, 2003; Miyake et al., 2000; Miyake & Friedman, 2012; van der Sluis, de Jong, & van der Leij, 2007). Traditionally, executive function was viewed and measured as a unified cognitive construct with complex EF tasks (such as the Wisconsin Card Sort Task). However, Miyake and Friedman's (2012) comprehensive research on the latent factor structure of executive function indicates that EF is comprised of a set of abilities both related through common EF (synonymous with response inhibition) and distinct to each other (updating specific and switching specific) (*see Figure 6*). Inhibition is the ability to override inappropriate responses, regulate appropriate behaviour and control attention by focussing on relevant information and filtering out distracting information; updating is the ability to hold and continuously update information in working memory from moment to moment; and switching is the ability to rapidly adapt to changing task demands (Diamond, 2013; Miyake et al., 2000; Miyake & Friedman, 2012).

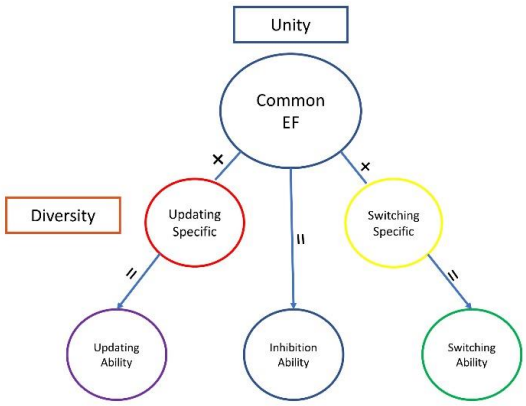


Figure 6 Miyake and Friedman's (2012) 3-factor model of EF

Extensive research confirms the 3-factor structure of EF proposed by the model (Collette et al., 2005; Friedman et al., 2006, 2007, 2008; Huizinga et al., 2006; Lehto et al., 2003; Miyake et al., 2000; Miyake & Friedman, 2012; van der Sluis et al., 2007); and the structure is relatively stable across development as it is confirmed to be present in children (Huizinga et al., 2006; Lehto et al., 2003; Rose, Feldman, & Jankowski, 2011; van der Sluis et al., 2007), adolescents (Huizinga et al., 2006), and adults (Friedman et al., 2006, 2007, 2008; Miyake et al., 2000). These EFs develop gradually from early childhood reaching maturity in early adulthood (Huizinga et al., 2006; Lehto et al., 2003; van der Sluis et al., 2007).

A range of brain areas play a role in competent executive functioning (*see Figure 7)*, the main area of importance is the prefrontal cortex, although other subcortical areas (basal ganglia, thalamus and cerebellum) play a role through their rich connections to pre-frontal brain areas (Powell & Voeller, 2004). The main prefrontal areas necessary for executive function are: (1) the anterior cingulate circuit (important for attentional control, error awareness, and tasks requiring effort) (Powell & Voeller, 2004), (2) the dorsolateral circuit (important for filtering distractions, phonological decoding, set maintenance, and working memory) (Powell & Voeller, 2004), and (c) orbitofrontal circuit (important for decision making, self-monitoring and integrating emotion and cognition) (Powell & Voeller, 2004).

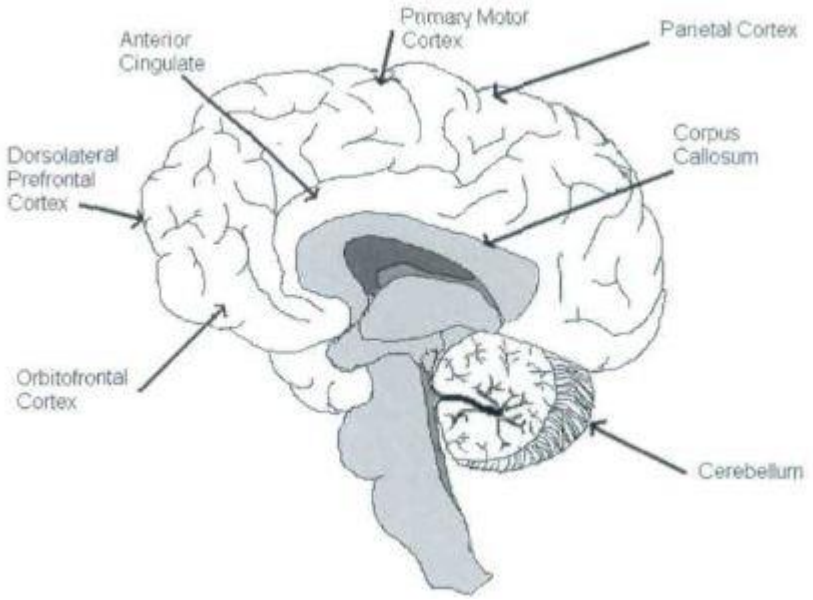


Figure 7 Powell and Voeller's (2004) Diagram of brain areas underpinning EF

Response Inhibition appears to be supported by activation in the anterior cingulate cortex, left inferior frontal gyrus, temporo-parietal regions, dorsolateral prefrontal cortex, frontal striatal regions and inferior parietal cortex (Alvarez & Emory, 2006; Bench et al., 1993; Booth et al., 2005; Casey et al., 1997; Garavan, Ross, Murphy, Roche, & Stein, 2002; Kiefer, Marzinzik, Weisbrod, Scherg, & Spitzer, 1998; Liotti, Woldorff, Perez, & Mayberg, 2000; Taylor, Kornblum, Lauber, Minoshima, & Koeppe, 1997). Working memory updating appears to be underpinned by activation in fronto-polar, left middle frontal area, dorsal cingulate, pre-motor cortex, dorsolateral cortex and ventro-lateral prefrontal cortex, as well as posterior parietal cortex (Collette et al., 1999; Owen, McMillan, Laird, & Bullmore, 2005). Switching appears to be underpinned by activation in temporo-parietal cortex, dorsolateral prefrontal cortex, right orbitofrontal cortex, left middle and inferior frontal regions, as well as additional parietal brain regions (Collette et al., 2005; Fink et al., 1997). The neural underpinnings of EFs appear to be consistent with Miyake and Friedman's (2012) model of executive function, as shared and distinct activation is found (Collette et al., 2005).

Core EFs – response inhibition, updating, switching- are differentially implicated in and facilitate higher order cognitive processes such as planning, reasoning, fluid intelligence

(Diamond, 2013; Friedman & Miyake, 2016; Miyake et al., 2000, p. 200; Miyake & Friedman, 2012; Snyder et al., 2015). Diamond's (2013) outlines an EF framework for understanding how the core EFs are related to each other and how in combination they facilitate higher order cognitive processes such as planning, reasoning and fluid intelligence and self-regulation (*see Figure 8*). This facilitation to "higher-order cognitive processes" could theoretically be extended to a wide range of complex human behaviours, for instance EFs have been found to contribute also to reading ability, math ability, self-regulation and socio-emotional wellbeing (Blair & Razza, 2007; Carlson & Wang, 2007; Christopher et al., 2012; Diamond, 2013; Friedman et al., 2006, 2008; Miyake et al., 2000; Vohs & Baumeister, 2011). EFs appear distinguishable at the behavioural level, as they contribute differentially to complex human behaviours. For instance, inhibition is found to uniquely relate to attentional problems, cognitive failures, emotional regulation, math ability and emerging literacy (Carlson & Wang, 2007; Friedman et al., 2007; Friedman & Miyake, 2004; van der Sluis et al., 2007); updating is found to relate to fluid intelligence, crystallised intelligence, verbal reasoning and attentional problems (Friedman et al., 2006, 2007; van der Sluis et al., 2007): and switching is found to relate to reading ability, non-verbal reasoning and effortful control (Blair & Razza, 2007; van der Sluis et al., 2007). This highlights the importance for implementing measures of key EFs (instead of higher order cognitive processes) as a first step in understanding how they may be implicated in behaviourally diverse disorders.

Diamond's (2013) framework has implications for understanding how impairments within an EF brain system may have knock on effects for a range of behavioural level impairments. If the key EFs are a cognitive hub for facilitating a wide range of complex behaviours, then a disorder characterised by EF impairments may have additional (non-core) symptoms as well as core symptoms (which are required for diagnosis of a specific condition), and may result in comorbid diagnosis such as is the case between dyslexia and ADHD. Understanding each condition within an EF framework emphasises the redundancy and limitation of diagnosing disorders at the symptom level, as an EF dysfunction category may more appropriately explain conditions, enhance diagnostics and targeted intervention. Such a framework may provide an explanation of core (reading) and non-

core (socio-emotional) symptoms of dyslexia and why dyslexia is highly comorbid with ADHD. An adapted version of Diamond's (2013) framework extending to reading ability is outlined in Figure 8. Extending this framework to include reading ability has potential for explaining the core and non-core features of dyslexia, however it is unclear from typical and atypical populations which key EFs are predictive of reading ability.

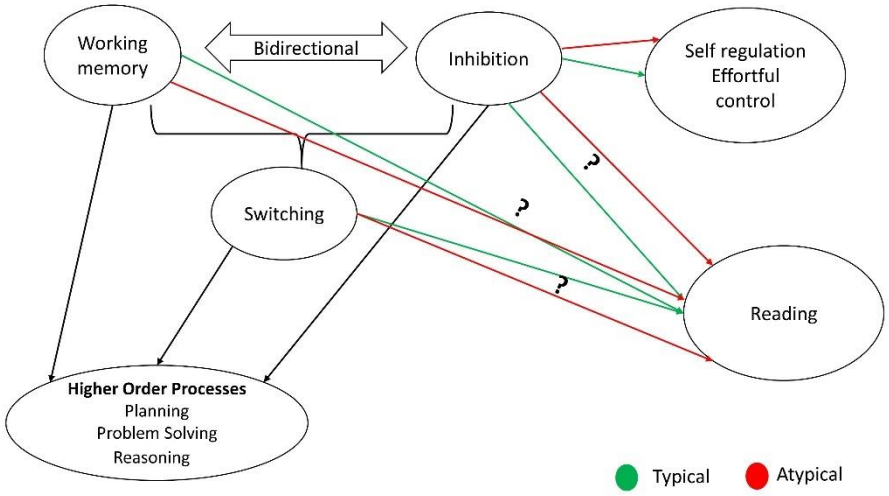


Figure 8 Diamond's (2013) EF Framework adapted to include reading ability, question marks indicate that paths (direct/indirect) to reading ability are unclear from previous research

Key EF impairments have been implicated in a range of psychological disorders which appear distinct at the behavioural level such as autism and ADHD (Barkley, 1997; Biederman et al., 2004; Gau & Chi-Yung Shang, 2010; Ozonoff & Jensen, 1999; Ozonoff, Pennington, & Rogers, 1991). This highlights the strength of EF as a neuro-cognitive endophenotype for a range of disorders. A number of researchers suggest that common EF (response inhibition) mechanisms may be the EF that explains overlapping disorders. Robbins et al. (2012) argue that a response inhibition endophenotype may be a useful transdiagnostic endophenotype for explaining a range of complex disorders and the range of behaviours associated with them. They suggest response inhibition is at the core of

both impulsive and compulsive behaviours which are capable of characterising psychological disorders ranging from ADHD to schizophrenia and autism (Robbins et al., 2012) (*see Figure 9)*. It is important to note however that dyslexia is not included under Robbins et al. (2012) framework of disorders characterised by common EF impairments. This may be due to no study to date exploring EF as an endophenotype in dyslexia, and, a lack of clarity on whether dyslexia is associated with an EF impairment (see section 2.6 for detailed discussion).

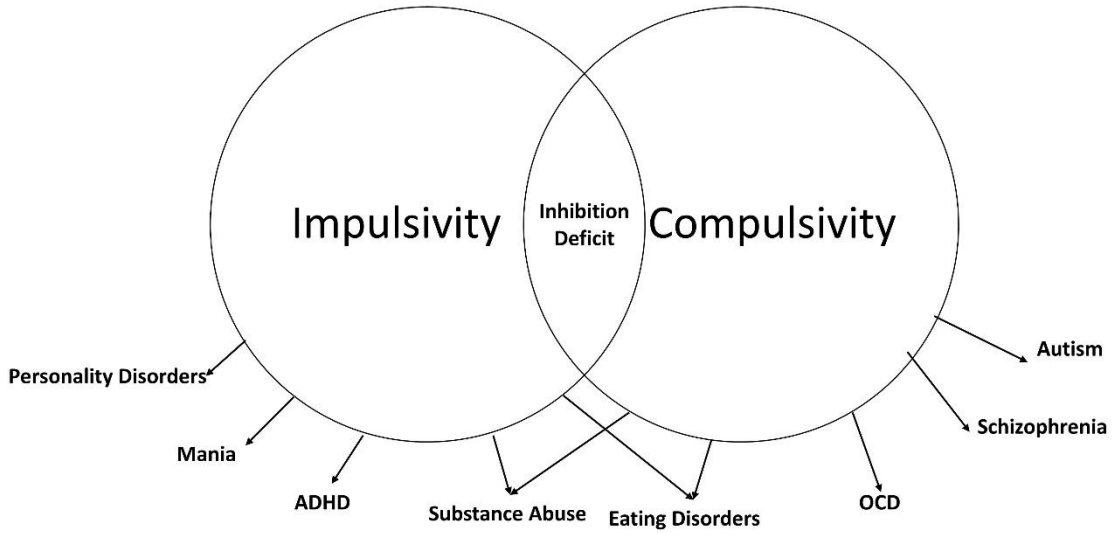


Figure 9 Robbins et al. (2012) depiction of response inhibition as a central mechanism in impulsive-compulsive behaviours

Common EF (response inhibition) mechanisms could be a potential explanation for the overlap between dyslexia and ADHD. ADHD has previously been conceptualised as a disorder stemming from response inhibition impairments (Barkley, 1997) which result in higher order cognitive impairments and self-regulatory difficulties. Response inhibition (Brosnan et al., 2002) and other key EF impairments are also observed in dyslexia (Moura et al., 2015), as well as socio-emotional issues which could be due to self-regulatory

difficulties (Dahle et al., 2011; Heiervang et al., 2001; Knivsberg & Andreassen, 2008; Mugnaini et al., 2009). EF is highly heritable, linked to psychopathology and self-regulatory behaviour (Friedman et al., 2008), and has been proposed as a candidate endophenotype for explaining ADHD and comorbid reading problems (Kegel & Bus, 2013; Rommelse et al., 2009). Key EFs appear to be differentially implicated in a range of complex behaviours, suggesting that they may also differentially relate to core and non-core behaviour in dyslexia and possibly explain overlap with behaviourally distinct ADHD features.

However, issues in establishing which EFs are impaired in dyslexia and comorbid dyslexia-ADHD make it difficult to extend an explanation to overlapping impairments and to core and non-core issues of dyslexia.

2.6 Executive Function in Dyslexia

The extent to which EF is implicated in dyslexia alone remains unclear within current literature. Several studies find dyslexia to be associated with an EF impairment (Beneventi et al., 2010(a); Brosnan et al., 2002; Helland & Asbjørnsen, 2000; Poljac et al., 2010; Reiter et al., 2005; Rucklidge & Tannock, 2002; Willcutt, Pennington, Olson, Chhabildas, & Hulslander, 2005); while several other studies find dyslexia is not associated with an EF impairment (Bental & Tirosh, 2007; Marzocchi et al., 2008; Peng, Sha, & Li, 2013; Reiter et al., 2005; Tiffin-Richards, Hasselhorn, Woerner, Rothenberger, & Banaschewski, 2008).

The role of the common EF (response inhibition) in dyslexia remains unclear, with a number of studies finding an impairment (Booth, Boyle, & Kelly, 2014; Brosnan et al., 2002; De Lima, Salgado-Azoni, Travaini, & Ciasca, 2012; Proulx & Elmasry, 2014; Willcutt et al., 2001, 2005) and a number of studies finding no impairment (Bental & Tirosh, 2007; Bexkens, van den Wildenberg, & Tijms, 2014; Marzocchi et al., 2008; Reiter et al., 2005; Schmid, Labuhn, & Hasselhorn, 2011). Findings appear to differ depending on the task employed to measure inhibition. For instance, there is evidence of an impairment with Stroop task, Group Embedded Figures task, and Stop Signal Task (Booth et al., 2014; Brosnan et al., 2002; De Lima et al., 2012; Proulx & Elmasry, 2014; Wang & Yang, 2014; Willcutt et al., 2001, 2005). Whereas, there is no evidence of an impairment with the Change task, Matching Familiar Figures task, Go No Go task and in some cases the Stop

Signal task (Bental & Tirosh, 2007; Bexkens et al., 2014; Marzocchi et al., 2008; Reiter et al., 2005; Schmid et al., 2011; Wang & Yang, 2014). However, inconsistent evidence of a response inhibition impairment in dyslexia makes it difficult to determine whether this EF is implicated, and the role it may play in symptom expression. Task discrepant findings of an inhibition deficit are also indicative of task impurity issues (Miyake et al., 2000).

The role of updating (working memory) in dyslexia also remains unclear, with a number of studies finding a deficit (Bental & Tirosh, 2007; Brosnan et al., 2002; McGee, Brodeur, Symons, Andrade, & Fahie, 2004; Rucklidge & Tannock, 2002; Smith-Spark, Fisk, Fawcett, & Nicolson, 2003; Willcutt et al., 2005), and a number failing to find a deficit in dyslexia (Marzocchi et al., 2008; Peng et al., 2013; Willcutt et al., 2005). Within the working memory literature, there may be differences depending on the type of content employed in measures (verbal not visual). For instance, when tasks with verbal or language-based stimuli are used such as in the listening sentence span (where participants had to recall a number of spoken words), there is evidence for a deficit in dyslexia (Bental & Tirosh, 2007; Brosnan et al., 2002; Chiappe, Siegel, & Hasher, 2000; Rucklidge & Tannock, 2002; J. Smith-Spark et al., 2003; Willcutt et al., 2005); yet when tasks employing visuo-spatial stimuli are used, such as in the spatial span tasks (where participants have to recall a sequence of visually presented spatial locations), there is little or no evidence for a working memory impairment in dyslexia (Brosnan et al., 2002; Peng et al., 2013; Willcutt et al., 2005).

However, some studies using visual stimuli related to linguistic information (e.g. picture-phoneme updating (*see Figure 10)* or letter updating tasks) have demonstrated an impairment in dyslexia (Beneventi et al., 2010(a); Smith-Spark et al., 2003). The picture-phoneme updating task employed by Beneventi et al. (2010a) required participants to view a stream of pictures and decide if the first letter of the current picture on screen matched the first letter of the picture on screen two back. Beneventi et al. (2010a) found that children with dyslexia were impaired on this task even while controlling for phonological awareness. This suggests that there may be a disorder-specific working memory updating deficit in dyslexia relating to linguistic information - particularly with phoneme information (Beneventi et al., 2010a). Overall, it is unclear if dyslexia is

associated with working memory updating impairment, or whether it is disorder-specific to processing phoneme information, and the role it may play in symptom expression.

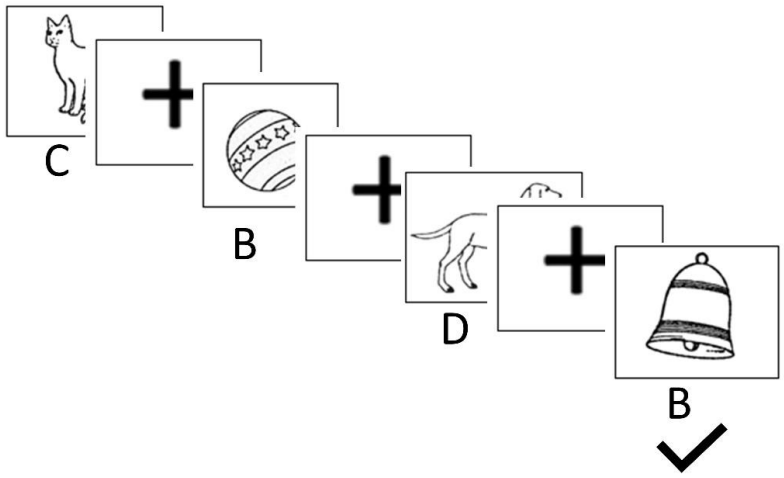


Figure 10 Beneventi et al.'s (2010a) Disorder specific (phoneme) working memory updating task. In this task, participants were presented with an image for 1,000ms and a fixation for 1,000ms. Participants were required to sound out the word for the image and decide if it matched the image presented 2-times ago based on the first letter sound. For example, ball matches bell because they both begin with a b-sound.

The role of switching in dyslexia also remains unclear. A number of studies report a switching impairment associated with dyslexia (De Lima et al., 2012; Helland & Asbjørnsen, 2000; Poljac et al., 2010), and a number of studies find no switching impairment (Bental & Tirosh, 2007; Marzocchi et al., 2008; Menghini et al., 2010; Reiter et al., 2005; Tiffin-Richards et al., 2008). An added complication interpreting the extent to which switching is implicated in dyslexia is related to the range of tasks used to measure switching. For instance, impairments are found using Trail Making task, Wisconsin Card Sort task (WCST), and Shape-Colour switch task (De Lima et al., 2012; Helland & Asbjørnsen, 2000; Poljac et al., 2010), yet other studies which use the Trail Making and WCST find no evidence of an impairment (Bental & Tirosh, 2007; Marzocchi et al., 2008;

Menghini et al., 2010; Reiter et al., 2005; Tiffin-Richards et al., 2008). There are major criticisms of using complex EF tasks such as the Trail Making Task and WCST when trying to examine EF, and this is due to all 3 core EFs contributing to task performance (Miyake et al., 2000; Snyder et al., 2015). It is unclear if dyslexia is associated with a switching impairment, and the role it may play in symptom expression. An added complication with employing complex tasks to measure EF is that they cannot address how key EF abilities may help (common EF and updating) or hinder (common EF and switching) each other (Friedman & Miyake, 2016; Snyder et al., 2015). This suggests that if measured with sensitive tools, EF abilities may manifest in a strengths and impairments pattern.

2.7 Executive Function in Comorbid Dyslexia-ADHD

The association between compromised EF and comorbid dyslexia-ADHD is more consistent than dyslexia alone, with most studies finding evidence of an impairment (McGee et al., 2004; Rucklidge & Tannock, 2002; Tiffin-Richards et al., 2008; Willcutt et al., 2001, 2005). Studies have found evidence for (Rucklidge & Tannock, 2002; Willcutt et al., 2005), and against a common EF (response inhibition) impairment (Bental & Tirosh, 2007); for a working memory impairment (McGee et al., 2004; Rucklidge & Tannock, 2002; Tiffin-Richards et al., 2008; Willcutt et al., 2001); and, for (Tiffin-Richards et al., 2008) and against a switching impairment in comorbid dyslexia-ADHD (Bental & Tirosh, 2007). Although there is debate surrounding which specific aspects of EF are compromised in comorbid dyslexia-ADHD, there are difficulties also in understanding the source of impairments in the comorbid condition, such that some find deficits associated with each pure form of condition are additive in the comorbid condition (Willcutt et al., 2001) while others suggest that they are more severe (Rucklidge & Tannock, 2002).

Neale and Kendler (1995) proposed a number of explanations for comorbidity between behaviourally distinct conditions. These explanations suggest that comorbidity may be due to chance (artefact of chance), a single impairment manifesting differently at the behavioural level (alternate forms), one condition increasing risk for the behavioural expression of another condition (multiform), each isolated condition and comorbid condition being separate (independent conditions) and each isolated condition having

shared impairments which result in the comorbid condition (correlated liabilities) (Neale & Kendler, 1995). The alternate forms explanation of comorbidity proposes that isolated conditions may be characterised by a single shared underlying impairment which manifests differently at the behavioural level and results in comorbidity due to environmental risk factors interacting with genetic risk factors. The multiform explanation of comorbidity proposes that one condition characterised by a single impairment increases likelihood of the behavioural manifestation only of the other condition. The independent conditions explanation of comorbidity proposes that each isolated condition and the comorbid instance are independent. The correlated liabilities explanation suggests that each isolated condition share some impairments which explain comorbidity.

A number of these explanations have been explored in comorbid dyslexia-ADHD. Comorbidity between these conditions does not appear to be a product of chance, as both conditions co-occur at a greater than chance rate (American Psychiatric Association, 2013; Gilger et al., 1992; Willcutt & Pennington, 2000). The phenocopy hypothesis (multiform) (Pennington, Groisser, & Welsh, 1993) suggests that comorbid dyslexia-ADHD is characterised by the same underlying impairments as dyslexia alone and is only associated with symptoms of ADHD due to frustration with reading. The cognitive subtype hypothesis (independent conditions) (Rucklidge & Tannock, 2002) suggests that comorbid dyslexia-ADHD is a unique subtype as it appears to be associated with more severe and additional impairments than either isolated condition. While the multiple deficit hypothesis (correlated liabilities) (McGrath et al., 2011; Willcutt et al., 2010) suggests that each isolated condition is underpinned by distinct impairments as well as shared impairments which result in comorbidity.

Pennington et al. (1993) proposed the phenocopy explanation of comorbid dyslexia-ADHD, employing a double dissociation design the found impaired phonological abilities in dyslexia, impaired EF abilities in ADHD and only impaired phonological abilities in comorbid dyslexia-ADHD, suggesting that the comorbid group exhibited the same underlying impairments of dyslexia alone yet expressed the symptoms of ADHD. However, subsequent studies failed to replicate these findings and instead suggested that the comorbid group exhibit an additive combination of impairments from dyslexia and ADHD

alone (Willcutt et al., 2001). Employing a similar design, Willcutt et al. (2001) found that comorbid dyslexia-ADHD expressed the impairments associated with dyslexia alone (phonological, working memory) and ADHD alone (response inhibition) in an additive manner. Further studies have replicated this additive effect, of phonological impairments associated with dyslexia and EF impairments associated with ADHD expressing in an additive manner in the comorbid condition (Gooch, Snowling, & Hulme, 2011). Findings of additivity and a failure to replicate the phenocopy explanation suggests that it is not a sufficient explanation of comorbidity between dyslexia and ADHD. However, double dissociation studies of dyslexia and ADHD suggest that dyslexia alone is associated with a single phonological deficit and ADHD alone is associated with a single EF deficit, which does not consider findings of impaired EF in dyslexia alone (see section 2.6).

Rucklidge and Tannock (2002) proposed the cognitive subtype hypothesis when they found that the comorbid group demonstrated an additive and more severe profile of impairments (speed, naming) than either dyslexia alone (verbal working memory) or ADHD alone (speed, naming, inhibition). Studies supporting this explanation of comorbid dyslexia-ADHD have found phonological impairments in dyslexia alone, executive impairments in ADHD alone and additional rapid naming and working memory impairments in the comorbid condition (Bental & Tirosh, 2007). This strengthens the explanation of the comorbid condition as a unique cognitive subtype, although neither provide an explanation of findings of impaired EF in dyslexia alone (see section 2.6).

The multiple deficit/shared aetiology hypothesis (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010) suggests that complex neurodevelopmental conditions such as dyslexia and ADHD are unlikely to arise from a single deficit (e.g. phonological- dyslexia, EF- ADHD) rather each isolated condition is associated with multiple distinct and shared risk factors, and shared risk factors explain comorbidity. Pennington (2006) suggests that phonological impairments appear to be a specific risk for dyslexia, inhibition appears to be a specific risk for ADHD while processing speed appears to be a shared risk factor for both and therefore may explain comorbidity. However, studies differ with regard to the profile of impairments in each case, Willcutt et al. (2010) found that dyslexia, ADHD and comorbid dyslexia-ADHD were impaired relative to control participants on working

memory, inhibition, processing speed, phonological awareness and verbal reasoning and that the comorbid group had more severe processing speed and response inhibition impairments, suggesting that each condition is associated with EF. However, at a predictive level processing speed appeared to be the only shared risk factor, as ADHD symptoms were predicted by speed and inhibition and dyslexia symptoms were predicted by working memory, phonological awareness, speed and verbal reasoning. Processing speed as a shared overlapping risk factor has been replicated by other studies suggesting that it may explain overlap (Shanahan et al., 2006; Willcutt et al., 2005). These studies determine overlap based on shared cognitive processes implicated in core symptomatology but do not extend explanations to non-core symptomatology. These studies typically suggest that although EF is impaired it is not related to core symptoms in dyslexia, yet a number of studies suggest that EF impairments are associated with dyslexia (see section 2.6) and appear to be implicated in core reading symptoms (see section 2.8). This suggests the importance of exploring the role of EF in dyslexia while systematically accounting for processing speed impairments.

For now, at the level of impairments it appears that both dyslexia and ADHD appear to be underpinned by multiple cognitive deficits including EF, and the multiple deficit hypothesis may provide the optimum explanation for comorbidity (Germanò et al., 2010).

2.8 EF Involvement in Core (Reading) and Non-Core (Socio-Emotional) Issues Associated with Dyslexia Alone

As discussed in section 2.5, there is evidence to suggest that key EFs (response inhibition, updating and switching) may facilitate higher order cognitive abilities such as reasoning, problem solving and decision making, but also reading ability, math ability, self-regulation and socio-emotional wellbeing in typically developing populations (Blair & Razza, 2007; Carlson & Wang, 2007; Christopher et al., 2012; Diamond, 2013; Friedman et al., 2006; Miyake et al., 2000; van der Sluis et al., 2007; Vohs & Baumeister, 2011). Within Diamond's (2013) framework, a combination of common EF (response inhibition) and other core EFs of updating and switching may facilitate higher order cognitive processes like reading, while common EF may facilitate efficient self-regulatory skills (such as

effortful control and socio-emotional wellbeing). Given that dyslexia is associated with reading (core) and self-regulatory (non-core) problems, this framework may help isolate which aspects of EF, common (response inhibition) and/or specific (updating and switching) contribute to reading and socio-emotional problems in dyslexia alone.

EF Involvement in Core Issues (Reading)

Previous research suggests that EF may be involved in typical and atypical reading abilities, however, it is unclear which specific aspects of EF are necessary for typical reading and are compromised in atypical reading.

EF appears to play a role in typically developing reading skills, although different key EFs are found to be implicated in reading skills across studies. In typically developing participants it appears as though EF plays a role in reading ability; however, it is unclear which key EF factors are important. Some find that response inhibition is important for reading ability (Blair & Razza, 2007), some find that updating is important for reading ability (Christopher et al., 2012), and some suggest that switching is important reading ability (Cartwright, 2012). Other authors find that a combination of key EF abilities are predictive of reading abilities, such as updating and switching combined (van der Sluis et al., 2007) and response inhibition and updating combined (Arrington, Kulesz, Francis, Fletcher, & Barnes, 2014; Welsh, Nix, Blair, Bierman, & Nelson, 2010). All of these studies suggest that increased efficiency in EF is associated with better reading skills suggesting that EF may play a role in reading ability.

EF also appears to play a role in atypically developing reading skills/reading problems. In atypical reading, there is conflicting findings for which EFs are crucial, some find response inhibition and working memory updating to predict reading impairment in dyslexia (Booth et al., 2014; Wang & Yang, 2014), while other find inhibition and switching combined predict reading impairment in dyslexia (Altemeier, Abbott, & Berninger, 2008).

EF Involvement in Non-Core Issues (Socio-Emotional)

Conscious control and regulation of behaviour e.g. socio-emotional competence, has been

related to EF – particularly in the case of response inhibition (Diamond, 2013; Vohs & Baumeister, 2011). Self-regulatory and EF processes overlap in the frontal areas of the brain - particularly in the anterior cingulate cortex (Holroyd & Coles, 2002) - and are crucial for socialisation, emotional regulation, future planning and learning from mistakes (Vohs & Baumeister, 2011). In ADHD, this theory of self-regulation has been explored, and attention, executive function and inhibition are found to relate to surface problems with socio-emotional functioning (Barkley, 1997; Barkley, Fischer, Smallish, & Fletcher, 2006; Wheeler Maedgen & Carlson, 2000). This suggest that common EF (response inhibition) may be at the forefront when it comes to efficient self-regulation of emotion (Diamond, 2013).

Common EF (response inhibition) is consistently found to be necessary for typical socio-emotional behaviour regulation (Bohlin, Eninger, Brocki, & Thorell, 2012; Brunnekreef et al., 2007; Carlson & Wang, 2007; Eisenberg et al., 2009; Rhoades, Greenberg, & Domitrovich, 2009) and may be sensitive to detecting type of socio-emotional difficulties (internalizing, externalizing) (Albrecht, Banaschewski, Brandeis, Heinrich, & Rothenberger, 2005; Brunnekreef et al., 2007; Young et al., 2009).

Response inhibition may be a central transdiagnostic factor for explaining socio-emotional problems across a range of psychopathologies such as ADHD, obsessive compulsive disorder (OCD), and conduct disorder (CD) (Albrecht et al., 2005; Bohlin et al., 2012). These socio-emotional issues are also present in dyslexia (Knivsberg, Reichelt, & Nødland, 1999; Mugnaini et al., 2009). However, little research has been conducted on the predictors of socio-emotional problems associated with dyslexia. One study explored the predictive relationship between EF and socio-emotional problems in dyslexia and found that response inhibition and updating were predictive of the severity of externalizing problems expressed (Wang & Yang, 2014).

2.9 Neural Evidence for Compromised EF in Dyslexia Alone

At the neural level, there is evidence for impaired executive function in dyslexia. Poor performance on executive function tasks in dyslexia is correlated with under-activation of frontal brain areas important for executive functioning (Beneventi et al., 2010a; Horowitz-

Kraus, 2014). Common EF (response) inhibition abilities in dyslexia have been explored with ERPs (EEG). ERPs are measures of electrophysiological activity in the brain time locked to a specific cognitive process (Luck, 2014). N2 (occurring between 200-350ms) and P3 (occurring between 250-500ms) ERPs are useful indexes of inhibition in Go No-Go and stop signal task paradigms (Johnstone et al., 2007; Jonkman, Lansbergen, & Stauder, 2003; Pires, Leitão, Guerrini, & Simões, 2014). Typically, these ERPS are of a larger magnitude for inhibition compared to non-inhibition trials (Johnstone et al., 2007; Jonkman et al., 2003; Pires et al., 2014). Studies exploring inhibition ERPS in dyslexia suggest an abnormality in No-Go P3 amplitude in children with dyslexia relative to typically developing children (Liotti et al., 2010; van der Schoot, Licht, Horsley, & Sergeant, 2002).There is also evidence of abnormal frontal Pe amplitude (which is an error processing ERP) in dyslexia during a stop signal task (Van De Voorde et al., 2010).

Updating abilities in dyslexia have been explored with fMRI which indexes blood flow to brain regions during cognitive processes. Beneventi et al. (2010a) found evidence to suggest dyslexia is associated with an updating deficit in processing disorder specific (phoneme) information (see section 2.6), this study also employed fMRI to explore the neural underpinnings of disorder specific updating in dyslexia, and, found under-activation in frontal areas crucial for EF such as the inferior frontal gyrus, middle frontal gyrus, precentral gyrus, and the left cingulate gyrus (Beneventi et al., 2010a). Similar activation deficits are observed in dyslexia with fMRI also when completing a letter working memory updating task (Beneventi, Tønnessen, & Ersland, 2009). Switching abilities have been explored in dyslexia with ERPs during a Wisconsin Card Sort Task (Horowitz-Kraus, 2014). Horowitz-Kraus (2014) found that dyslexia is associated with decreased N1 and P3 ERPs compared to typically developing participants which are neural indices of attention (N1) and switching (P3) in this task. These findings suggest that dyslexia is associated with frontal under-activation during executive processing tasks. Unfortunately, there are only a few studies examining brain activation underpinning EF in dyslexia, making it difficult to comment on the extent to which EF is impaired.

However, functional activation during reading and phonological tasks in dyslexia suggest a role for frontal brain areas in the high-level reading and phonological impairments

observed in dyslexia. Reading impairments in dyslexia are found to be characterised by under activation of the left precentral gyrus, left temporal gyrus, inferior frontal gyrus, middle frontal gyrus, and left orbital frontal gyrus (Turkeltaub et al., 2002). It has been suggested that frontal areas may play a top down role in phonological processing. For instance, Richlan et al. (2010) found that dyslexia readers compared to control readers demonstrate under-activation in the left occipito-temporal region, the inferior frontal gyrus and the inferior parietal lobule when reading pseudo-words. The authors argue that this is evidence of top down attentional control of phonological representations in the inferior frontal gyrus because the inferior parietal lobule plays a role in attentional mechanisms (Richlan, 2012). Another study found under-activation in the inferior frontal gyrus, left inferior temporal gyrus, left inferior parietal and middle temporal gyrus in dyslexia compared to controls during a phoneme rhyme task (Cao, Bitan, Chou, Burman, & Booth, 2006). Cao et al. (2006) suggest that under-activation in inferior parietal lobe and inferior frontal gyrus in dyslexia indicates that they do not demonstrate top down executive control (manipulation) of phoneme representations as the control participants do.

In a similar vein, brain activation differences after reading interventions suggest that improved reading and phonological processing are associated with pre-post improvements in frontal and parietal brain areas. Pre-post intervention improvements in phoneme and morpheme mapping are found to be underpinned by activation changes in frontal (right superior frontal gyrus, left middle frontal gyrus, inferior frontal gyrus) and parietal (bilateral superior parietal) regions (Aylward et al., 2003), suggesting that phonological abilities are underpinned by activation in frontal and parietal regions of the brain. Other intervention studies have demonstrated that reading improvements are correlated with improved activation in left prefrontal cortex, left fusiform gyrus and right anterior cingulate cortex (Gaab et al., 2007; Horowitz-Kraus & Holland, 2015; Temple et al., 2003).

Overall the neural underpinnings of reading in dyslexia suggest a role of frontal brain areas in reading and phonological processing, and findings by Beneventi et al. (2010a) suggest executive impairments in processing of phoneme information, which may be reflective of

a disorder specific EF impairment in dyslexia.

2.10 Critical Issues Across EF Profiling and Predictive Studies

The EF profile associated with dyslexia and whether this profile is overlapping, additive or more severe in comorbid dyslexia-ADHD is unclear from previous research. It is also unclear whether EF is implicated in the core (reading) and non-core (socio-emotional) issues that characterise dyslexia alone. Several critical issues apparent across profiling and predictive studies point to potential reasons for inconsistent findings. These include discrepancies with: (1) sample characteristics/inclusion criteria, (2) theoretically informed profiling and measurement approach, (3) task content, and (4) systematic control of confounding variables.

EF profiling and predictive studies differ in how they classify participants with dyslexia and how they screen for potentially undiagnosed/elevated ADHD within the sample. Some studies include only those with a diagnosis of dyslexia carried out by a certified psychologist (de Jong et al., 2009; Gooch et al., 2011; Moura et al., 2016; Varvara, Varuzza, Sorrentino, Vicari, & Menghini, 2014), while others classify participants with dyslexia on the basis of standardised tools which vary in cut off criteria (Bexkens et al., 2014; Peng et al., 2013; Wang & Yang, 2014). In addition, most EF profiling and predictive studies do not systematically screen for ADHD. For example, Brosnan et al. (2002) found evidence for a response inhibition impairment in dyslexia but did not account for ADHD in the sample, while Reiter et al. (2005) accounted for ADHD in the sample and found no evidence of a response inhibition impairment. This is unsatisfactory, as both conditions frequently co-occur, and ADHD is characterised by EF deficits (Barkley, 1997). This also makes it difficult to determine if EF impairments are associated with dyslexia alone or manifest due to the presence of elevated ADHD within the sample. This above highlights the importance of exploring how an EF profile manifests in dyslexia alone screened for elevated ADHD and how this compares to those with a comorbid diagnosis of dyslexia and ADHD.

Studies also differ greatly in terms of profiling approach and impurity of measures employed. Several studies view EF as a unitary construct (employing complex measures such as Wisconsin Card Sort Task or unitary EF composites) (Beidas, Khateb, & Breznitz,

2013; Pennington et al., 1993), as multiple but separate abilities (employing multiple complex measures such as planning, switching, inhibition, interference control and verbal fluency) (De Lima et al., 2012; Menghini et al., 2010; Moura et al., 2016, 2015; Willcutt et al., 2005) or look at separate processes in isolation with single tasks (Beneventi et al., 2010a; Poljac et al., 2010; Schmid et al., 2011). Different EF tasks are often used interchangeably to measure different underlying constructs without any justification for why they purportedly mean one thing in a particular context and another in a different context. For example, the Stroop task (read the ink colour of a colour word, such as RED) is consistently used to measure response inhibition as the word RED interferes with naming the colour of the ink GREEN (Reiter et al., 2005), yet is also used in some studies to measure switching (Helland & Asbjørnsen, 2000); and working memory tasks range from simple memory span to complex updating and manipulation of information, which differ greatly in the underlying task demands. The range of tasks used to measure different EFs makes it difficult to understand what is being measured, thus impacting upon conclusions about EF involvement in dyslexia.

Complex tasks lack specificity in isolating key EF impairments (section 2.5 for outline of key EFs), as performance is driven by a range of these key EFs (response inhibition, updating and switching) as well as non-EF processes (e.g. learning from feedback in WCST) (Miyake et al., 2000; Miyake & Friedman, 2012; Snyder et al., 2015). Viewing EF as a number of separate unrelated abilities or looking at single processes in isolation is problematic because it fails to address the theoretical understanding that these abilities are facilitated by a number of core underlying processes which are both related (common EF: response inhibition) and unique (updating and switching) and sometimes antagonistically related (trade-offs between common EF and switching) (Snyder et al., 2015). If EFs operate in a trade-off manner, this suggests that the profile of abilities associated with a condition may manifest in a strengths and impairments pattern. An assumption of many profiling studies is that impaired EF abilities are related to severity of symptoms. Yet, a line of literature exploring EF in relation to socio-emotional problems suggests that the relationship may not be linear. Some studies suggest that enhanced as well as impaired effortful control skills are linked to socio-emotional problems, for

instance those with enhanced skills expressed more internalizing type problems while those with impaired skills expressed more externalizing type problems (Eisenberg et al., 2005). This suggests that a moderate level of EF may be conducive to adaptive outcomes, other studies have found that reduced or enhanced EF abilities are associated with socio-emotional problems (Carlson & Wang, 2007), or that children with enhanced inhibitory control more likely to have internalizing and those with impaired inhibitory control are more likely to demonstrate externalizing (Kooijmans, Scheres, & Oosterlaan, 2000). This may also be the case for other outcomes related to EF, yet studies typically explore only impairments in relation to core and non-core symptoms of conditions.

A meta-analysis exploring the effects of tasks used in identifying EF deficits in dyslexia indicated that there are major problems with task impurity, and that no concrete conclusion on which EFs are implicated in dyslexia can be made until researchers begin considering the underlying task demands when choosing tasks (Booth, Boyle, & Kelly, 2010). Extensive research suggests that EF is comprised of related (common EF: response inhibition) yet separable abilities (updating and switching) (Miyake & Friedman, 2012) which are sensitively measured at the latent level with multiple tasks of each ability (Friedman et al., 2007, 2008; Miyake & Friedman, 2012). Yet, most EF profiling and predictive studies fail to theoretically inform research with validated models of EF and employ sensitive measures.

To understand exactly how key EFs are implicated in dyslexia (and subsequently manifest in comorbid dyslexia) and how they are related to core and non-core symptoms, profiling studies should be informed by validated EF models and employ the most sensitive measures (Goschke, 2014; Snyder et al., 2015). Latent variable analysis is the most suitable and sensitive approach to measuring EF (Friedman & Miyake, 2016; Miyake & Friedman, 2012), however large sample sizes are required which is not practical for clinical research where typically smaller sample sizes are employed. A solution is to use EF z-mean composites of each construct with clinical samples as they provide cleaner measures by filtering out any non-EF noise – effectively, z-mean composites are similar to latent (Snyder et al., 2015). By systematically accounting for task impurity issues within EF

measurement, studies should be able to explore core EFs and their predictive utility for symptom severity.

The majority of EF studies in dyslexia do not address disorder specificity (phoneme) of impairment, despite a recent meta-analysis indicating that it is not clear whether EF deficits in dyslexia are disorder specific (manifesting with verbal, language related content such as phonemes) or general (manifesting with all types of content) (Booth et al., 2010). The only emerging area within EF research that is currently examining disorder specific versus general problems is working memory/updating research, and most of the literature to date suggests that dyslexia may be associated with disorder specific impairments. For example, Beneventi et al. (2010a) adapted a working memory 2-back task to have a disorder specific phoneme processing rule, in this task (*see Figure 10*) participants had to decide if a current image matched an image presented 2-back based on first phoneme sound of the pictures presented. For example, if the participant viewed a picture of a dog, then a cat, and then a dress, they would press '*match*' for dress because it begins with the same first phoneme as dog. Essentially, participants were required to sound out and parse the phonemes and update this information in working memory. Participants with dyslexia were significantly impaired on this task at the behavioural and neural levels. Impaired behavioural performance was correlated with under-activation in frontal areas related to executive processing – under activated inferior frontal gyrus, middle frontal gyrus and superior parietal lobule, left cingulate gyrus and precentral gyrus compared to controls (Beneventi et al., 2010a).

However, Beneventi et al. (2010a) did not compare performance on the phoneme-updating task to a visual picture-updating control task (match is visual) to determine if the EF deficit was disorder-specific to processing phoneme information. A confound of the phoneme updating rule is that it may place additional demands on inhibitory control, with a phoneme updating rule the match is based on sounds of pictures which are not visually matched (e.g. bat, ball), if a picture is presented that matches the visual features then inhibitory control may be required to resolve this interference as well as update information based on the sound. With the picture task, although the name of the picture may come to mind, no interference resolution is involved as the picture names are the

same and are matched based on visual features. Disorder specificity (phoneme) of impairment has remained largely unexplored with other key EFs such as response inhibition and switching. Given that the most consistent impairment found in dyslexia is a phonological processing impairment, it may be the case that EF deficits in dyslexia are disorder-specific to processing phoneme information. Indeed, phonological deficits appear to manifest more so on tasks tapping EF processes (Ramus & Szenkovits, 2008) and neuro-imaging studies suggest top down EF control of phonological information may underlie task performance (Richlan, 2012).

Based on the behavioural and neural evidence of a disorder specific (phoneme) updating impairment in dyslexia (Beneventi et al., 2010a) (outlined in section 2.6 and 2.9), it is important to explore if this disorder specificity (phoneme) emerges in other EFs such as response inhibition and switching. Disorder specificity (phoneme) of EF in dyslexia remains unexplored with other EFs (response inhibition and switching), and it is unclear whether this disorder specific EF processing impairment would manifest more severely when ADHD co-occurs as may be the case with non-specific general EFs. To understand the specificity of EF in dyslexia and how this relates to comorbid dyslexia-ADHD, profiling studies need to explore disorder specific patterns of EF by adapting pre-existing validated measures grounded in EF theory to include disorder specific content (e.g. phoneme information in dyslexia) (Goschke, 2014).

Another problem limiting the understanding of the EF profile associated with dyslexia and comorbid dyslexia-ADHD, and EF involvement in core and non-core issues associated with dyslexia, is a lack of control of potential confounding variables. Processing speed is a confound to understanding the role of EF in each condition and severity of symptoms expressed. Previous research indicates that processing speed is impaired in dyslexia, and ADHD and may be a shared risk factor (Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2005). This is problematic due to EF tests being scored based on speed and accuracy, meaning that if processing speed is not accounted for, evidence for an EF impairment may really be due to a general processing speed impairment and not due to high-level EF problem per se. One study examining EF in dyslexia found evidence for a number of core EF impairments (response inhibition and updating), but when processing

speed was controlled, the impairments disappeared (Peng et al., 2013). Therefore, studies are limited by the fact that they mostly do not control for processing speed, and this makes it difficult to understand if EF is implicated in dyslexia, whether EF impairments are compounded when dyslexia and ADHD co-occur, and if EF is implicated in core and non-core issues associated with dyslexia alone. To account for this confound, profiling and predictive studies should account for processing speed abilities.

2.11 A Framework for Exploring EF: Profile and Predictive Utility

The EF profile associated with dyslexia and comorbid dyslexia-ADHD and the role of EF in core and non-core issues associated with dyslexia is unclear from previous research. Limitations in previous research include discrepancies with: (1) sample characteristics/inclusion criteria, (2) theoretically informed profiling and measurement approach, (3) task content, and (4) systematic control of confounding variables.

These issues need to be addressed if progress is to be made in understanding how the EF profile manifests in dyslexia and comorbid dyslexia-ADHD, and whether it is involved in symptom expression. Recruiting a sample with a clinical diagnosis of dyslexia and ADHD and employing a standardised screening tool to account for elevated ADHD in dyslexia may address sampling issues within previous research. Informing EF with validated models of key EFs such as Miyake and Friedman's (2012) model and Diamond's (2013) model may enhance the understanding of how key EFs are implicated in dyslexia and comorbid dyslexia-ADHD, and whether they can feasibly explain core and non-core symptoms. Issues of task impurity from previous research could be addressed by employing multiple measures of each key EF and creating z-mean composite scores for group comparisons (Snyder et al., 2015). Individual EF z-mean composite scores could be created for each construct by standardising performance on each measure of a key EF and dividing it by the number of tasks. Sensitive measures of EF could be adapted to include disorder specific (phoneme) information to address content issues in previous research (Goschke, 2014). To account for the confound of processing speed, these abilities could be statistically controlled for while exploring the profile of EF associated with each condition and the role of EF in symptom expression. Addressing these issues may allow more fine-grained

conclusions on which aspects of EF are associated with each condition and which aspects are important for core and non-core outcomes.

Incorporating all of these issues, within the Miyake and Friedman (2012) and Diamond (2013) frameworks (*see Figure 11*), provides a viable approach for understanding the profile of key EFs associated with dyslexia and comorbid dyslexia-ADHD, and, for exploring the predictive ability of key EFs for core (reading) and non-core (socio-emotional) issues associated with dyslexia alone. Exploring EF profile associated with each condition at the EF z-mean composite while controlling for processing speed enables an exploration of common (response inhibition) and unique (updating, switching) EF abilities associated with dyslexia and comorbid dyslexia-ADHD compared to controls, and for an exploration of whether EF profile is more severe in the comorbid group. Computing z-mean composite scores of common (response inhibition) and unique (updating, switching) EF requires multiple measures tapping different domains (e.g. picture, phoneme). This requirement allows for the framework to address the additional question of whether dyslexia is associated with a disorder specific (phoneme) executive processing impairment a the common (response inhibition) and unique (updating, switching) levels, and, to explore whether this also manifests more severely in comorbid dyslexia-ADHD. After confirming whether key EFs are associated with dyslexia alone and manifest more severely in comorbid dyslexia-ADHD, this framework will allow for an exploration of how common (response inhibition) and unique (updating and switching) aspects of EF contribute to core (reading) and non-core (socio-emotional) symptoms associated with dyslexia alone. Controlling for individual differences in processing speed at all stages will enable firm conclusions on EF involvement independent of processing speed impairment.

This framework has implications for understanding EFs which may be targeted to improve symptom expression in dyslexia alone, and will be employed as a framework to explore EF in dyslexia and comorbid dyslexia-ADHD (see Chapter 3) and to explore the role in core and non-core behaviours associated with dyslexia (see Chapter 4).

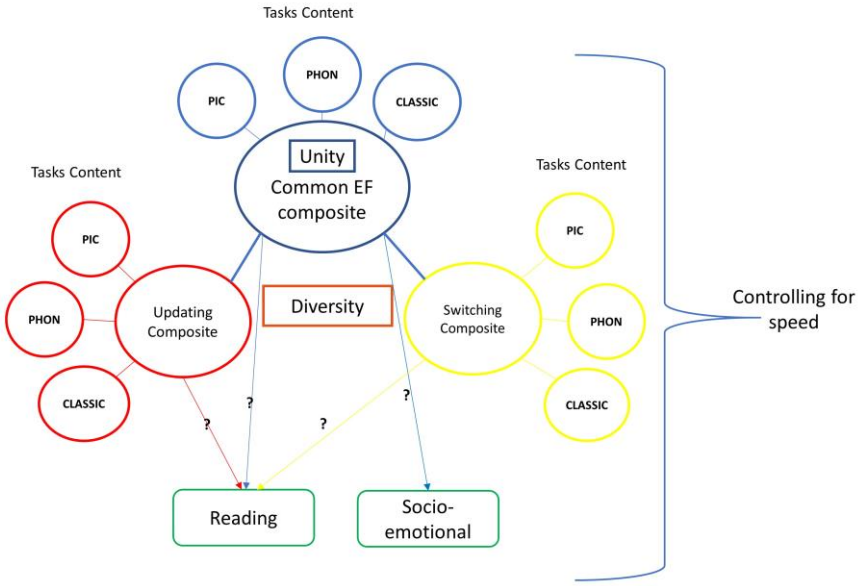


Figure 11 Miyake and Friedman's (2012) and Diamond's (2013) EF frameworks adapted to explore EF profile in Dyslexia and Comorbid Dyslexia-ADHD, and Exploring EF involvement in Core and Non-Core Issues in Dyslexia

2.12 Targeting EF Impairments: Modifiability of Executive Function

Our proposed framework has implications for targeted interventions aimed at reducing symptom expression in dyslexia, because it can elucidate the EF profile (strengths and impairments in common: response inhibition, and unique: updating and switching abilities) associated with dyslexia and isolate key EFs implicated in core and non-core symptoms. Previous research suggests that EF is modifiable, with training interventions resulting in changes to EF and unrelated outcomes such as reading ability, reasoning and behavioural problems(Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Klingberg, 2010; Loosli et al., 2012; Mezzacappa & Buckner, 2010). Therefore, key EFs implicated in the aetiology and symptom severity of dyslexia may be modifiable with a targeted training intervention.

Training approaches differ greatly across the EF literature with different studies training different EF processes (response inhibition, working memory/updating, switching), including variability in sample and age ranges, and further variability in how successful training gains are measured in terms of behavioural outcomes. Operational definitions of

"success" in training transfer also differ within the literature depending on whether the sample is typical or atypical. Training studies with typical samples generally target a cognitive process shown to be important for a behavioural outcome, as is the case for working memory and intelligence or reading outcomes (Baddeley, 2012). These cognitive processes and behavioural outcomes are not impaired in typical samples, so the overall aim is to see if they can be enhanced but not restored. Success of transfer of training is usually based on direct measures of the trained cognitive process (e.g. working memory) and on related behavioural outcomes (e.g. intelligence). In contrast, training studies with atypical samples target a cognitive process shown to be implicated in the aetiology and symptom severity of a clinical condition, as in the case of response inhibition and symptoms of ADHD (Barkley, 1997). These cognitive and behavioural outcomes are impaired in atypical samples, so the overall aim is to see if the underlying cognitive process and behavioural outcome can be restored to typical function. Success of transfer of training is usually based on direct measures of the trained cognitive process which is impaired in the condition (e.g. response inhibition and ADHD) and measures of symptom expression (e.g. inattention and impulsivity).

In typical populations, common EF (response inhibition) appears to improve as a function of training, with evidence of improvement at the cognitive (Berkman et al., 2014; Enge et al., 2014; Johnstone et al., 2010; Spierer, Chavan, & Manuel, 2013) and underlying neural levels (Berkman et al., 2014). However, successful transfer of training is debated, with some reporting that training transfers to improvements in a wide range of regulatory behaviours (such as food consumption, alcohol intake and gambling (Spierer et al., 2013). However, others have reported little or no transfer to untrained EF measures and fluid intelligence (Enge et al., 2014; Thorell, Lindqvist, Bergman Nutley, Bohlin, & Klingberg, 2009). In typical populations, working memory/updating training has resulted in direct transfer to improved working memory/updating (Dunning, Holmes, & Gathercole, 2013; Holmes, Gathercole, & Dunning, 2009; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Jaeggi et al., 2011; Karbach, Strobach, & Schubert, 2015; Loosli et al., 2012). However, studies differ in the extent to which they find transfer to other behaviours with some studies finding transfer to improvements in reading and fluid intelligence (Jaeggi et al., 2008;

Loosli et al., 2012), while others find no transfer to fluid intelligence, reading or math ability (Holmes et al., 2009; Karbach et al., 2015). Although less work has been conducted on the effects of switching training, there is evidence of direct transfer to switching abilities and transfer to working memory, fluid intelligence and response inhibition (Karbach & Kray, 2009). This suggests that EF processes are modifiable at the direct level in typical samples and may transfer to improved outcomes in closely related behaviours.

EF training has been proposed as a potential intervention for ameliorating cognitive deficits associated with symptoms in complex neurodevelopmental conditions (Keshavan, Vinogradov, Rumsey, Sherrill, & Wagner, 2014). In atypical samples, to our knowledge the transfer effects of isolated common EF training remains unexplored. Working memory training has been explored in atypical populations, and, has resulted in direct improvements in working memory abilities in those with dyslexia and special education needs (Dahlin, 2011; Luo, Wang, Wu, Zhu, & Zhang, 2013; Shiran & Breznitz, 2011). Working memory training was found to transfer to reduced symptom expression (reading and phoneme problems) in children (Luo et al., 2013) as well as adults with dyslexia (Shiran & Breznitz, 2011). One study found that these improvements were greater than what was observed with a reading intervention targeted at the behavioural level of impairments (Shiran & Breznitz, 2011), suggesting that targeting underlying cognitive factors which may be implicated in symptom severity may be more beneficial than targeting the symptom. There is evidence of switching training improving switching abilities in ADHD, as well as other EFs and fluid intelligence (Kray, Karbach, Haenig, & Freitag, 2012), however this study did not track transfer to reduced symptom expression in ADHD.

Mixed training approaches (where more than one EF is trained) have also been explored in atypical samples. Horowitz-Kraus (2015) explored transfer of combined training (working memory, naming, speed, inhibition, flexibility) in children with ADHD and comorbid dyslexia-ADHD and found differential effects in each subgroup. Training transferred to improved reading ability, speed and spatial abilities in those with comorbid dyslexia-ADHD and improved working memory and speed but not reading ability in those with ADHD alone (Horowitz-Kraus, 2015), suggesting that an impairment in outcome may be a

necessary pre-requisite for transfer at the behavioural level in clinical conditions. Combined working memory and response inhibition training has been explored in ADHD (Johnstone et al., 2012, 2010), and direct improvements in working memory and response inhibition are found to transfer to reduced symptoms of ADHD (Johnstone et al., 2012, 2010), which were sustained at 6-week follow up (Johnstone et al., 2012). These findings suggest that EF training may have potential for targeting the core and non-core issues in dyslexia. However, it is difficult to conclude which trained factor contributed to overall changes as both working memory and inhibition were trained.

Although there is debate regarding the transfer of EF training to behavioural outcomes in typical samples, the pattern of results emerging from atypical samples suggests that EF training targeted at underlying impairments can improve executive processes underpinning the disorder, and in some cases, generalise to improvements in the severity of symptoms associated with clinical conditions. Although some reviews suggest that training efficacy is not fully established for clinical conditions, and fundamental issues within the research field need to be addressed to progress in this field (Keshavan et al., 2014; Kirk, Gray, Riby, & Cornish, 2015). According to Kirk et al. (2015, p. 157) "many current cognitive training programs lack a clear underlying theoretical model, which makes it hard to ascertain which domain the programs are truly targeting". This highlights the importance of exploring EF training in dyslexia, especially if our proposed theoretical framework can elucidate common (response inhibition) or unique (working memory updating, switching) EF impairments which are implicated in core (reading) and non-core (socio-emotional) issues associated with the condition. Before we can train EF in dyslexia, fundamental issues in EF profiling and predictive studies (see section 2.10) need to be addressed in order to target clinically relevant EFs in dyslexia (i.e. EFs which are predictive of core symptoms).

2.13 Conclusion

EF may be candidate cognitive level endophenotype for explaining overlap between dyslexia and ADHD (two behaviourally distinct neurodevelopmental conditions) and for explaining the range of core and non-core behaviours associated with dyslexia. As such, EF

may be an early and modifiable risk factor associated with dyslexia which could be targeted prior to reading instruction to prevent symptom expression or after reading instruction to reduce severity of symptom expression. However, problems across previous literature relating to sample characteristics, theoretical approach to profiling and task selection, task content, and a lack of control for confounding variables, make it difficult to isolate key EFs implicated in disorder etiology and symptom severity which can be targeted with training. Before progressing with targeted training, problems with the literature need to be tackled and incorporated into a research design that addresses current knowledge gaps. It's currently unclear what exact profile of EF is associated with and implicated in the symptoms of dyslexia, and, whether this EF profile manifests more severely in comorbid dyslexia-ADHD at the construct and disorder-specific content level while controlling for processing speed abilities. Indeed, EF may offer a viable treatment option, however, previously mentioned gaps need to be addressed in order to decide most appropriate type (inhibition, updating or switching) and domain of training (visual or verbal) for children with dyslexia. In addition, the role of key EFs in core and non-core symptoms of dyslexia needs to be established to theoretically inform the link between trained EF and transfer to improved symptoms in dyslexia.

2.14 PhD Aims

In order to establish EF as a candidate early and modifiable risk factor implicated in the etiology and symptom severity of dyslexia this PhD aims to:

(1) Establish the EF profile (strengths and impairments in common: response inhibition, and unique: updating and switching abilities) associated with dyslexia and whether this manifests more severely in comorbid dyslexia-ADHD at the EF z-mean composite level using Miyake and Friedman's (2012) framework while controlling for individual differences in processing speed.

(2) Determine whether EF profile manifests differently in dyslexia and comorbid dyslexia-ADHD with disorder specific information (phoneme task content).

(3) Develop and validate EF z-mean predictive models of clinically-relevant core and non-

core symptoms associated with dyslexia alone while systemically screening for potentially undiagnosed ADHD, and, controlling for individual differences in processing speed.

(4) Assess whether training targeted at key EFs implicated in core and non-core symptoms of dyslexia are modifiable with training at cognitive and neural levels and capable of inducing change at the level of symptom expression.

These aims will be addressed by implementing our proposed framework outlined in section 2.11 which accounts for issues across previous profiling and predictive studies.

Chapter 3: Profiling Executive Function in Dyslexia and Comorbid Dyslexia ADHD

3.1 Introduction

At the symptom level dyslexia and ADHD appear distinct, yet they co-occur at a greater than chance rate (comorbidity estimated in 20-40% of cases) (Wadsworth, DeFries, Willcutt, Pennington, & Olson, 2015; Willcutt & Pennington, 2000), suggestive of shared genetic, neural and cognitive underpinnings (Gottesman & Gould, 2003; Rommelse et al., 2009). Both disorders have been linked at the genetic level via pleiotropic risk genes (Gayan et al., 2005) and genes crucial for the development of dopamine receptors in prefrontal brain areas necessary for the development of EF (Kegel & Bus, 2013). EF abilities appear to be highly heritable at the latent level (common EF: response inhibition-96%; and specific: updating- 100%, switching-79%) and although EF abilities develop with age heritability estimates remain relatively stable across a 6-year developmental period which transitions from late adolescence to early adulthood (17-21 years) (common EF: 86%; specific: updating- 100%, switching- 91%) (Friedman et al., 2016). In middle childhood (7-15 years), there is evidence for high heritability of a common EF factor (100%) and unique switching factor (59%) (Engelhardt, Briley, Mann, Harden, & Tucker-Drob, 2015).Given the strong genetic influence, EF has been proposed as a useful cognitive level endophenotype (intermediate in the gene-symptom pathway) for sensitively detecting prodromal phases and predicting severity of functional outcome (Glahn et al., 2014, 2016; Goschke, 2014; Miller & Rockstroh, 2013; Snyder et al., 2015), and, for wide range of neurodevelopmental such as ADHD and ASD (Rommelse et al., 2009; Rommelse, Geurts, Franke, Buitelaar, & Hartman, 2011). EF has been implicated in ADHD and self-regulatory behaviours at the endophenotype level (Castellanos & Tannock, 2002; Crosbie et al., 2008; Friedman et al., 2008; Rommelse et al., 2009), and some researchers propose it as a candidate explanatory framework for understanding high co-occurrence of attentional and reading problems (Kegel & Bus, 2013; Rommelse et al., 2009).

As a candidate endophenotype, EF may be an early and modifiable risk factor associated with dyslexia and comorbid dyslexia-ADHD. However, as outlined in Chapter 2 (literature review), critical issues in previous literature such as – sample characteristics, theoretical approach to profiling and task selection, task content, and a lack of control of confounding variables – make it difficult to infer the EF profile associated with these clinical conditions and whether it sensitively predicts different levels of functional outcome at the level of symptoms (mild, moderate, severe). These issues need to be addressed before we can progress with targeted treatment aimed at key EF abilities implicated in disorder etiology and symptom severity. Previous research suggests that EF training may directly improve EF (cognitive and neural) (Berkman et al., 2014; Manuel et al., 2013) and may transfer to behavioural level improvements (transfer at phenotype level to reading and ADHD symptoms) (Johnstone et al., 2010; Loosli et al., 2012). If shown to be implicated in dyslexia and comorbid dyslexia-ADHD; and more importantly, of clinical relevance, then EF training will be a novel avenue for remediation of behavioural outcomes.

From previous research, the exact EF profile (strengths and impairments in response inhibition, updating and switching) (Friedman & Miyake, 2016; Miyake & Friedman, 2012) associated with dyslexia and whether this profile overlaps with or manifests more severely in comorbid dyslexia-ADHD, are unclear (Booth et al., 2010; Germanò et al., 2010). This is important to explore as both dyslexia and ADHD in isolation are associated with prefrontal brain abnormalities or activation differences (Beneventi et al., 2010a; Clark et al., 2014; Horowitz-Kraus, 2014; Qiu et al., 2011), EF impairments (Barkley, 1997; Bental & Tirosh, 2007; Poljac et al., 2010; Willcutt et al., 2005),and socio-emotional problems (Knivsberg & Andreassen, 2008; Mugnaini et al., 2009; Wheeler Maedgen & Carlson, 2000).

Although some studies report that dyslexia is not associated with EF impairments (Bental & Tirosh, 2007; Bexkens et al., 2014; Peng et al., 2013; Smith-Spark & Fisk, 2007), the majority of the literature thus far suggests that dyslexia is associated with EF impairments (Beneventi et al., 2010a; Brosnan et al., 2002; Helland & Asbjørnsen, 2000; Menghini et al., 2010; Moura et al., 2016; Nydén, Gillberg, Hjelmquist, & Heiman, 1999; Poljac et al., 2010; van der Sluis et al., 2007; Willcutt et al., 2001, 2005) (see Table 2). What is lacking within the literature, however, is critical and in-depth knowledge of the profile of key EFs

(strengths and impairments in inhibition, updating and switching) associated with dyslexia (as discussed in section 2.10). EF impairments are also found in comorbid dyslexia-ADHD (Gooch et al., 2011; Moura et al., 2016; van der Sluis et al., 2007; Willcutt et al., 2001, 2005), but again more in-depth knowledge is needed of the profile of key EFs associated with comorbid dyslexia-ADHD – in particular how this manifests relative to each isolated condition. Previous literature cannot make firm conclusions on the key EF profile associated with each condition due to weak theoretical approaches to profiling and task selection, as well as methodological confounds (as discussed in section 2.10).

A number of hypotheses attempt to explain how the profile of cognitive impairments (not just EF) manifest across dyslexia, ADHD and comorbid dyslexia-ADHD. As we saw in section 2.7 of the literature review, most of these hypotheses approach explanations of comorbidity from a single deficit viewpoint (i.e. impaired phonology in dyslexia, impaired EF in ADHD) (Pennington et al., 1993; Rucklidge & Tannock, 2002; Willcutt et al., 2001). Typically, research studies exploring the profile associated with comorbid dyslexia-ADHD employ a double dissociation design, whereby manifestations of cognitive impairments associated with dyslexia (phonological) and ADHD (EF) are explored in comorbid dyslexia-ADHD. The initial phenocopy hypothesis proposed by (Pennington et al., 1993) explored comorbidity with this design and found that the profile associated with comorbid dyslexia-ADHD (phonological impairments) matched that of dyslexia alone (phonological impairments) and not ADHD (EF impairments), leading them to suggest that the frustrations associated with reading elicit ADHD-like symptoms in the absence of underlying EF impairments. Therefore, from a phenocopy perspective neither dyslexia or comorbid dyslexia-ADHD would be associated with EF impairments.

However, subsequent research failed to replicate these findings and instead suggested that the cognitive profile of comorbid dyslexia-ADHD is an *additive* combination of impairments associated with dyslexia alone (phonological) and ADHD alone (EF) (Gooch et al., 2011; Willcutt et al., 2001). Willcutt et al. (2001) found a pattern for a double deficit, such that the dyslexia groups (dyslexia alone and comorbid dyslexia-ADHD) were characterised by more severe phonological impairments while the ADHD groups (ADHD alone and comorbid dyslexia-ADHD) were characterised by more severe EF impairments.

This finding has been replicated by others, who also found an additive combination of impairments associated with dyslexia (phonological) and ADHD (EF) in the comorbid condition (Gooch et al., 2011). However, Willcutt et al. (2001) found that each clinical group was impaired relative to control participants on measures of EF, suggesting that the boundaries of these conditions may not be as discrete as suggested by single deficit explanations. Overall, these findings suggest that the phenocopy hypothesis is not a sufficient explanation for how the cognitive profile associated with comorbid dyslexia-ADHD manifests.

There is also evidence that the cognitive profile manifests more severely in the comorbid condition relative to each isolated condition, as impairments may not be simply additive (Willcutt et al., 2001), but instead *magnified* resulting in a unique cognitive subtype (Rucklidge & Tannock, 2002). Rucklidge and Tannock (2002) found that although the comorbid group demonstrated an additive profile of impairments associated with dyslexia alone (verbal working memory) and ADHD alone (speed, naming, inhibition) some of these impairments manifested more severely (speed, naming) than in either isolated condition. Other studies supporting the cognitive subtype view, found that the comorbid group may have additional impairments in rapid naming and working memory which are not found in either isolated condition (dyslexia-phonological, ADHD-EF) (Bental & Tirosh, 2007).

The phenocopy (Pennington et al., 1993) and cognitive subtype hypotheses (Rucklidge & Tannock, 2002) ultimately approach the understanding of comorbid dyslexia-ADHD from a single impairment viewpoint (i.e. phonological impairments in dyslexia, EF impairments in ADHD) which cannot account for findings of impaired EF in each clinical condition (Willcutt et al., 2001) or for the wealth of studies suggesting impaired EF in dyslexia alone (see section 2.6). This led to the multiple deficit hypothesis which suggests that dyslexia and ADHD are associated with *multiple distinct but also overlapping impairments* which may explain comorbidity (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010). This hypothesis may be the best explanation of comorbid dyslexia-ADHD thus far, as a comprehensive review of previous literature suggests that there is evidence for multiple cognitive impairments in each condition (Germanò et al., 2010).

Although multiple deficit explanations of comorbidity may provide more insight into why dyslexia and ADHD are highly comorbid (due to overlapping shared impairments) studies differ with regard to the unique and shared profile of impairments associated with each condition. At the level of associated impairments, Willcutt et al. (2010) found impaired inhibition, working memory, processing speed, phonology and verbal reasoning in all three conditions relative to control participants, as well as more severe impairments in processing speed and inhibition in the comorbid group relative to the other clinical groups, suggesting multiple cognitive processes are impaired and may manifest more severely in the comorbid condition. However, Willcutt et al. (2010) found that only some of these impairments were important for predicting dyslexia (underpinned by working memory, phonological, processing speed and verbal reasoning) and ADHD (underpinned by inhibition and processing speed), suggesting that processing speed may be an overlapping impairment. Yet, other studies exploring multiple deficits in relation to the severity of core symptoms (reading in dyslexia, inattention and hyperactivity in ADHD) suggest that phonological impairments are unique predictors of core dyslexia symptoms, inhibition impairments are unique predictors of core ADHD symptoms, while working memory and speed are shared overlapping predictors of dyslexia and ADHD symptoms (McGrath et al., 2011). Although studies differ with the extent to which cognitive impairments are unique or shared, one pattern that consistently emerges from studies exploring the multiple deficit hypothesis is that processing speed is a shared overlapping impairment (McGrath et al., 2011; Pennington, 2006; Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2010).

These studies define overlap as shared cognitive processes which are predictive of both dyslexia and ADHD diagnoses (Willcutt et al., 2010) or as cognitive processes which are implicated in core symptoms of each clinical condition (McGrath et al., 2011). Although some suggest that working memory may indeed be a shared overlapping risk factor, they also suggest that impaired EFs are not predictive of diagnostic status or symptom severity. These studies cannot account for conflicting findings that working memory and inhibition are predictive of core reading symptoms in dyslexia (Booth et al., 2014; Wang & Yang,

2014), and that inhibition is predictive of non-core socio-emotional symptoms in dyslexia (Wang & Yang, 2014).

A selective and critical review of previous research studies exploring EF in dyslexia alone and comorbid dyslexia-ADHD (see Table 2), highlights that studies profiling EF in dyslexia and comorbid dyslexia-ADHD are disparate: mainly due to differences in sample characteristics/criteria, theoretically informed profiling approach, measurement tools and systematic control of confounding variables. These issues make it difficult to infer the exact profile of EF associated with dyslexia and whether this profile is magnified in comorbid dyslexia-ADHD.

As will be discussed in Section 3.5, the current study aims to elucidate the profile of key EFs (strengths and impairments in response inhibition, updating and switching) (Friedman & Miyake, 2016; Miyake & Friedman, 2012) associated with dyslexia alone and comorbid dyslexia-ADHD compared to control children, and, to clarify whether this profile is overlapping with and manifests more severely in comorbid dyslexia-ADHD than dyslexia alone. Although an optimal approach would be to explore whether this profile manifests more severely in comorbid compared to dyslexia alone and ADHD alone, the current study (Study 1) did not allow us to address such questions due to difficulties encountered in recruiting an ADHD alone sample. Therefore, within the context of this research study, *overlapping* will be used to refer to a situation where dyslexia and comorbid dyslexia-ADHD are impaired or spared within the same cognitive domains relative to control participants, *additive* will be used to refer to a situation where the comorbid group demonstrates additional impairments that do not manifest in dyslexia alone, while more *severe* will be used to refer to a situation where the comorbid group demonstrates more severe impairments than dyslexia alone. This same terminology will be used to explore whether the profile of symptoms (core: reading, non-core: socio-emotional) associated with dyslexia and comorbid dyslexia-ADHD is overlapping or more severe. Core symptoms within the context of this research study will be used to refer to reading impairments as the central focus is on dyslexia, while non-core will be used to refer to socio-emotional problems. However, in a diagnostic sense it is also possible that ADHD symptoms are central in some children with comorbid dyslexia-ADHD. ADHD symptoms will be explored

as a behavioural outcome across groups, however, these symptoms will not be defined as core within the context of this thesis.

Sample characterisation

Across EF profiling studies there is a discrepancy between how dyslexia is classified within the sample (see Table 2). Some studies include only participants with a clinical diagnosis of dyslexia given by a clinical/educational psychologist and based on DSM criteria (de Jong et al., 2009; Gooch et al., 2011; Moura et al., 2016; Varvara et al., 2014), while others use researcher-administered standardised tools to classify dyslexia which vary in terms of cut-off points for classification (Bexkens et al., 2014; Peng et al., 2013; Wang & Yang, 2014; Willcutt et al., 2001, 2005). Studies also differ with regard to method for screening co-occurring ADHD or potentially undiagnosed ADHD from the dyslexia alone sample, although some studies implement a standardised tool to screen ADHD from the dyslexia sample (de Jong et al., 2009; Marzocchi et al., 2008; Pennington et al., 1993; Tiffin-Richards et al., 2008; Varvara et al., 2014; Willcutt et al., 2001, 2005), the majority just require no history of a diagnosis or report no method of tracking or screening ADHD from the dyslexia alone sample. Not screening ADHD from the dyslexia alone sample is problematic as these conditions frequently co-occur (Willcutt & Pennington, 2000), and ADHD alone is associated with EF deficits (Barkley, 1997). This makes it difficult to determine if EF impairments are associated with dyslexia alone or manifest due to the presence of elevated ADHD within the sample.

Study 1 aims to account for this by including a homogenous sample of participants with dyslexia alone and comorbid dyslexia-ADHD. Participants with a clinical diagnosis of dyslexia alone and comorbid dyslexia-ADHD will be recruited. To account for potential undiagnosed ADHD in the dyslexia alone sample, participants will be screened for ADHD features. Parents of participants will complete the Child Behaviour Checklist (Achenbach & Rescorla, 2001), which includes a standardised measure of ADHD which can detect pre-clinical and clinical ranges. Children with a diagnosis of dyslexia who score in the pre-clinical/clinical range on the Child Behaviour Checklist for their age and gender will be screened from the dyslexia alone sample and included in the comorbid dyslexia-ADHD sample.

EF as multiple but separate abilities

Studies profiling EF in dyslexia and comorbid dyslexia-ADHD also differ in terms of approach to profiling (see Table 2), a number of studies view EF as a unitary construct (employing complex measures such as Wisconsin Card Sort Task or unitary EF composites) (Beidas et al., 2013; Pennington et al., 1993), as multiple but separate abilities (employing multiple complex measures such as planning, switching, inhibition, interference control and verbal fluency) (De Lima et al., 2012; Menghini et al., 2010; Moura et al., 2016, 2015, Willcutt et al., 2001, 2005), or look at separate processes in isolation with single tasks (Beneventi et al., 2010a; Beneventi et al, 2010b; Poljac et al., 2010; Schmid et al., 2011). Extensive research carried out on the 3-factor model of executive function suggests: (a) EF is comprised of three key related (inhibition-common EF) but separable abilities (updating and switching) (Miyake & Friedman, 2012); (b) EF is most sensitively measured at the latent level with multiple tasks of each ability (common EF (inhibition), updating specific, and switching specific) (Friedman et al., 2007, 2008; Miyake & Friedman, 2012); and (c) the 3-factor structure of EF is present in childhood (Lehto et al., 2003) and adulthood (Friedman et al., 2007, 2008; Miyake & Friedman, 2012) demonstrating its developmental relevance for profiling cognitive change over time and cross study comparability. Yet, the majority of EF profiling studies in dyslexia and comorbid dyslexia-ADHD fail to theoretically inform research with validated models of EF.

Table 2 Summarising Characteristics of Previous EF Profiling Studies in Dyslexia and Comorbid Dyslexia-ADHD

Authors	Sample (N)	Age	Grouping	ADHD: Screened	Cont. speed	Profiling approach	Measure	Findings
Pennington et al., 1993	D:15 A:16 A+D:16 C:23	D:9.1 A:8.7 A+D:9.1 C:8.8	CD	ST	-	UA	EF comp. (TOH, MFF, CPT)	↓ A EF comp.
Nyden et al., 1999	D:10 C:10	D:10.1 C:10.1	CD	ST	-	MUP	GNG, WCST	↓ D GNG
Helland & Abjornsen 2000	D:43 C:20	D:12.67 C: 12.11	CD	NH	-	MUP	Stroop, WCST	↓ D Stroop + WCST
Palmer 2000	D: 16 C:16	D:14 C:14	CD	-	-	SM	WCST	↓ D WCST
Wilcutt et al 2001	D:93 A:52 A+D:48 C:121	D:10.4 A:10.8 A+D:10.6 C:10.7	RAST (SD 1.65)	ST	-	MUP	WCST, SST, TMT, Stroop	↓ D, A, A+D: WCST, TMT, SST, Stroop
Brosnan et al 2002	D: 30 C:30	D:14 C:13.8	CD	NH	-	SM	GEFT	↓ D GEFT
Jeffries & Everatt 2004	D:21 C: 40	D:10.8 C:11.07	CD	-	-	SM	Stroop	
Reiter et al 2005	D:42 C:42	D: 10.8 C:10.6	CD	NH	-	MUP	FT, GNG, Stroop, TOH, WCST, TMT	↓ D FT, Stroop, TOL

Authors	Sample (N)	Age	Grouping	ADHD: Screened	Cont. speed	Profiling approach	Measure	Findings
Wilcutt et al 2005	D:109 A:113 A+D:64 C:151	D:11 A:11.2 A+D:11.1 C:11.5	A: RAST D: RAST (SD 1.75)	ST	-	MUP	SST, CPT, WCST, TMT	↓D:SST, CPT, ↓A, A+D: SST, CPT, WCST, TMT.
Smithspark et al 2007	D:22 C:22	D:20.59 C:20.82	CD	-	-	SM	CU, SU	-
Bental & Tirosh 2007	D:17 A:19 A+D:27 C:23	D:9.96 A:9.76 A+D:9.24 C:9.75	CD	ST	-	MUP	MFF,PM, WCST	-
Tiffin-Richards et al 2008	D:20 A:20 A+D:20 C:19	D:11 A:11.6 A+D:11.8 C:11.7	CD	ST	-	SM	WCST	-
De Jong et al 2009	D:41 A:24 A+D:29 C:26	D:10.1 A:9.00 A+D:9.83 C:9.31	CD	ST	-	SM	SST	↓D, A, A+D: SST
Marzocchi 2009	D:22 C:25	D:9.43 C:9.72	CD	ST	-	MUP	OW	↓D OW
Menghini et al 2010	D:60 C:65	D:11.43 C:11.94	RAST (2 SD)	NH	-	MUP	FT, WCST	↓D FT

Authors	Sample (N)	Age	Grouping	ADHD: Screened	Cont. speed	Profiling approach	Measure	Findings
Kapoula et al 2010	D:10 C:14	D:15.1 C: 14.3	RAST (2SD)	NH	-	SM	Stroop	↓ D Stroop
Poljac et al 2010	D:25 C:27	D:15.4 C:15.2	CD	-	-	SM	MT	↓ D MT
Beneventi et al 2010b	D:12 C:14	D:13.2 C: 13.5	CD	NH	-	SM	L2-back	↓ D L2-back
Beneventi et al 2010a	D:11 C:13	D:13.2 C:13.5	CD	NH	-	SM	P2-back	↓ D P2-back
Gooch et al 2011	D:17 A:17 A+D:25 C:42	D:10.69 A:9.54 A+D:10.33 C:10.27	CD	NH	-	SM	SST	↓ A, A+D: SST
Schmidd et al 2011	D:20 C:16	D:9.7 C:9.3	RAST	NH	-	SM	SST	↓ D: SST
Beidas et al 2012	D:34 C:35	D:25.32 C:25.02	CD	NH	-	UA	EF Comp. (TOL, WCST, Stroop)	↓ D EF comp.
De Lima et al 2013	D:20 C:20	D: 9.7 C:9.05	CD	NH	-	MUP	TMT, Stroop, TOL, WCST	↓ D TMT, Stroop ↑ WCST
De Weerdt et al 2013	D:17 C:45	D:9.96 C:10.08	CD	NH	-	SM	AN-GNG, Pi-GNG	↓ D AN-GNG

Authors	Sample (N)	Age	Grouping	ADHD: Screened	Cont. speed	Profiling approach	Measure	Findings
Peng et al 2013	D:22 C:31	D:11.09 C:10.99	RAST (25th perc.)	NH	Yes	MUP	Stroop, Num-Stroop, W2-back, N2-back	-
Bexkens et al 2014	D:28 C:31	D:10.11 C:11.2	RAST (1 SD)	NH	-	SP	SST, Sim. T	-
Varvara et al 2014	D:60 C:65	D:11.4 C:11.9	CD	ST	-	MUP	WCST, FT	↓ D FT
Moura et al 2014	D:50 C:50	D:9.8 C:9.82	CD	NH	-	MUP	TMT, TOL, FT	↓ D TMT, FT
Wang & Yang 2015	D:37 C:37	D:10.1 C:10	RAST	-	-	SP	Cog inhib comp. (Stroop, GEFT), Behav. Inhib comp (GNG, SST)	↓ D Cog inhib comp
Moura et al 2016	D:32 A:32 A+D:18 C:34	D:9.00 A:8.25 A+D:8.94 C: 9.03	CD	NH	-	MUP	TMT, FT	↓ D TMT ↓ A + A+D: TMT, FT

Note: D= dyslexia, A=ADHD, A+D=comorbid, C=control, CD=clinical diagnosis, RAST= researcher administered standardised test, SD=standard deviation, ST=Standardised Tool, NH= no history, UA= unified ability, MUP= multiple unrelated processes, SM=single measure, SP=single process, EF=Executive function, Comp=composite score, TOH/L=Tower of Hanoi/London, MFF=Matching Familiar Figures, CPT=Continuous performance test, GNG=Go No-Go, WCST=Wisconsin Card Sort Test, SST=Stop Signal Task, Stroop=Stroop Task, TMT=Trail Making Task, GEFT=Group Embedded Figures Task, FT=Fluency Task, CU= consonant updating, SU= spatial updating, PM=Porteus Maze, OW= Opposite Worlds (TEACH), MT=Matching switch task, L2-back=Letter 2-back task, P2-back=phoneme 2-back, AN-Alphanumeric, Pi=Pic, Num=Number, W2-back= word 2-back task, N2-back=Number 2-back task, Sim. T= Simon Task, Cog=Cognitive, inhib=inhibition, Behav.=Behavioural, PC=phenocopy hypothesis, Add=Additive hypothesis, CS=Cognitive subtype hypothesis.

EF and Task Purity

Previous approaches to EF profiling in dyslexia and comorbid dyslexia-ADHD are problematic due to task impurity issues (see Table 2), complex tasks are poor profiling tools because they lack specificity in detecting key underlying impairments, as performance is driven by a range of EF (response inhibition, updating, and switching) and non-EF processes (e.g. learning from feedback in WCST) (Miyake et al., 2000; Miyake & Friedman, 2012; Snyder et al., 2015). Viewing EF as a number of separate unrelated abilities or looking at single processes in isolation is problematic because it fails to address the theoretical understanding that these abilities are facilitated by a number of core underlying processes which are both related (common EF: response inhibition) and unique (updating and switching) and sometimes antagonistically related (Snyder et al., 2015). For instance, trade-offs have been observed between response inhibition and switching due to the incompatibility of each demand (Blackwell, Chatham, Wiseheart, & Munakata, 2014; Goschke, 2000; Gruber & Goschke, 2004); response inhibition facilitates increased focus by filtering irrelevant information/distractions in a top down manner, while switching requires a degree of distraction to aid in considering alternative options in order to flexibly adapt to changing demands (Gruber & Goschke, 2004). These difficulties are manifest across cross-sectional, longitudinal and meta-analytic studies - thus hindering progress in understanding exactly how EF is implicated in dyslexia and comorbid dyslexia-ADHD.

A confounding factor which could also potentially explain how EF is implicated in dyslexia and comorbid dyslexia-ADHD is processing speed. Previous research suggests that processing speed is a risk factor for dyslexia and ADHD (McGrath et al., 2011; Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2010, 2005). This is problematic because performance on EF tasks is quantified with indices of speed and accuracy- if general speed of processing is not adequately controlled for it could lead to findings of false positive EF impairments that are reflective of a general slowness as opposed to an EF impairment per se. Peng et al. (2013) found updating and inhibition impairments in dyslexia, yet when they controlled for general processing speed impairments, updating and inhibition impairments no longer reached significance.

Disorder specific patterns of EF

There is a pattern across previous research which suggests that dyslexia alone may be characterised by a disorder specific deficit in EF processing of phoneme based content (Beneventi, et al., 2010a), however, the majority of established measures of EF employ basic visual/spatial content which limits the ability to capture disorder specific deficits if present (Booth et al., 2010). EF processing of phoneme content in dyslexia alone is worthy of further investigation because: (a) phoneme impairments appear to be a central deficit in dyslexia and are mostly found on complex tasks tapping executive abilities (Ramus & Szenkovits, 2008); (b) multiple deficit models suggest that phonological impairments are a unique risk factor for dyslexia alone (McGrath et al., 2011; Pennington, 2006); (c) brain imaging studies of phoneme impairments in dyslexia implicate frontal brain areas suggesting impairments in top down executive processing of phoneme content (Cao et al., 2006; Richlan et al., 2010; Richlan, 2012; Richlan et al., 2009, 2011); and (d) frontal brain areas are implicated in reading ability (Turkeltaub et al., 2002) and appear to facilitate pre-post intervention reading improvements (Gaab et al., 2007; Horowitz-Kraus & Holland, 2015; Temple et al., 2003).

The majority of EF studies in dyslexia do not address disorder specificity (phoneme) of impairment, despite a recent meta-analysis indicating that it is not clear whether EF deficits in dyslexia are disorder specific (manifesting with verbal, language related content such as phonemes) or general (manifesting with all types of content) (Booth et al., 2010). One study explored disorder specificity (phoneme) of updating in dyslexia by adapting a 2-back task to include phoneme content (match based on first/last phoneme of pictures) and found significant impairments and reduced activation in frontal areas facilitating EF (inferior frontal gyrus, middle frontal gyrus, precentral gyrus, and left cingulate gyrus) (Beneventi et al., 2010a). However, Beneventi et al. (2010a) failed to compare performance on the disorder specific (phoneme) updating task to a picture-control updating task, therefore, it cannot determine if the impairment manifests with disorder specific (phoneme) content alone (are more severe with phoneme content) or is generalised to all types of content. Disorder

specificity (phoneme) of EF in dyslexia remains unexplored with other EFs (response inhibition and switching), and it is unclear whether this disorder specific (phoneme) EF processing impairment would have a compound effect when ADHD co-occurs as may be the case with non-specific EFs.

To understand the disorder specificity of EF in dyslexia and how this relates to comorbid dyslexia-ADHD, it has been suggested that profiling studies need to explore disorder specific patterns of EF by adapting pre-existing validated measures grounded in EF theory to include disorder specific content (e.g. phoneme information in dyslexia) (Goschke, 2014). Previous work by Beneventi et al. (2010a) adapted a 2-back updating task to include phoneme content so that participants had to make a 2-back matching decision based either on the first phoneme (or sounding out the first phoneme of the common name of the object visually depicted) or the last phoneme. This study found that the first phoneme 2-back task was sensitive to detect impairments in dyslexia, however, the last phoneme 2-back task was too difficult to capture any differences as all groups performed poorly (Beneventi et al., 2010a). Based on these findings, this study will adapt EF tasks such that EF processing rule is based on first phoneme instead of last phoneme.

Profiling single and comorbid disorder dyslexia

To understand exactly how EF is implicated in dyslexia and comorbid dyslexia-ADHD, profiling studies should be informed by well validated models and employ the most sensitive measures to systematically reduce non-EF noise (Friedman & Miyake, 2016; Goschke, 2014; Miyake & Friedman, 2012; Snyder et al., 2015). The present study aims to profile EF in dyslexia using Miyake and Friedman's (2012) 3-factor model and to employ the most sensitive measures of each EF factor. Tasks were deemed sensitive measures if they: (1) demonstrated significant loadings onto key EF constructs within previous latent variable analyses studies; and (2) were underpinned by frontal brain activation. Multiple measures were employed for each EF construct (inhibition, updating, and switching) with different types of content (e.g. picture, phoneme, and alpha-numeric). Latent variable analysis could not be conducted in study 1 due to sample size constraints, however, EF z-mean composite scores were created for each

construct to provide cleaner measures by filtering out any non-EF noise (Snyder et al., 2015). By systematically accounting for task impurity issues within EF measurement, this study (1) should elucidate the exact EF profile of dyslexia and whether EF profile is overlapping and manifests more severely in comorbid dyslexia-ADHD.

Exploring EF in dyslexia with the 3-factor structure may also elucidate strengths and impairments, as well as potential trade-offs between EFs which often manifest between response inhibition and switching due to incompatibility of each demand (Blackwell et al., 2014; Goschke, 2000; Gruber & Goschke, 2004), thus allowing for the development of a more sensitive and specific EF profile of dyslexia and comorbid dyslexia-ADHD which cannot be captured with previous profiling tools. Common EF (response inhibition) impairments are associated with a wide range of psychopathologies at the behavioural and endophenotypic level (Robbins et al., 2012) and more specifically demonstrate potential for explaining overlap between ADHD and its comorbidity with OCD (Fineberg et al., 2014), suggesting response inhibition may be a transdiagnostic risk factor capable of explaining overlap between symptomatically discrete conditions. It has been suggested that a range of neuro-developmental disorders including dyslexia and ADHD should be collapsed more broadly into neuro-developmental delay (due to high comorbidities) (Pauc, 2005). Therefore, a neuro-cognitive framework which enables a fine-grained understanding of EF (common and specific aspects) involvement in dyslexia and comorbid dyslexia-ADHD may shed light on possible candidates for overlap.

Study 1 aims – Profiling EF in Dyslexia and Comorbid Dyslexia (PhD aims 1 and 2)

Overall there is difficulty in determining the exact (strengths and impairments) of key EFs associated with dyslexia alone and whether the profile overlaps with or is magnified in comorbid dyslexia-ADHD. Potential reasons for inconsistent findings include (a) task impurity, (b) specificity of impairment, and (c) lack of control for confounds.

(A) To address task impurity issues, this study will profile EF using Miyake and Friedman's (2012) 3-factor model and will employ sensitive EF z-mean

composite measures of each construct which systematically accounts for any non-EF noise (Snyder et al., 2015).

(B) To address specificity of impairment, this study aims to explore phoneme specificity across groups by adapting tasks that load onto EF constructs and are underpinned by frontal brain activity. Adapted phoneme versions of EF tasks employed in the present study have not yet been validated, so the present study will also report concurrent validity.

(C) To address potential confounds by screening the dyslexia sample for elevated ADHD features and to also control for general processing speed abilities while exploring dyslexia and comorbid dyslexia-ADHD EF performance (see figure 12 below).

In summary, while incorporating and addressing potential reasons for inconsistent findings this chapter aims to: (1) establish the EF profile (strengths/impairments in common (response inhibition) and specific (updating, switching) EFs associated with dyslexia and whether this overlaps with or manifests more severely in comorbid dyslexia-ADHD using EF z-mean composite scores; and (2) determine if EF profile manifests differently in dyslexia and comorbid dyslexia-ADHD with disorder specific information (phoneme task content).

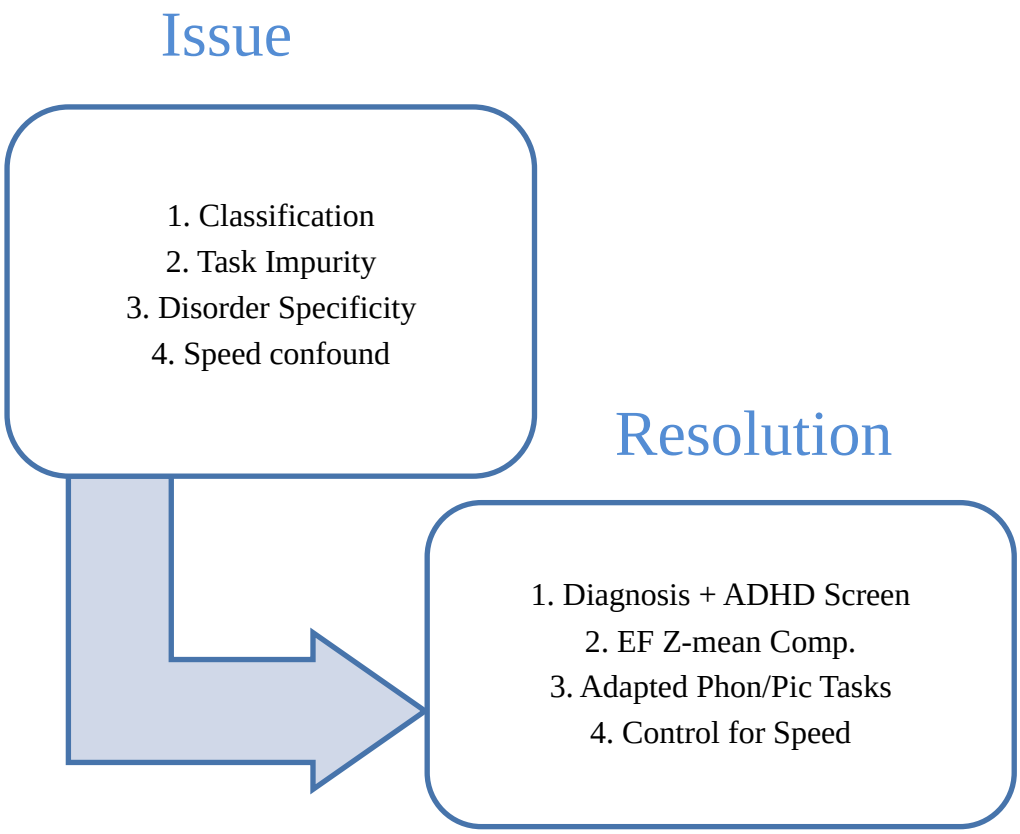


Figure 12 Key issues identified across EF profiling studies and proposed resolution

3.2 Method

3.2.1 Participants

Seventy-one participants aged 10-12 years took part in this research study: 27 (female:13, male:14) participants with dyslexia alone (mean age: 10.78 years), 15 (female: 7, male: 8) participants with comorbid dyslexia-ADHD (mean age: 10.53 years) and 29 (female:12, male: 17) participants with no clinical diagnosis. Participant diagnoses (Dyslexia; ADHD) was confirmed by parents and a copy of the psychological assessment report was requested. In the dyslexia group, two participants did not have a formal diagnosis of dyslexia but were enrolled on a dyslexia support workshop at their primary school. Diagnostic reports were submitted for 17 participants with dyslexia and all assessments were conducted by an educational psychologist, 16 of these participants were referred for reading difficulties whilst one participant was referred for reading difficulties and emotional distress induced by reading difficulties. Of these 17 participants, four were diagnosed at 7 years of age, five were diagnosed at 8 years of age, six were diagnosed at 9 years of age, and two were diagnosed at 10 years of age. Eight parents did not submit the diagnosis report but reported that their child had received a diagnosis of dyslexia. Twenty-six of those with dyslexia were enrolled in primary school when they participated, and one participant with dyslexia took part in the summer prior to starting secondary school. Twenty-one participants with dyslexia were right-handed, five were left-handed and one was ambidextrous. In the comorbid group, four participants did not have a formal diagnosis of ADHD, initially they were allocated to the dyslexia group but moved to the comorbid group due to scoring in the clinical range on the combined ADHD scale of the Child Behaviour Checklist (Achenbach & Rescorla, 2001). Of these four participants two were diagnosed by an educational psychologist at 10 years of age and were referred for reading difficulties, parent confirmation of a diagnosis was received for the other two participants, but they did not submit the report. One participant in the comorbid group, initially had a formal diagnosis of ADHD confirmed by their parent and was allocated to the comorbid group as they scored in the low-range (6^{th} percentile) for reading on a standardised reading assessment. Diagnostic reports were submitted for four participants

with comorbid dyslexia-ADHD, all assessments were conducted by a clinical psychologist and all participants were referred for inattentive, hyperactive, behavioural problems and reading difficulties. One participant was diagnosed with inattentive subtype of ADHD, while the other three were diagnosed with the combined subtype of ADHD. Three of these participants received a diagnosis at 7 years of age and one received a diagnosis at 8 years of age. Six parents did not submit the diagnostic report but confirmed that their child had received a diagnosis of comorbid dyslexia-ADHD. Two participants with comorbid dyslexia-ADHD were on medication for ADHD during the testing session. All fifteen participants in the comorbid dyslexia-ADHD group were enrolled in primary school when they participated. Ten participants with comorbid dyslexia-ADHD were right handed, while five were left handed. In the control group, twenty-seven were enrolled in primary school when they participated, while one had transitioned to 1st year of secondary school. Twenty-five participants in the control group were right handed, while three were left handed. Although some participants failed to submit the diagnostic report, all participants were screened for ADHD with the combined-ADHD scale of the child behaviour checklist and reading was assessed with a standardised reading test (Wilkinson & Robertson, 2006). All participants were Caucasian, monolingual English speakers, with normal or corrected vision and hearing. Participants had no additional diagnosis of a psychological disorder. Informed consent and assent were obtained from participating parents and children. Ethical approval for this research project was granted by Dublin City University's Research Ethics Committee (DCUREC/2014/167). Participants were recruited through Dyslexia Association Ireland and local primary schools.

3.2.2 Procedure

The research study was carried out in the psychology laboratories in the School of Nursing and Human Sciences at Dublin City University. All participants were assessed individually in the presence of their parent or guardian. The testing session took approximately two hours to complete and a break was given half way through. During the testing session children completed a battery of neuro-cognitive (EF), reading, phonological and processing speed measures. Parents or guardians of children completed a measure of

their child's socio- emotional behaviour problems. The order of tasks was counterbalanced for each participant to control for fatigue effects. All neuro-cognitive measures were created with E-Prime Software and responses were recorded on a Cedrus RB-50 response pad.

3.2.3 Measures

Phonological processing: Participants completed the first sound comparison task (Wagner, Torgesen, & Rashotte, 1994) as a baseline measure of phonological processing abilities. In this test participants were shown a row of four pictures and asked to circle the picture that begins with the same sound as the first picture. All picture names were read aloud by the researcher. There were 15 sets of four pictures which consisted of one syllable names. Pictures were selected from the Snodgrass and Vanderwart (1980) collection on the basis of having a high name agreement and acquisition in children at 8 years of age (Cycowicz, Friedman, Rothstein, & Snodgrass, 1997). The first sound comparison task loaded highly onto phonological analysis latent variable (.72) (Wagner et al., 1994).

Processing speed: Participants completed a computerized version of the coding task (Wechsler, 2003) as a measure of processing speed. On screen participants viewed a row of letters with a row of numbers directly underneath while a letter was presented centrally. Participants were tasked with searching for the centrally presented letter on the letter row and pressing the number on the keypad which was directly underneath the letter. This task consisted of 30 trials and a practice block of 10 trials where feedback was given. A latent analysis of the coding task revealed that it loads highly (.68) onto general processing speed factor (Keith, Fine, Taub, Reynolds, & Kranzler, 2006).

Executive Function Measures

Inhibition Measures

Stroop Task: Participants completed the Stroop Task (Balota et al., 2010) as a measure of response inhibition. In this task participants were presented with four colour words (red,

blue, green, yellow) and four non-colour words (poor, deep, legal, bad) which were presented on screen in varying ink colours (red, blue, green, yellow) (*See Figure 13 for sample stimuli and timings*). In the first block (colour naming) participants had to press the button on the response pad corresponding to the ink colour of the word. In the second block (word naming) participants had to press the button on the response pad corresponding to the meaning of the word (e.g. press red for word red only). Practice blocks were given before each experimental block which consisted of 16 trials. Experimental blocks consisted of 104 trials. Stimuli appeared on screen for 5,000ms with an inter-stimulus fixation of 500ms. The Stroop task significantly loads onto inhibition latent variable (Friedman & Miyake, 2004; Miyake et al., 2000), and is underpinned by frontal brain activation (Bench et al., 1993; Collette et al., 2005; Taylor et al., 1997).

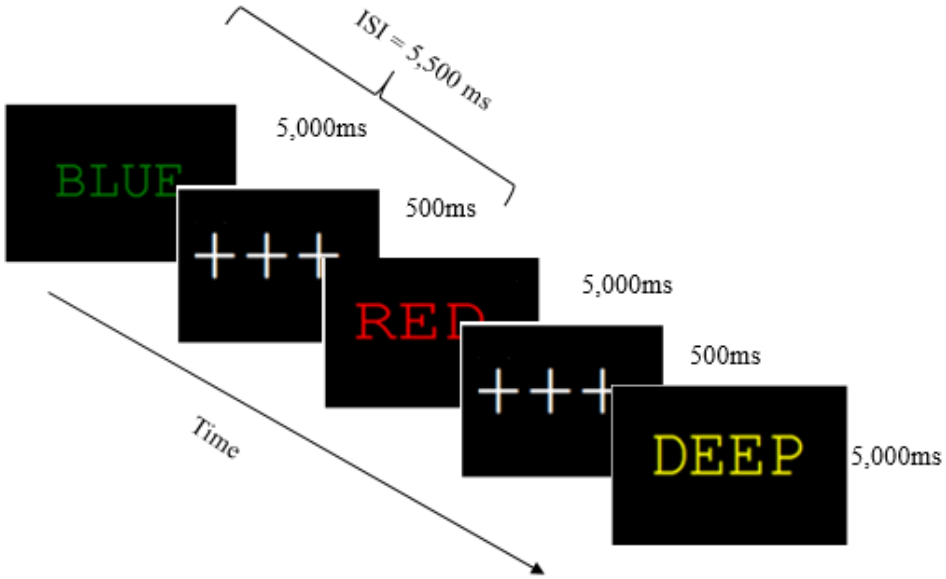


Figure 13 Stroop stimuli and timings

Picture Go No-Go task: Participants completed the picture Go No-Go task as a measure of visual response inhibition. This task was an adapted version of the Go No-Go task (Brocki & Bohlin, 2004; McAuley & White, 2011) to include pictures of common objects from the Snodgrass and Vanderwart (1980) collection. Stimuli were chosen on the basis of having

an age of acquisition below 8 years and a name agreement level of over 65% in children aged 5-6 years (Cycowicz et al., 1997; Snodgrass & Vanderwart, 1980). Participants viewed a sequence of object pictures which appeared centrally on screen and were required to press the green button for all Go pictures (manmade objects) and to withhold response for No-Go pictures (natural objects) (*see Figure 14 for sample stimuli and timings*). The experimental block consisted of 100 trials (75 go trials and 25 no-go trials). A practice block of 20 trials with feedback was given prior to experimental block. Stimuli appeared on screen for 2,000ms with an inter-stimulus fixation for 1,000ms. Stimuli were presented in the same pseudo-random order for each participant. The Go No-Go paradigm of task significantly loads on to an inhibitory control factor (Archibald & Kerns, 1999), and is underpinned by frontal brain activation (Booth et al., 2005; Casey et al., 1997).

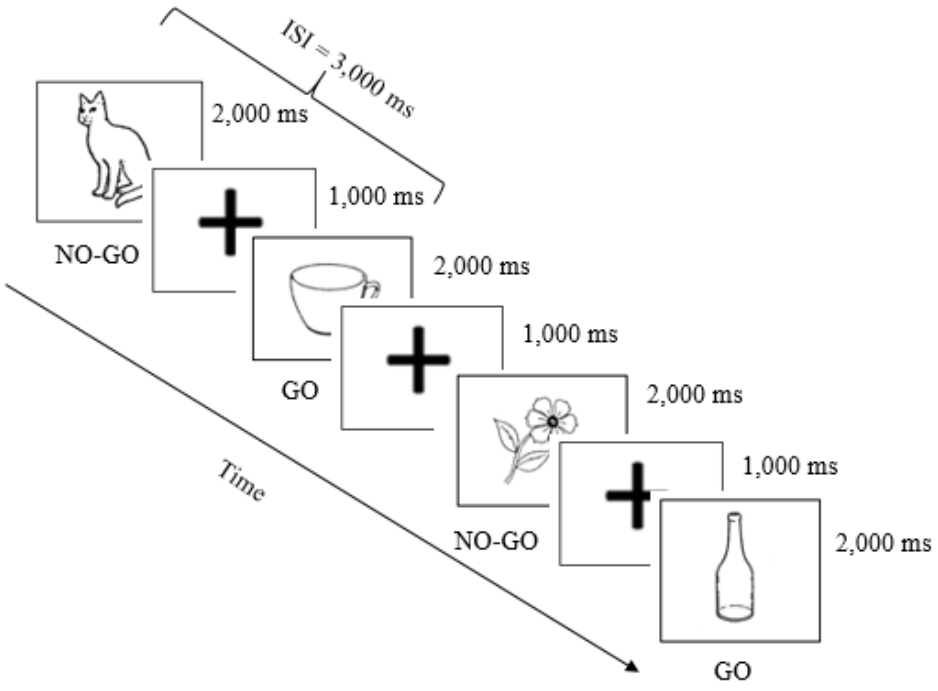


Figure 14 Picture Go No-Go task sample stimuli and timings

Phoneme Go No-Go Task: Participants completed the phoneme Go No-Go task as a measure of visual response inhibition. This task was an adapted version of the Go No-Go task (Brocki & Bohlin, 2004; McAuley & White, 2011) to include phoneme-picture information. Stimuli were selected from the Snodgrass and Vanderwart (1980) collection on the basis of picture name being monosyllabic or bi-syllabic, having an age of acquisition below 8 years and a name agreement level of over 65% in children aged 5-6 years (Cycowicz et al., 1997; Snodgrass & Vanderwart, 1980). Participants viewed a sequence of pictures which appeared centrally on screen and were required to press the green button for Go stimuli (pictures beginning with a consonant) and to withhold response for No-Go stimuli (pictures beginning with a vowel) (*see Figure 15 for sample stimuli and timings*). The experimental block consisted of 100 trials (75 go trials and 25 no-go trials). A practice block of 20 trials with feedback was given prior to experimental block. Stimuli appeared on screen for 2,000ms with an inter-stimulus fixation for 1,000ms. Stimuli were presented in the same pseudo-random order for each participant. The Go No-Go paradigm of task significantly loads on to an inhibitory control factor (Archibald & Kerns, 1999), and is underpinned by frontal brain activation (Booth et al., 2005; Casey et al., 1997).

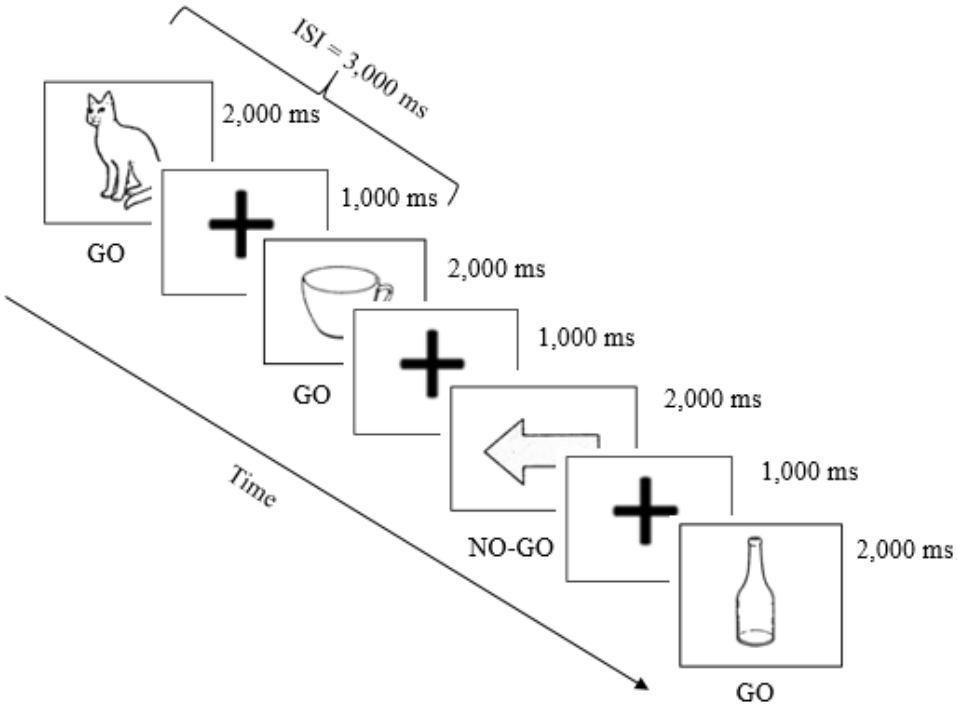


Figure 15 Phoneme Go No-Go stimuli and timings

Sustained Attention to Response Task (SART): Participants completed the random SART task as a measure of response inhibition (Johnson et al., 2007; Robertson, Manly, Andrade, Baddeley, & Yiend, 1997). Participants viewed a random sequence of single digits (1-9) on screen and were instructed to respond to all digits (go trials) with a button press except 3 (no-go trial) (*see Figure 16 for sample stimuli and timings*). The experimental block consisted of 225 trials. A practice block consisting of 18 trials with feedback was administered prior to the experimental block. Single digits (1-9) appeared on screen for 313ms, followed by a response cue for 563ms and a fixation cross for 563ms. Participants were instructed to respond when the response cue was on screen. The random SART places demands on response inhibition (Johnson et al., 2007), is similar in task procedure to Go No-Go task which significantly loads on to inhibitory control (Archibald & Kerns, 1999) and is underpinned by frontal brain activation (Fassbender et al., 2004).

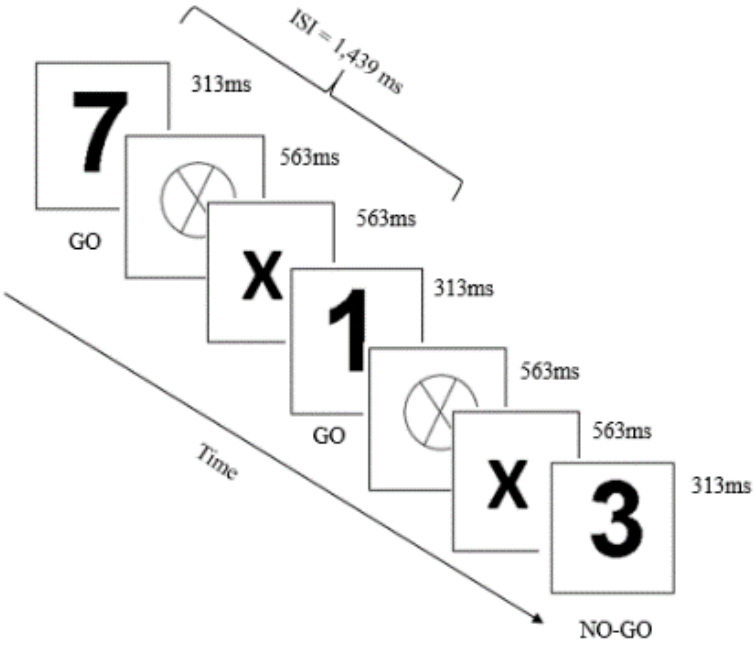


Figure 16 SART stimuli and timings

Updating measures

Letter N-Back Task: Participants completed the letter N-back (Kane, Conway, Miura, & Colflesh, 2007) task as a measure of working memory updating. Participants viewed a continuous stream of letters presented centrally on screen and were required to decide if the current letter on screen matched the letter presented 2 times ago (*see Figure 17 for sample stimuli and timings*). If the letters matched participants were instructed to press the green button on the response pad and if the letters did not match participants were instructed to press the red button on the response pad. The experimental block consisted of 96 trials. Stimuli were presented on screen for 1,000ms with an inter stimulus fixation for 100ms. Participants completed a practice block of 7 trials with feedback given prior to the experimental block. The N-back task loads on to a working memory updating factor (Wilhelm, Hildebrandt, & Oberauer, 2013), and is underpinned by frontal brain activation (Owen et al., 2005).

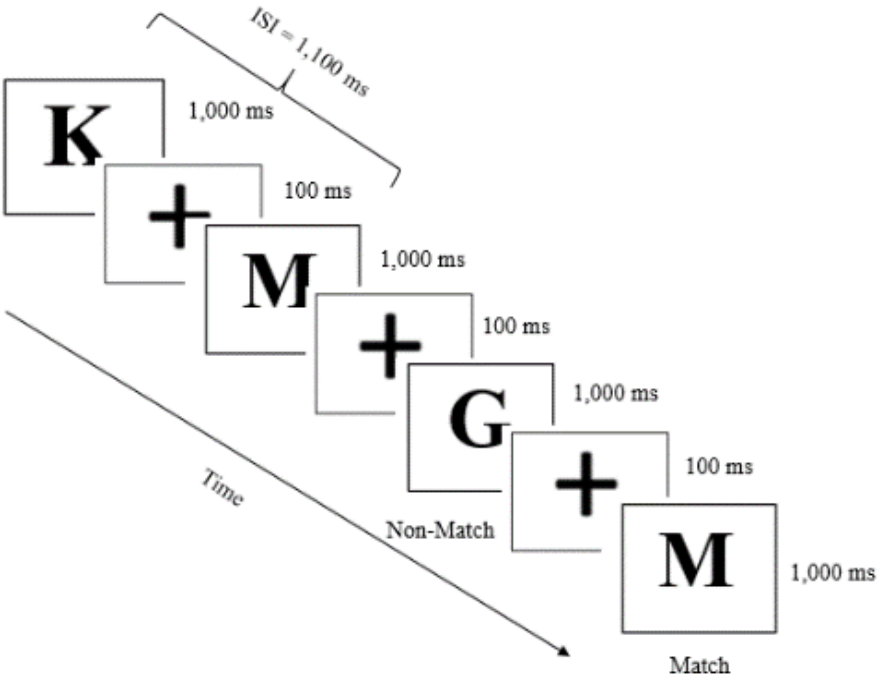


Figure 17 Letter N-back Task sample stimuli and timings

Picture N-Back Task: Participants completed the picture N-back task as a measure of visual updating. This task was modified (Beneventi, et al., 2010a) to include basic visual information. Stimuli were selected from the Snodgrass and Vanderwart (1980) collection on the basis of having an age of acquisition below 8 years and a name agreement level of over 65% in children aged 5-6 years (Cycowicz et al., 1997; Snodgrass & Vanderwart, 1980). Participants were presented with a continuous stream of pictures appearing centrally on screen and were required to decide if the current picture on screen matched the picture that was on screen 2 times ago (*see Figure 18 for sample stimuli and timing*). If the pictures matched participants were instructed to press the green button on the response pad and if pictures did not match participants were instructed to press the red button on the response pad. The experimental block consisted of 100 trials (33 of which were target matches). Participants completed a practice block of 20 trials with feedback prior to the experimental block. Stimuli appeared on screen for 1,000ms with an inter-stimulus fixation for 1,500ms. The N-back task loads on to a working memory updating

factor (Wilhelm et al., 2013), and is underpinned by frontal brain activation (Beneventi, et al., 2010a; Owen et al., 2005).

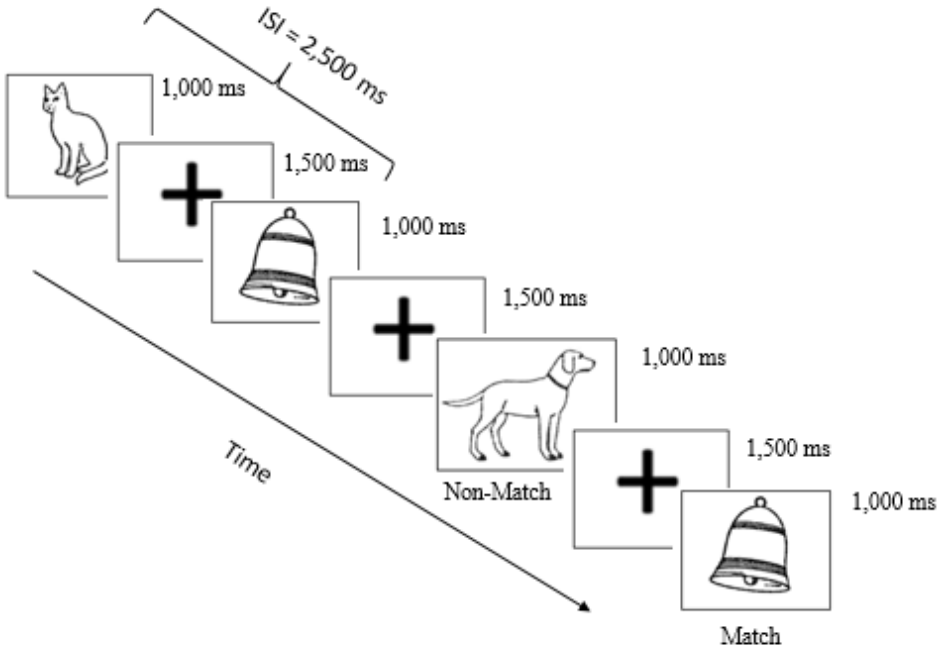


Figure 18 Picture N-back Task sample stimuli and timings

Phoneme N-back task: Participants completed the phoneme N-back task as a measure of phoneme updating. This task was a modified version of the phoneme updating task used by Beneventi et al. (2010a). This task was adapted for English speaking participants and only the first phoneme 2-back condition is used in the current study. Stimuli were selected from the Snodgrass and Vanderwart (1980) collection on the basis of picture name being monosyllabic or bi-syllabic, having an age of acquisition below 8 years and a name agreement level of over 65% in children aged 5-6 years (Cycowicz et al., 1997; Snodgrass & Vanderwart, 1980). Participants viewed a continuous sequence of pictures presented centrally on screen and were required to decide if the first phoneme of the current picture on screen matched the first phoneme of the picture presented on screen two times ago (*see Figure 19 for sample stimuli and timings*). If the phonemes matched participants were instructed to press the green button on the response pad and if phonemes did not match participants were instructed to press the red button on the response pad. The experimental block consisted of 100 trials (33 of which were target matches). Participants

completed a practice block of 20 trials with feedback prior to the experimental block. Stimuli appeared on screen for 1,0000ms with an inter-stimulus fixation for 1,500ms. The N-back task loads on to a working memory updating factor (Wilhelm et al., 2013), and is underpinned by frontal brain activation (Beneventi, et al., 2010a; Owen et al., 2005).

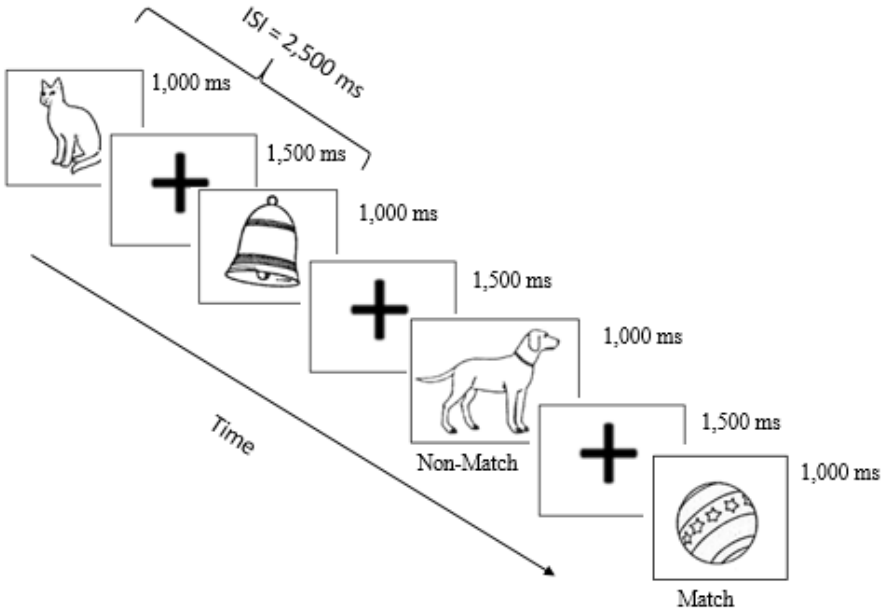


Figure 19 Phoneme N-back task sample stimuli and timings

Switching Measures

Number-Letter Switch Task: Participants completed the number-letter switch task as a measure of switching ability. An adapted version of the number-letter task (Miyake et al., 2000; Rogers & Monsell, 1995) was used where switch is based on colour of stimuli instead of location of stimuli. Participants were presented with different number letter pairs (e.g. 2A) centrally on screen and were required to decide on the number if green or to decide on the letter if red. If the number letter pair appeared in red participants had to focus on the letter and decide if it was a consonant or a vowel. If the number letter pair appeared in green participants had to focus on the number and decide if it was even or odd (*see Figure 20 for sample stimuli and timings*). In the first block of 20 trials the number letter pair only appeared in red. In the second block of 20 trials the number letter pair only appeared in green. In the third block of 116 trials the number letter pair changed between red and green and participants were required to switch between processing

number or letter- switch occurred on every 4th trial. Participants completed a practice block of 12 trials with feedback prior to each experimental block. Stimuli appeared on screen for 5,000ms with an inter-stimulus fixation for 150ms. The number-letter switch task loads onto switching construct (Collette et al., 2005; Miyake et al., 2000), and is underpinned by frontal brain activation (Collette et al., 2005).

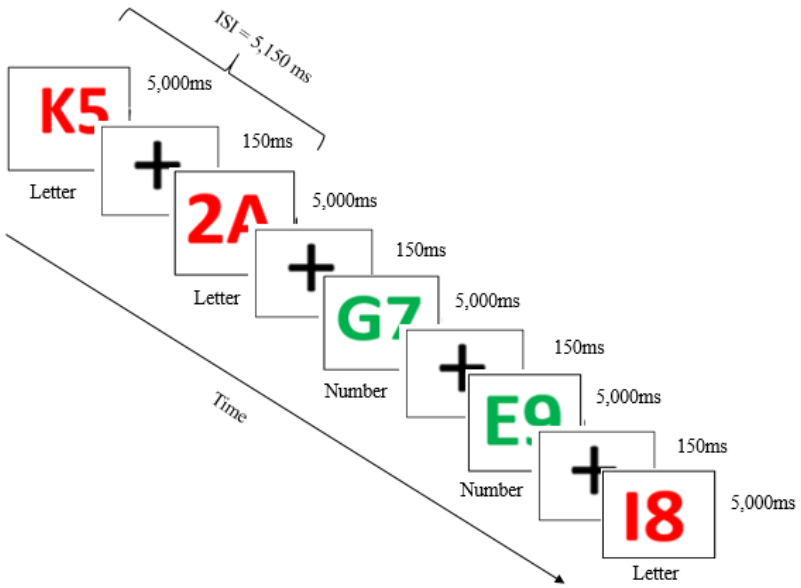


Figure 20 Number- Letter Switch task sample stimuli and timings

Phoneme Switch Task: Participants completed the phoneme switch task as a measure of phoneme switching ability. The number letter-task procedure (Miyake et al., 2000; Rogers & Monsell, 1995) was adapted to contain phoneme information. Stimuli for this task were pictures of common objects from the Snodgrass and Vanderwart (1980) collection on the basis of picture name being monosyllabic or bi-syllabic, having an age of acquisition below 8 years and a name agreement level of over 65% in children aged 5-6 years (Cycowicz et al., 1997; Snodgrass & Vanderwart, 1980). Participants viewed a different number of pictures (e.g. 2 apples, 1 star, 3 balloons) on screen in light (light red, green, or blue) or dark colours (dark red, green or blue). Participants were required to do one of two things depending on the first phoneme (letter sound) of the pictures (*see Figure 21 for sample stimuli and timings*). If the first phoneme was a consonant-sound, participants had to decide if the pictures were light or dark in colour. If the first phoneme was a vowel-sound,

participants had to decide if the number of pictures was even or odd. In the first block of 20 trials only first phoneme consonant pictures appeared on screen. In the second block of 20 trials only first phoneme vowel pictures appeared on screen. In the third block of 116 trials the pictures changed between first phoneme consonant and vowel, and participants were required to switch between processing number or colour- switch occurred on every 4th trial. Participants completed a practice block of 12 trials with feedback prior to each experimental block. Stimuli appeared on screen for 5,000ms with an inter-stimulus fixation for 150ms. A similar task the number-letter switch task loads onto switching construct (Collette et al., 2005; Miyake et al., 2000), and is underpinned by frontal brain activation (Collette et al., 2005).

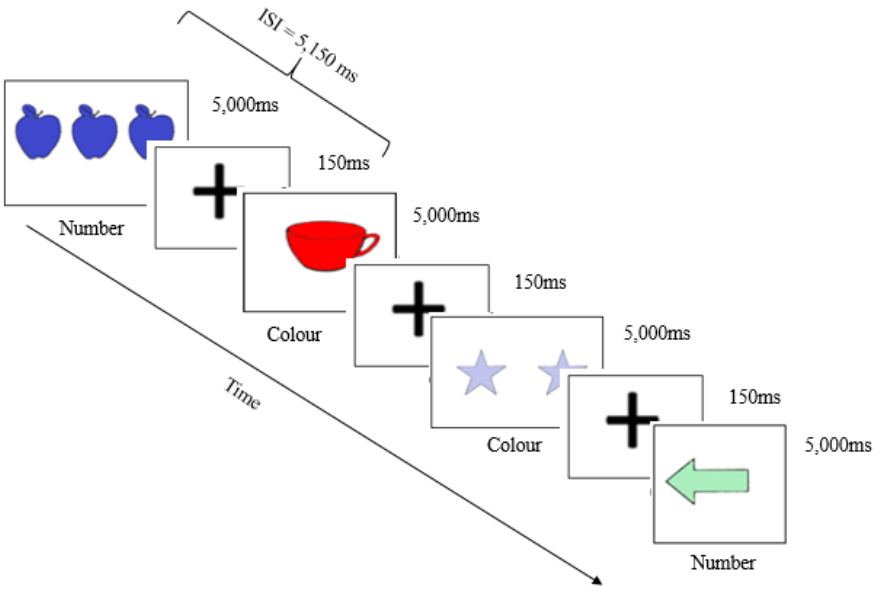


Figure 21 Phoneme Switch Task sample stimuli and timings

Clinically-relevant Symptom Outcomes

Reading ability: Participants completed the Green word reading list from the Wide Range Achievement Test 4 (WRAT-4) (Wilkinson & Robertson, 2006) as a measure of reading ability. The word reading subtest from WRAT-4 requires participants to read from a list of 55 items increasing in difficulty. The assessment was discontinued if participants had 10 consecutive errors. The WRAT-4 word reading subtest demonstrates good test retest reliability (subtest= .86) and consistency (subtest= .87) (Wilkinson & Robertson, 2006).

Social and emotional problems: The Parent Child Behaviour Checklist (CBCL) (Achenbach & Rescorla, 2001) was employed as a measure of social and emotional behaviour problems. The total problems subscale was employed as a measure of socio-emotional problems. The CBCL demonstrates good test retest reliability (competence items= 1; individual items=.95), and consistency (competence items= .69, problem items= .72) (Achenbach & Rescorla, 2001).

ADHD Symptoms: The ADHD subscale of the Parent Child Behaviour Checklist (CBCL) (Achenbach & Rescorla, 2001) was employed to measure ADHD symptoms. The CBCL demonstrates good test retest reliability (competence items= 1; individual items=.95), and consistency (competence items= .69, problem items= .72) (Achenbach & Rescorla, 2001).

3.3 Data Analyses

Hypothesis and analysis plans for research questions: (1) What is the EF profile (strengths/impairments in common (response inhibition) and specific (updating, switching) EFs) associated with dyslexia and comorbid dyslexia-ADHD?; (2) Is the EF profile associated with comorbid dyslexia-ADHD more severe than dyslexia alone?; and (3) Does the EF profile of Dyslexia and Comorbid Dyslexia-ADHD differ as a function of processing rule (visual based versus phoneme based)?, are summarised in Table 3. To establish validity of adapted EF tasks correlations were explored between adapted version, classic version and EF composite scores. A Bonferroni correction ($p<.004$) was applied to all analyses to account for inflated type I error rate due to multiple comparisons. The Bonferroni correction was calculated based on apriori research

questions only to ensure that resulting alpha level would not lead to an increase in type II error rate.

3.4 Results

3.4.1 Preliminary Analysis

Preliminary analyses were conducted to ensure that variables did not violate the assumptions of normality, homogeneity of variance, homogeneity of regression slopes and groups did not significantly differ on the covariate processing speed. Phoneme processing and Stroop effect (error) violated the assumption of normality and homogeneity of variance, suitable non-parametric analyses were conducted.

3.4.2 Descriptive Statistics

Descriptive statistics for dyslexia, comorbid dyslexia-ADHD and control group are summarised in Table 4.

Table 3 Hypotheses and Analyses Plan for Three Primary Research Questions

RQ	Hypothesis	Analysis		Post-Hoc Tests
1 & 2	**A. Not Controlling for Speed** H_o: $\mu_{RI}^{Dys} = \mu_{RI}^{Con}$; $\mu_{RI}^{Com} = \mu_{RI}^{Con}$; $\mu_{RI}^{Com} = \mu_{RI}^{Dys}$ H_o: $\mu_{UP}^{Dys} = \mu_{UP}^{Con}$; $\mu_{UP}^{Com} = \mu_{UP}^{Con}$; $\mu_{UP}^{Com} = \mu_{UP}^{Dys}$ H_o: $\mu_{SW}^{Dys} = \mu_{SW}^{Con;}$ $\mu_{SW}^{Com} = \mu_{SW}^{Con}$; $\mu_{SW}^{Com} = \mu_{SW}^{Dys}$	3 (Group: Dyslexia, Comorbid Control) x 3 (EF: Inhibition, Updating, Switching) Mixed Design ANOVA	**If results differ after controlling for speed**	Separate ANOVAs for each EF (inhibition, updating, switching) 2 (Group: Dyslexia-Control; Comorbid-Control; Comorbid-Dyslexia) x 1(EF) ANOVA
	B. Controlling for Speed H_o: $\mu_{RI}^{Dys}{}_{/PS} = \mu_{RI}^{Con}{}_{/PS}$; $\mu_{RI}^{Com}{}_{/PS} = \mu_{RI}^{Con}{}_{/PS}$; $\mu_{RI}^{Com}{}_{/PS} = \mu_{RI}^{Con}{}_{/PS}$ H_o: $\mu_{UP}^{Dys}{}_{/PS} = \mu_{UP}^{Con}{}_{/PS;}$ $\mu_{UP}^{Com}{}_{/PS} = \mu_{UP}^{Con}{}_{/PS;}$ $\mu_{UP}^{Com}{}_{/PS} = \mu_{UP}^{Dys}{}_{/PS}$ H_o: $\mu_{SW}^{Dys}{}_{/PS} = \mu_{SW}^{Con}{}_{/PS;}$ $\mu_{SW}^{Com}{}_{/PS} = \mu_{SW}^{Con}{}_{/PS;}$ $\mu_{SW}^{Com}{}_{/PS} = \mu_{SW}^{Dys}{}_{/PS}$	3 (Group: Dyslexia, Comorbid Control) x 3 (EF: Inhibition, Updating, Switching) Mixed Design ANCOVA controlling for processing speed	**If not**	Separate ANCOVAs for each EF (inhibition, updating, switching) 2 (Group: Dyslexia-Control; Comorbid-Control; Comorbid-Dyslexia) x 1(EF) ANCOVA **If Significant**
3	**A. Not Controlling for Speed** H_{o1}: $\mu_{RI\text{-}pic/phon}^{Dys} = \mu_{RI\text{-}pic/phon}^{Con}$; $\mu_{RI\text{-}pic/phon}^{Com} = \mu_{RI\text{-}pic/phon}^{Con}$; : $\mu_{RI\text{-}pic/phon}^{Com} = \mu_{RI\text{-}pic/phon}^{Dys}$ H_{o2}: $\mu_{UP\text{-}pic/phon}^{Dys} = \mu_{UP\text{-}pic/phon}^{Con}$; $\mu_{UP\text{-}pic/phon}^{Com} = \mu_{UP\text{-}pic/phon}^{Con}$; $\mu_{UP\text{-}pic/phon}^{Com} = \mu_{UP\text{-}pic/phon}^{Dys}$ H_{o3}: $\mu_{SW\text{-}pic/phon}^{Dys} = \mu_{SW\text{-}pic/phon}^{Con}$; $\mu_{SW\text{-}pic/phon}^{Com} = \mu_{SW\text{-}pic/phon}^{Con}$; $\mu_{SW\text{-}pic/phon}^{Coms} = \mu_{SW\text{-}pic/phon}^{Con}$	3 Separate Mixed ANOVAs for each EF 2 (Group: Dyslexia-Control; Comorbid-Control; Comorbid-Dyslexia) x 2 (Content: Pic, Phon) Mixed ANOVAs	**If Sig. interaction**	2 (Group: Control-Dyslexia, Comorbid-Control, Comorbid- Dyslexia) x 1 (phoneme cost: phoneme error/rt – picture error/rt) ANOVA Independent sample T-test to explore possible floor/ceiling effects
	B. Controlling for Speed H_{o1}: $\mu_{RI\text{-}pic/phon}^{Dys}{}_{/PS} = \mu_{RI\text{-}pic/phon}^{Con}{}_{/PS;}$ $\mu_{RI\text{-}pic/phon}^{Com}{}_{/PS} = \mu_{RI\text{-}pic/phon}^{Con}{}_{/PS;}$ $\mu_{RI\text{-}pic/phon}^{Com}{}_{/PS} = \mu_{RI\text{-}pic/phon}^{Dys}{}_{/PS}$ H_{o2}: $\mu_{UP\text{-}pic/phon}^{Dys}{}_{/PS} = \mu_{UP\text{-}pic/phon}^{Con}{}_{/PS;}$ $\mu_{UP\text{-}pic/phon}^{Com}{}_{/PS} = \mu_{UP\text{-}pic/phon}^{Con}{}_{/PS;}$ $\mu_{UP\text{-}pic/phon}^{Com}{}_{/PS} = \mu_{UP\text{-}pic/phon}^{Dys}{}_{/PS}$ H_{o3}: $\mu_{SW\text{-}pic/phon}^{Dys}{}_{/PS} = \mu_{SW\text{-}pic/phon}^{Con}{}_{/PS;}$ $\mu_{SW\text{-}pic/phon}^{Com}{}_{/PS} = \mu_{SW\text{-}pic/phon}^{Con}{}_{/PS;}$ $\mu_{SW\text{-}pic/phon}^{Com}{}_{/PS} = \mu_{SW\text{-}pic/phon}^{Dys}{}_{/PS}$	3 Separate Mixed ANCOVAs 2 (Group: Dyslexia-Control; Comorbid-Control; Comorbid-Dyslexia) x 2 (Content: Pic, Phon) Mixed ANCOVAs	**If Sig. interaction**	2 (Group: Control-Dyslexia, Comorbid-Control, Comorbid- Dyslexia) x 1 (phoneme cost: phoneme error/rt – picture error/rt) ANCOVA Independent sample T-test to explore possible floor/ceiling effects

Note: RQ= research question, RI= response inhibition, UP= updating, SW= Switching, Dys= Dyslexia, Com=Comorbid, Con= Control, PS= Processing Speed, Pic= Picture, Phon= Phoneme, EF= Executive Function.

Table 4 Means and Standard deviations for Dyslexia, Comorbid and Control Groups on all EF and Processing Resource Measures

		Dyslexia			Comorbid			Control	
Measure	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age	27	10.78	.85	15	10.53	.74	29	10.93	.80
Response Inhibition									
Stroop RT effect	27	170.86	88.03	15	260.24	142.27	29	157.18	81.15
Stroop err. Effect	27	5.44	4.36	15	9.82	7.01	29	4.17	6.59
Pic. GNG % Comm.	27	20.33	13.37	15	27.43	21.33	28	9.43	8.93
Pic. GNG RT	27	680.06	91.08	15	754.25	150.04	28	711.82	124.21
Phon. GNG % Comm.	27	24.15	12.67	15	31.14	16.54	29	16.55	12.27
Phon. GNG RT	27	926.63	167.41	15	937.22	138.21	29	990.67	199.35
SART % Comm.	27	41.48	16.94	15	48.57	15.60	29	31.31	12.61
SART RT	27	487.95	56.05	15	524.48	49.58	29	474.46	52.16
Response Inhibition Comp	27	.135	.499	15	.555	.711	29	-.391	.546
Updating									
Let. 2-back % error	27	59.25	16.51	15	60.26	13.78	29	41.37	13.17
Let. 2-back RT	27	578.57	90.3	15	523.17	104.93	29	611.56	55.43
Pic. 2-back % error	27	47.22	18.74	15	61.29	13.01	29	34.64	13.23
Pic. 2-back RT	27	624.01	81.23	15	558.08	93.99	29	616.75	58.62
Phon. 2-back % error	27	67.92	12.78	15	65.14	12.22	29	65.82	13.08
Phon. 2-back RT	27	610.34	88.64	15	514.52	80.09	29	650.57	74.46
Updating Comp	27	.169	.78	15	.371	.62	29	-.462	.679
Switching									
Num-Let SW err. Cost	27	3.33	4.65	15	1.50	5.67	29	2.00	4.22
Num-Let SW RT cost	27	511.80	395.82	15	466.61	406.64	29	690.18	336.02
Phon. SW err. Cost	27	1.67	4.84	15	1.93	4.76	29	2.55	4.31
Phon. SW RT cost	27	490.92	533.30	15	168.40	289.69	29	749.95	558.58
Switch Comp.	27	.036	.826	15	-.135	.971	29	-.024	.62
Processing resources									
Proc. Speed (no. items)	27	7.96	2.05	15	7.14	2.07	29	9.31	2.49
Phoneme Proc. (0-15)	27	14.85	.46	15	14.86	.36	29	15	0
Digit Span F	27	4.33	.68	15	4.21	.80	29	4.89	.9
Digit Span B	27	3.52	.64	15	3.29	.47	29	3.93	.59

Symptom Expression									
Reading	27	34.85	8.17	15	33.21	6.54	29	50.59	7.48
Socio-emotional	27	26.05	15.58	15	43.21	18.41	29	10	11.85
ADHD	27	3.48	2.06	15	8.57	3.67	29	1.48	1.86

Note. Stroop RT= Stroop effect in reaction time, Stroop err.= Stroop effect in error, GNG= GoNoGo, Comm= Commission errors, Comp= composite score, ACC= accuracy, RT= reaction time, Num-Let SW error= Number-Letter switch cost in errors, Num-Let SW RT= Number-Letter switch cost in reaction time, Phon SW err.= Phoneme switch cost in errors, Phon SW RT= phoneme switch cost in reaction time, Proc. Speed= processing speed, Phoneme proc.= phoneme processing, F= forward, B= backward. For between group differences at individual task level see Appendix F.

3.4.3 Validating Adapted (picture and phoneme) EF Tasks

Correlations between adapted (Visual/Phoneme rule based) task, classic or well-established task(s) and Z-mean composite scores for each EF construct are summarised in Table 5 in order to determine concurrent validity of adapted tasks. Pearson correlation coefficients are reported for all variables except for those violating parametric assumptions (Stroop Effect) where Spearman correlations are reported.

Table 5 Establishing Construct Validity of Adapted EF Measures and EF Z-Mean Composite Scores

1. Convergent and Discriminant Validity of Adapted Visual-Phoneme Rule Based EF Measures

RI	**RI**	**SART**	**Stroop Effect**	**Pic RI Comm**	**UP**	**Let. UP Err.**	**Pic UP Err.**	**SW**	**SW Err.**	**SW RT**
Pic. RI Comm.	**.69****	.203	**.35****	1	.16	.27*	.25*	-.07	-.03	-.31*
Phon. RI Comm.	**.75****	**.31***	**.36****	**.37****	.27*	.34*	.31*	-.16	-.09	-.25*
UP										
Pic. UP error	.41**	.28*	.24*	.25*	**.84****	**.54****	1	.01	-.1	-.51**
Phon. UP error	-.08	.02	-.12	-.14	**.78****	**.39****	**.49****	.13	.08	-.14
SW										
Phon. SW err. Cost	-.15	-.12	-.41**	-.08	.13	.07	.11	**.76****	.21*	.07
Phon. SW RT cost	-.49**	-.29*	-.11	-.36**	-.19	-.17	-.35**	.07	-.03	**.31****

2. Convergent and Discriminant Validity of EF Z-Mean Composite Scores

	RI	**UP**	**SW**
RI	1	.29*	-.22~
UP	.29*	1	.13
SW	-.22	.13	1

Note: RI= response inhibition, UP= updating, SW= switching, Pic=picture, Let=letter Phon=phoneme, GNG= Go No-Go Comm. =commission error, Err= error, RT= reaction time. P<.08~ ,*p<.05 (trend), **p<.004 (significant with Bonferroni correction)

Convergent Validity

Response Inhibition (Common EF)

A response inhibition z-mean composite score was calculated to provide a cleaner measure of inhibition between groups and to increase power due to small sample size $\left(\frac{ZPicGNGComm+ZPhonGNG+ZSARTComm+ZStroopError}{4}\right)$.

Both adapted (visual-phoneme) measures of response inhibition significantly correlated with the response inhibition composite score, the classic Stroop task and SART task (phoneme only), and with each other (see Table 5). The adapted response inhibition measures demonstrated convergent validity suggesting that they are measuring response inhibition (medium to high correlations across all response inhibition measures: (.31 - .75).

Updating

An updating z-mean composite score was calculated to provide a cleaner measure of updating between groups and to increase power due to small sample size $\left(\frac{ZPic2backerror+ZPhonbackerror+ZLett2backerror}{3}\right)$.

Both adapted measures of updating significantly correlated with the updating composite score, the classic updating task and with each other (see Table 5). Adapted measures of updating demonstrated convergent validity suggesting that they are measuring updating (medium to high correlations across all updating measures: (.39-.84).

Switching

A switching z-mean composite score was calculated to provide a cleaner measure of switching between groups and to increase power due to a relatively small sample size $\left(\frac{ZNumLettswitcherrorcost+ZPhonswitcherrorcost}{2}\right)$.

The adapted measure of switching significantly correlated with the composite score (error cost only) and the classic measure of switch (reaction time only) (see Table 5). The adapted task demonstrated convergent validity suggesting that it is measuring switching (medium to high correlations with switching measures: (.31-.76).

Discriminant Validity

Adapted EF Measures

The adapted response inhibition measures demonstrated a trend for medium correlations (-.25-.34) with updating and switching composites/classic measures. Both measures have a medium positive correlation with updating, which is expected given that response inhibition is the common-EF. Both measures also have medium negative correlations with switching, which may represent the antagonistic relationship between response inhibition and switching.

The adapted updating measures demonstrated a trend for medium correlations (-.51-41) with response inhibition and switching composites/classic measures. Both measures have a medium positive correlation with inhibition, and the picture task demonstrates a medium-large negative correlation with switching. Again, this may be reflective of response inhibition demands in updating and antagonistic relationship of response inhibition demands with switching demands at the individual task level.

The adapted switching measure demonstrates medium negative correlations (-.29 to -.49) with response inhibition and updating composites/classic measures. This further suggests that response inhibition and updating may have an antagonistic relationship with switching potentially due to the common EF: response inhibition.

EF Z-Mean Composite Scores

EF z-mean composites provide a cleaner measure of each EF as they extract what is common across tasks and remove any content (visual, phoneme, alphanumeric) based confounds which are often implicated at the individual task level.

The unity-diversity framework appears to manifest at the composite level, with response inhibition demonstrating a trend for a positive correlation with updating (.29) and almost a trend (p=.06) for a negative correlation with switching. No correlations are observed between updating and switching, suggesting that the EF z-mean constructs provide purer measures of the common (response inhibition) and specific (updating, switching) aspects of EF.

3.4.4 RQ1: What is the EF profile (strengths/impairments in common (response inhibition) and specific (updating, switching) EFs) and behavioural profile associated with dyslexia and comorbid dyslexia-ADHD?

To explore the EF z-mean profile associated with dyslexia and comorbid dyslexia-ADHD and whether this differed when accounting for baseline processing speed abilities, a 3 x 3 (EF) mixed design ANOVA was conducted with group as a between factor (3 levels: Dyslexia, Comorbid, Control) and EF as a within factor (3 levels: Inhibition, Updating, Switching). To explore whether this profile differed while controlling for baseline processing speed abilities a 3 x 3 mixed design ANCOVA was conducted (see Table 6).

Results from the 3 x 3 ANOVA indicate a non-significant main effect of EF, a significant main effect of group ($F(2,67)=12.57$, $p<.004$) and a trend for an interaction effect between EF and group ($F(4,134)=3.74$, $p<.05$). After controlling for low-level processing speed, there was a trend for a main effect of EF ($F(1,132)=4.05$, $p<.05$), a significant main effect of group ($F(2,66)=7.73$, $p<.004$), and a non-significant interaction effect.

Separate post hoc 2 (Group: dyslexia and control; comorbid and control) x 1 (EF: response inhibition, updating or switching) ANCOVAs controlling for speed were conducted to further explore the significant main effect of group. When controlling for baseline processing speed abilities, children with dyslexia alone demonstrated a significant response inhibition impairment ($F(1,52)=9.29$, $p<.004$, Cohen's $d=1.01$) and a trend for an updating impairment ($F(1,53)=5.68$, $p<.05$, Cohen's $d=.86$). When controlling for baseline processing speed abilities, children with comorbid dyslexia-ADHD also demonstrated a significant response inhibition impairment ($F(1,40)=11.55$, $p<.004$, Cohen's $d=1.49$) and a trend for an updating impairment ($F(1,41)=8.49$, $p<.05$, Cohen's $d=1.28$). Both dyslexia and comorbid dyslexia-ADHD did not significantly differ from the control group on switching. Overall significance of post hoc results did not differ when not controlling for speed (See Table 6 for summary). See Figure 22 for EF profile of dyslexia and comorbid dyslexia-ADHD.

To explore processing resources, separate 2 (Group: dyslexia and control; comorbid and control) x 1 (Speed, or Phoneme Processing, or Digit Span forward, or Digit Span

Backward) ANOVAs were conducted. Dyslexia was associated with trends for speed ($F(1,54)=4.84$, $p<.05$, Cohen's $d=.60$) and working memory capacity impairments (forward: $F(1,54)=6.9$, $p<.05$, Cohen's $d=.70$; backward: $F(1,54)=6.24$, $p<.05$, Cohen's $d=.66$) compared to the control group. Comorbid dyslexia-ADHD was also associated with significant backward working memory capacity impairments ($F(1,42)=14.32$, $p<.004$, Cohen's $d=1.19$), a trend for forward working memory capacity ($F(1,42)=6.48$, $p<.05$, Cohen's $d=.80$), speed ($F(1,42)=9.46$, $p<.01$, Cohen's $d=.95$) and phoneme processing impairments ($U=188.5$, $Z=-1.99$, $p<.05$, Cohen's $d=.55$) compared to the control group.

To explore behavioural outcomes, separate 2 (Group: dyslexia and control; comorbid and control) x 1 (reading, or, socio-emotional) ANOVAs were conducted. Dyslexia was associated with significantly impaired reading ($F(1,54)=56.60$, $p=.000$, Cohen's $d=2$) and significantly more socio-emotional problems ($U=148$, $Z=-3.99$, $p=.000$, $d=1.16$) compared to the control group. Comorbid dyslexia was also associated with significantly impaired reading ($F(1,42)=59.58$, $p=.000$, $d=2.47$) and significantly more socio-emotional problems ($U=32$, $Z=-4.6$, $p=.000$, $d=2.15$) compared to the control group.

RQ2: Is the EF profile and behavioural profile associated with comorbid dyslexia-ADHD more severe than dyslexia alone?

Separate post hoc 2 (Group: dyslexia and comorbid) x 1 (EF: response inhibition, updating or switching) ANCOVAs controlling for speed were conducted to further explore the significant main effect of group, and, whether the EF profile manifested more severely in comorbid dyslexia-ADHD than dyslexia alone. While controlling for speed, there was almost a trend for a more severe response inhibition impairment in comorbid dyslexia-ADHD compared to dyslexia alone ($F(1,39)=3.54$, $p=.067$, Cohen's $d=.68$). Dyslexia and comorbid dyslexia-ADHD did not significantly differ from each other on updating and switching (See Table 6).

To explore whether dyslexia and comorbid dyslexia-ADHD differed on processing resources, 2 (Group: dyslexia and control; comorbid and control) x 1 (Speed, or Phoneme Processing, or Digit Span forward, or Digit Span Backward) ANOVAs were conducted. Comorbid dyslexia-ADHD did not significantly differ from dyslexia alone on any of the

processing resource measures (Speed: $F(1,40)=2.12$, $p>.05$; phoneme processing: $U=199$, $Z=-.16$, $p>.05$; forward working memory capacity: $F(1,40)=.336$, $p>.05$; backward working memory capacity: $F(1,40)=1.79$, $p>.05$).

To explore whether dyslexia and comorbid dyslexia-ADHD differed on severity of symptoms expressed, separate 2 (Group: dyslexia and comorbid) x 1 (Reading, or, Socio-Emotional, or ADHD) ANOVAs were conducted. Comorbid dyslexia-ADHD was associated with significantly more severe ADHD symptoms ($F(1,37)=31.00$, $p=.000$, Cohen's $d=1.71$) and a trend for more severe socio-emotional problems ($U=105$, $Z=-2.56$, $p=.01$, $d=1.0$) than dyslexia alone. Comorbid dyslexia-ADHD did not significantly differ from dyslexia participants in severity of reading problems expressed ($F(1,40)=.496$, $p=.48$, Cohen's $d=.22$) (*see Figure 23*).

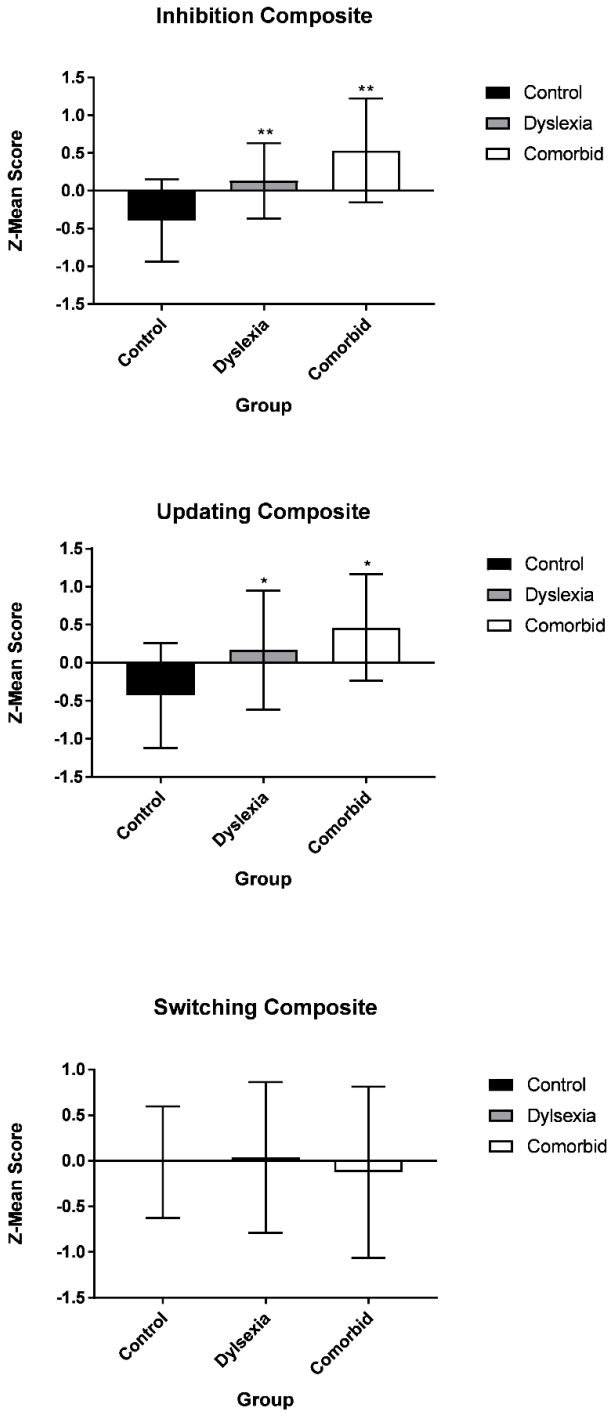


*Figure 22 Dyslexia, Comorbid dyslexia-ADHD and Control group on EF error z-mean composite scores. *p<.05 **p<.004*

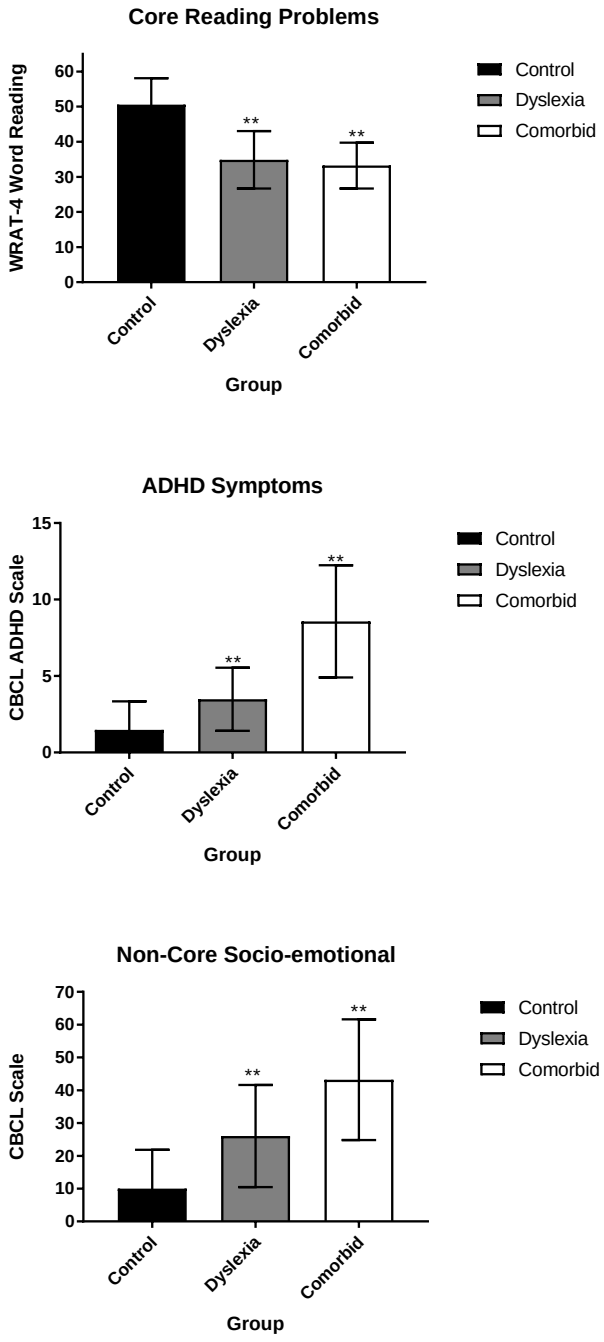


*Figure 23 Dyslexia, Comorbid dyslexia-ADHD and Control group severity on core reading, ADHD and non-core socio-emotional symptoms. *p<.05 **p<.004*

Table 6 RQ1 & RQ2: EF profile associated with Dyslexia and Comorbid Dyslexia-ADHD while controlling (ANCOVA) and not controlling for speed (ANOVA)

RQ	**Not Controlling for Speed**			**A/R**	**Controlling for Speed**				**A/R**	**Diff.**
1 & 2	$\mu_{RI}^{Dys} = \mu_{RI}^{Con}$; $\mu_{RI}^{Com} = \mu_{RI}^{Con}$; $\mu_{RI}^{Com} = \mu_{RI}^{Dys}$			**R**	$\mu_{RI}^{Dys}{}_{/PS} = \mu_{RI}^{Con}{}_{/PS}$; $\mu_{RI}^{Com}{}_{/PS} = \mu_{RI}^{Con}{}_{/PS}$; $\mu_{RI}^{Com}{}_{/PS} = \mu_{RI}^{Con}{}_{/PS}$				**R**	
	$\mu_{UP}^{Dys} = \mu_{UP}^{Con}$; $\mu_{UP}^{Com} = \mu_{UP}^{Con}$; $\mu_{UP}^{Com} = \mu_{UP}^{Dys}$			**R**	$H_{o:}\ \mu_{UP}^{Dys}{}_{/PS} = \mu_{UP}^{Con}{}_{/PS;}\ \mu_{UP}^{Com}{}_{/PS} = \mu_{UP}^{Con}{}_{/PS;}\ \mu_{UP}^{Com}{}_{/PS} = \mu_{UP}^{Dys}{}_{/Ps}$				**R**	
	$\mu_{SW}^{Dys} = \mu_{SW}^{Con;}\ \mu_{SW}^{Com} = \mu_{SW}^{Con}$; $\mu_{SW}^{Com} = \mu_{SW}^{Dys}$			**A**	$\mu_{SW}^{Dys}{}_{/PS} = \mu_{SW}^{Con}{}_{/PS;}\ \mu_{SW}^{Com}{}_{/PS} = \mu_{SW}^{Con}{}_{/PS;}\ \mu_{SW}^{Com}{}_{/PS} = \mu_{SW}^{Dys}{}_{/PS}$				**A**	
M1	**F**	***Df***	**P**		**M2**	**F**	***Df***	**P**		
EF	.61	2, 134	.547	**A**	EF	4.05	2, 132	.020	**R**	**Y**
Group	12.57	2, 67	.000	**R**	Group	7.72	2,66	.001	**R**	**N**
EF * Group	3.74	4, 134	.006	**R**	EF * Group	1.71	4, 132	.152	**A**	**Y**
					PS	4.11	1, 66	.047		
					EF * PS	3.54	2, 132	.032		

P-H	Dys – Con			Com – Con			Com - Dys				P-H	Dys - Con			Com – Con			Com - Dys				
	F	***Df***	**P**	**F**	***Df***	**P**	**F**	***Df***	**P**			**F**	***Df***	**P**	**F**	***Df***	**P**	**F**	***Df***	**P**		
RI	13.85	*1,53*	.000	23.4	1,41	.000	4.73	*1,40*	.036	**R**	RI	9.29	1,52	.004	11.55	1,40	.002	3.54	1,39	.067	**R**	**N**
UP	9.22	*1,54*	.004	16.42	*1,42*	.000	1.49	*1,40*	.23	**R**	UP	5.68	1,53	.021	8.49	1,41	.006	.61	1,39	.44	**R**	**N**
SW	.07	*1,54*	.793	.214	*1,42*	.65	.33	*1,40*	.571	**A**	SW	.13	1,53	.719	.011	1,41	.918	.20	1,39	.657	**A**	**N**

Note: RQ= Research Question, RI= response inhibition composite, UP= updating composite, SW= Switching composite, Dys= Dyslexia, Com=Comorbid, Con= Control, PS= Processing Speed, A= Accept, R= Reject, Diff.=Difference, Y=Yes, N=No M1= Model 1; M2=Model 2, EF= Executive Function, P-H= Post Hoc. * p<.05 (trend), **p<.004 (significant with Bonferroni correction). Trends and significant differences at composite level will continue to research question two analysis. At composite level switching is removed from analysis.

3.4.5 RQ3: Does the EF profile of Dyslexia and Comorbid Dyslexia-ADHD differ as a function of processing rule (visual based versus phoneme based)?

To explore whether inhibition and updating impairments associated with dyslexia and comorbid dyslexia-ADHD manifest more severely as a function of disorder specific processing rule -visual based versus phoneme based- separate 2 (Group: dyslexia and control; comorbid and control) x 2 (Rule: Visual and Phoneme) mixed ANCOVAs controlling for speed were conducted (see Table 7).

Post Hoc between differences on disorder specific cost variables in error or RT scale $(PhonemeNbackError/RT - PictureNbackError/RT)$, and one sample t-tests were employed to further explore any significant effects or trends from ANCOVA analysis.

Response Inhibition

Dyslexia: for commission errors, there was no main effect of processing rule (visual only or phoneme only); a trend for a main effect of group ($F(1,52)=7.15$, $p<.05$) but no interaction effect. Dyslexia participants made more errors than control participants regardless of whether they processed visual or phoneme content (collapsed across rule). For reaction time, there was a significant main effect of rule type ($F(1,52)=9.76$, $p<.004$), no main effect of group and no interaction effect. When group was collapsed, all participants took significantly longer to successfully complete the phoneme-based rule compared to the visual-based rule.

Comorbid dyslexia-ADHD: for commission errors, there was a trend for a main effect of rule ($F(1,40)=5.77$, $p<.05$) and group ($F(1,40)=8.84$, $p<.05$), but no interaction effect. When group was collapsed, all groups made more errors for the phoneme based rule than for the visual based rule. When rule was collapsed, comorbid participants had more errors than control participants. For reaction time, no main effect of rule and group, and no interaction effect were observed.

Updating

Dyslexia: for errors, there was no main effect of rule or group, but there was a trend for an interaction effect ($F(1,53)=5.21$, $p<.05$). For reaction time, there was no main effect of rule and group, and no interaction effect. Post-Hoc differences on a phoneme error cost (controlling for speed) and independent samples t-test (50% error rate) were conducted to further explore the trend for a significant group x rule error interaction effect (see Table 8). Control participants demonstrated a greater phoneme error cost than dyslexia participants ($F(1,53)=5.21$, $p<.05$, control: $M=31.14$, $SD=11.07$; dyslexia: $M=20.70$, $SD=15.06$). Independent sample t-tests (compared to chance performance 50% error rate) suggest that this may be due to task difficulty, both groups performed significantly worse than chance on the phoneme rule based task (dyslexia: $T(26)=-7.29$, $p<.004$; control: $T(28)=-6.6$, $p<.004$); while both groups performed similar to or better than chance on the visual rule based task (dyslexia: $T(26)=.77$, $p>.05$; control: $T(28)=5.7$, $p<.004$). This suggests that the phoneme rule based task may have been too difficult to sensitively profile between group updating differences, floor effects in this task are further depicted in figure 24.

Comorbid dyslexia-ADHD: for errors, there was no main effect of rule, a trend for a main effect of group ($F(1,41)=6.52$, $p<.05$) and a significant interaction effect ($F(1,41)=29.48$, $p<.004$). When rule was collapsed, the comorbid group demonstrated more errors than the control group. For reaction time, there was no main effect of rule, a significant main effect of group ($F(1,41)=14.10$, $p<.004$) and a trend for an interaction effect ($F(1,41)=6.88$, $p<.05$). When rule was collapsed, the comorbid group had lower reaction time than the control group. Post-Hoc differences on a phoneme error/RT cost (controlling for speed) and independent samples t-test (50% error rate) were conducted to further explore the group x rule interaction effects (see Table 8). Control participants demonstrated greater phoneme error ($F(1,41)=29.47$, $p<.004$, control: $M=31.14$, $SD=11.07$, comorbid: $M=5.07$, $SD=15.38$) and reaction time cost ($F(1,41)=6.88$, $p<.05$, control: $M=33.82$, $SD=72.99$, comorbid: $M=-43.55$, $SD=70.57$) than comorbid participants. Independent sample t-tests (compared to chance performance 50% error rate) suggest again that this may be due to task difficulty: Both groups performed significantly worse than chance on the phoneme

rule based task (comorbid: T(14)=-4.56, p<.004; control: T(28)=-6.6, p<.004); while the comorbid group performed worse than chance on the visual rule based task (T(14)=-3.62, p<.004) and the control group performed significantly better than chance on the visual rule based task (T(28)=5.7, p<.004). Again, this suggests that the phoneme rule based task may have been too difficult to sensitively profile between group updating differences, floor effects in this task are further depicted in figure 24.

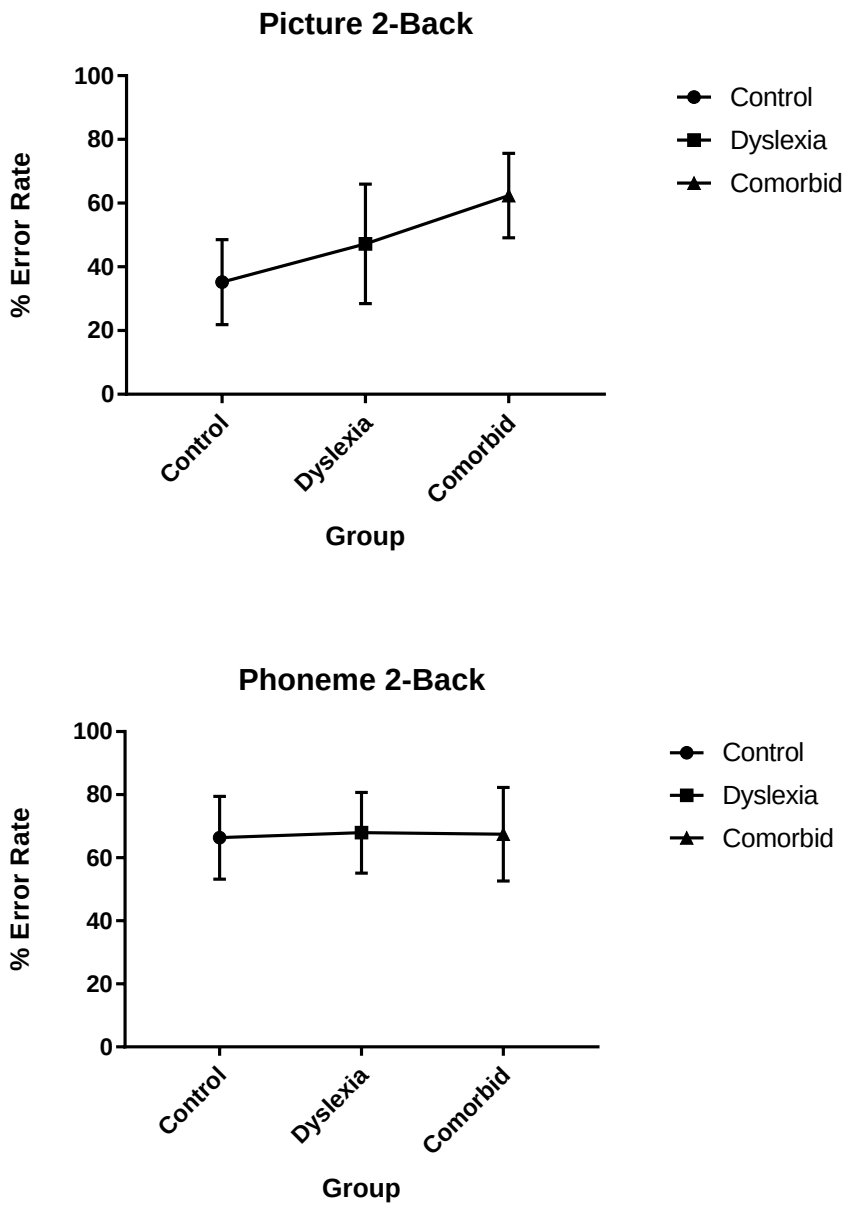


Figure 24 Floor effects on Picture rule based 2-back task compared to the phoneme rule based 2-back task across dyslexia, comorbid and control groups

Table 7 RQ3: Does EF profile of Dyslexia and Comorbid Dyslexia-ADHD differ as a function of processing rule (visual, phoneme)?

RQ	Controlling for Speed	A/R	Controlling for Speed	A/R
3	H_o: $\mu_{RI\text{-}pic/phon}{}^{Dys}{}_{/PS} = \mu_{RI\text{-}pic/phon}{}^{Con}{}_{/PS}$; $\mu_{RI\text{-}pic/phon}{}^{Com}{}_{/PS} = \mu_{RI\text{-}pic/phon}{}^{Con}{}_{/PS}$	A	H_o: $\mu_{UP\text{-}pic/phon}{}^{Dys}{}_{/PS} = \mu_{UP\text{-}pic/phon}{}^{Con}{}_{/PS}$ $\mu_{UP\text{-}pic/phon}{}^{Com}{}_{/PS} = \mu_{UP\text{-}pic/phon}{}^{Con}{}_{/PS}$	A

Model 3. Response Inhibition Rule (Phoneme, Visual)

	Dys - Con			Com – Con		
Error	**F**	***Df***	**P**	**F**	***Df***	**P**
Group	7.15	1,52	.01*	8.84	1,40	.005*
Rule	1.72	1,52	.19	5.77	1,40	.02*
Group * Rule	1.15	1,52	.29	1.05	1,40	.312
PS * Rule	.34	1,52	.57	3.09	1,40	.09
PS	6.94	1,52	.01*	8.97	1,40	.005
	Dys - Con			**Com – Con**		
RT	**F**	***Df***	**P**	**F**	***Df***	**P**
Group	2.69	1,52	.12	.03	1,40	.89
Rule	9.76	1,52	.003**	3.58	1,40	.07
Group * Rule	.25	1,52	.62	.87	1,40	.36
PS * Rule	.01	1,52	.95	.46	1,40	.50
PS	2.28	1,52	.14	.95	1,40	.34

Model 4. Updating Rule (Phoneme, Visual)

	Dys - Con			Com - Con		
Error	**F**	***Df***	**P**	**F**	***Df***	**P**
Group	1.47	1,53	.23	6.52	1.41	.014*
Rule	2.49	1,53	.12	2.74	1,41	.12
Group * Rule	5.21	1,53	.026*	29.48	1.41	.000**
PS * Rule	5.62	1,53	.021*	.91	1,41	.35
PS	6.71	1,53	.012*	5.16	1,41	.028*
	Dys - Con			**Com - Con**		
RT	**F**	***Df***	**P**	**F**	***Df***	**P**
Group	.21	1,53	.65	14.10	1,40	.001**
Rule	.23	1,53	.64	1.09	1,40	.30
Group * Rule	3.38	1,53	.07	6.88	1,40	.012*
PS * Rule	.53	1,53	.47	.93	1,40	.34
PS	2.87	1,53	.10	1.65	1,40	.21

Note: RQ= Research Question, Dys= Dyslexia, Con= Control, PS= Processing Speed, IS=Independent Sample. * p<.05 (trend), **p<.004 (significant with Bonferroni correction). Post-Hoc T-Tests explored only for significant interaction effects.

Table 8 Post-Hoc Tests for whether EF profile differs as a function of processing rule

RQ	**Post Hoc: Phoneme Updating Error Cost**						**Post Hoc: Phoneme Updating RT Cost**					
3	**Dys – Con**			**Com – Con**			**Dys - Con**			**Com – Con**		
	F	***Df***	**P**	**F**	***Df***	**P**	**F**	***Df***	**P**	**F**	***Df***	**P**
Group	5.21	1,53	.026*	29.47	1,41	.000**	3.38	1,53	.07	6.88	1,41	.012*
PS	5.62	1,53	.021*	.91	1,41	.35*	.53	1,53	.47	.93	1,41	.34
	Post Hoc: Independent Sample T-Test (50% error rate)											
	Dyslexia			**Comorbid**			**Control**					
	T	***Df***	**P**	**T**	***Df***	**P**	**T**	***Df***	**P**			
Picture	.77	26	.48	-3.62	14	.003**	5.70	28	.000**			
Phoneme	-7.29	26	.000**	-4.56	14	.000**	-6.6	28	.000**			

Note: RQ= Research Question, Dys= Dyslexia, Con= Control, PS= Processing Speed, RT= reaction time. * p<.05 (trend), **p<.004 (significant with Bonferroni correction). Post-Hoc Tests explored only for significant interaction effects.

3.4.6 Summary

RQ1: The EF profile associated with dyslexia and comorbid dyslexia-ADHD compared to controls is *overlapping* as both groups are associated with impaired response inhibition and updating (trend) and unimpaired in switching abilities at the EF z-mean composite level while controlling for low-level processing speed. The profile of processing resources associated with each condition also appears to be overlapping as both groups are associated with working memory (dyslexia-trend, comorbid- significant) and processing speed impairments (both trend, p<.05). However, the comorbid group demonstrates a trend for additional phoneme processing impairments (trend). The profile of symptoms associated with both conditions also appears to be overlapping as both groups demonstrate significant reading impairments, socio-emotional problems and ADHD problems relative to control participants.

RQ2: EF profile *does not manifest more severely* in comorbid dyslexia-ADHD compared to dyslexia alone, however there is almost a trend ($p < .05$) for more severe response inhibition impairments in comorbid dyslexia-ADHD. Dyslexia and comorbid dyslexia-ADHD did not differ on any processing resources. At the level of symptom expression, comorbid dyslexia-ADHD had more severe ADHD symptoms and a trend for more sever socio-emotional problems than dyslexia alone.

RQ3: Response inhibition impairments associated with dyslexia and comorbid dyslexia-ADHD did not differ as a function of processing rule (visual/phoneme based). For updating, there was a significant group x processing rule interaction where control participants experienced a phoneme rule cost compared to both dyslexia and comorbid dyslexia-ADHD. However, post-hoc analyses revealed that this cost was due to floor effects in the phoneme task compared to the visual task.

3.5 Discussion

From previous research, the key EF profile (common: response inhibition; specific: updating and switching) associated with dyslexia alone and whether this profile overlaps with or manifests more severely in comorbid dyslexia-ADHD is unclear. Inconsistent impairments are found across a range of EF measures in dyslexia alone: response inhibition (Bental & Tirosh, 2007; Booth et al., 2014; Brosnan et al., 2002), updating (Marzocchi et al., 2008; McGee et al., 2004; Willcutt et al., 2005), and switching (Menghini et al., 2010; Poljac et al., 2010). Although the multiple deficit hypothesis may be the best explanation for comorbid dyslexia-ADHD thus far studies typically do not suggest EF to be an overlapping factor (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010) which is inconsistent with findings that EF is implicated in symptoms (core and non-core) associated with dyslexia alone (Booth et al., 2014; Wang & Yang, 2014). Potential reasons for inconsistent findings across the literature include discrepancies: (a) with group classifications and methods of screening ADHD, (b) with profiling approach and measurement issues, (d) with task content, and (c) with not controlling for confounding effect of processing speed. These issues make it increasingly difficult to infer the exact EF profile associated with dyslexia alone and comorbid dyslexia-ADHD compared to control

participants, whether this EF profile is overlapping with or manifests more severely in comorbid dyslexia-ADHD compared to dyslexia alone, and whether this profile manifests differently with processing of disorder specific information (phoneme versus visual processing rule).

This study incorporated and addressed potential reasons for inconsistent findings by: (a) including a homogenous sample of dyslexia alone (clinical diagnosis, screened for elevated ADHD with a standardised measure) and a sample of comorbid dyslexia-ADHD (clinical diagnosis); (b) informing profiling approach with the 3-factor model of EF and employing sensitive measures of each construct (z-mean composites) (Miyake et al., 2000; Miyake & Friedman, 2012; Snyder et al., 2015); (c) adapting EF measures to explore disorder specificity (phoneme) of impairment; and (d) controlling for low-level processing speed abilities while exploring between group EF differences. Findings suggest that dyslexia and comorbid dyslexia-ADHD are associated with an overlapping EF profile of impaired response inhibition and updating, and unimpaired switching abilities at the EF z-mean composite level while controlling for low-level processing speed. Both conditions also appear to be overlapping on some processing resources such as working memory (dyslexia-trend, comorbid- significant) and processing speed impairments (both trend), but not on others such as phoneme processing which are additional in comorbid dyslexia-ADHD (trend). The symptom level profile is also overlapping as both conditions are associated with significant reading, socio-emotional and ADHD problems.

Although dyslexia and comorbid dyslexia-ADHD do not significantly differ from each other on any EF or processing resources, there is a trend for more severe response inhibition impairments in comorbid dyslexia-ADHD and this is a medium effect (.68) according to Cohen (1988). The pattern of effect sizes emerging across each condition when compared to control participants is also in support of a view that impairments manifest more severely in comorbid dyslexia-ADHD across response inhibition (dyslexia= 1.01; comorbid= 1.49), updating (dyslexia= .86; comorbid= 1.28), working memory forward (dyslexia= .70; comorbid= .80) and backward capacity (dyslexia= .66; comorbid = 1.19), and processing speed (dyslexia= .60; comorbid= .95). Comorbid dyslexia-ADHD is also associated with more severe ADHD and socio-emotional outcomes than dyslexia alone, and this pattern of

severity also emerges with increased effect sizes in the comorbid group for ADHD (dyslexia= 1.02; comorbid= 2.44) and socio-emotional problems (dyslexia= 1.16; comorbid= 2.15). According to Cohen (1988) all of these effects sizes can be classified as large (d=.8). These findings are consistent with the multiple deficit hypothesis of comorbid dyslexia-ADHD which suggests that each condition is associated with multiple impairments (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010). However, our findings suggest that EF impairments may be overlapping and effect size analysis suggests that these impairments are more severe in each condition than processing speed impairments. The overlapping profile manifests more severely in comorbid dyslexia-ADHD across each cognitive domain and there is also evidence of additional phoneme processing impairments which may support the view that comorbid dyslexia-ADHD is a unique cognitive subtype characterised by more severe and additional impairments (Rucklidge & Tannock, 2002). Although it is not clear within the current study whether additional impairments in comorbid dyslexia-ADHD are due to ADHD diagnosis as this study did not include an isolated ADHD sample.

Response inhibition impairments associated with each condition did not significantly differ in severity as a function of processing disorder specific phoneme information, in fact effect size analysis suggests that in dyslexia the effects for impaired response inhibition are larger for the picture (Cohen's d=.96) compared to the phoneme task (Cohen's d=.61). While in comorbid dyslexia-ADHD the effects for impaired response inhibition are similar across all types of content (picture: Cohen's d=1.1; phoneme: Cohen's d=1.0). When comparing dyslexia and comorbid dyslexia-ADHD the effect for impaired response inhibition are also similar across all types of content (picture: Cohen's d=.40; phoneme: Cohen's d=.48). For updating impairments, there was a significant group x processing rule interaction whereby control participants experienced a phoneme rule cost compared to both conditions, however post-hoc analyses suggest that this may be due to floor effects in the phoneme task compared to the control visual task.

The EF profile of dyslexia alone and comorbid dyslexia-ADHD (impaired: inhibition and updating; unimpaired: switching) found in the present study is consistent with previous studies finding impaired inhibition and updating (Booth et al., 2014; de Jong et al., 2009;

Wang & Yang, 2014) and unimpaired switching abilities in these conditions (Menghini et al., 2010; Tiffin-Richards et al., 2008). Both dyslexia and comorbid dyslexia-ADHD were associated with a trend for processing speed impairments, and the ANCOVA suggested a significant speed x EF interaction (highlighting that speed may play a role in EF impairments at a unified construct level). Similarly, Peng et al. (2013) found that after controlling for processing speed, EF impairments were no longer significant in dyslexia. However, in the present study additional post-hoc analysis indicated that the overall significance level for each group remained the same at the z-mean composite level (response inhibition- significant impairments; updating trend for significant impairments) when controlling and not controlling for speed- suggesting that EF impairments are associated with each condition while controlling for processing speed impairments. These findings are consistent with studies suggesting that processing speed is impaired in both dyslexia and comorbid dyslexia-ADHD (McGrath et al., 2011; Willcutt et al., 2005), but not with those suggesting that processing speed abilities explain EF impairments (Peng et al., 2013). These findings suggest that the EF profile associated with dyslexia alone and comorbid dyslexia-ADHD is not solely driven by processing speed problems - rather it reflects EF problems.

The EF profile of comorbid dyslexia-ADHD did not statistically differ from the EF profile associated with dyslexia alone at the EF z-mean composite level, however there was almost a trend for more severe impairments in common EF (response inhibition) associated with comorbid dyslexia-ADHD. This suggests a possible compound effect of response inhibition impairment in comorbid dyslexia-ADHD, as this EF may manifest more severely due to a dual diagnosis. Effect size analysis suggests that impairments may manifest more severely in comorbid dyslexia-ADHD across all EF, processing resources and behavioural outcomes. Larger effect sizes across each outcome in comorbid dyslexia-ADHD is in support of the multiple deficit theory as these impairments are overlapping (McGrath et al., 2011; Willcutt et al., 2010) and the cognitive subtype hypothesis as these impairments manifest more severely in comorbid dyslexia-ADHD (Rucklidge & Tannock, 2002). These findings do not support the initial phenocopy explanation of comorbid dyslexia-ADHD (Pennington et al., 1993) which suggested that comorbid dyslexia-ADHD

was associated with the same phonological impairments as dyslexia alone. Although this study did find a trend for a phoneme processing impairment in comorbid dyslexia-ADHD this was not found in dyslexia. In addition, EF impairments were found across both conditions and manifested more severely in comorbid dyslexia-ADHD which is inconsistent with the phenocopy explanation of comorbidity proposed by Pennington et al. (1993).

The findings from this study are more *consistent with the cognitive subtype hypothesis* (Rucklidge & Tannock, 2002) of comorbidity, which suggests more severe impairment(s) in comorbid dyslexia-ADHD. Although, it is important to note that the design of the present study (i.e. lack of ADHD alone group) necessarily limits the conclusions that can be drawn regarding status of comorbid dyslexia-ADHD within the cognitive subtype (Rucklidge & Tannock, 2002) framework. For instance, it cannot be confirmed whether the trend for a compound effect (response inhibition) in comorbid status is due to a level of impairment that would be typically associated with ADHD alone (additive effect) or due to the compound effect of dual diagnoses (cognitive subtype).

Considering this limitation, the findings from this study will be interpreted within the context of the *multiple deficit/shared aetiology* hypothesis (McGrath et al., 2011; Willcutt et al., 2010). Multiple impairments (EF, processing speed and working memory) were associated with both dyslexia and comorbid dyslexia-ADHD, highlighting how multiple processes are implicated in each condition. However, the considerable overlap in EF impairments suggests that EF may be a shared risk factor for both conditions. Findings from this study are consistent with previous work finding impairments in dyslexia and comorbid dyslexia-ADHD in working memory (Bental & Tirosh, 2007; Moura et al., 2016; Tiffin-Richards et al., 2008; Willcutt et al., 2005) and response inhibition (Willcutt et al., 2001, 2005), and inconsistent with those suggesting that EF is not an overlapping feature (Peterson et al., 2016). Peterson et al. (2016) found that processing speed is an overlapping feature, which is not inconsistent with the present findings as a trend for a processing speed impairment was found for each group. However, this study found that EF is an overlapping shared impairment in dyslexia and comorbid dyslexia-ADHD even when accounting for processing speed abilities. Effect size analysis suggests that at the cognitive level the common EF (response inhibition) is the most significantly impaired

ability across all groups. This suggests that EF (in particular response inhibition) may be a candidate for explaining overlap between dyslexia and ADHD independent of processing speed.

Although findings are consistent with some previous research, this research is difficult to interpret due to how EF is viewed (unitary or multiple separate abilities) (Goschke, 2000) and measured (complex measures tapping range of EFs) (Miyake & Friedman, 2012; Snyder et al., 2015). By creating EF z-mean composite scores, the present study was able to elucidate both the exact EF profile associated with dyslexia and comorbid dyslexia-ADHD while systematically reducing non-EF noise of measures (Snyder et al., 2015).

By profiling EF in dyslexia and comorbid dyslexia-ADHD using Miyake and Friedman's (2012) three factor model, it is apparent that inhibition (common EF) may be the central EF impairment associated with dyslexia and compounded in comorbid dyslexia-ADHD. This 'common EF' impairment may lead to impaired updating and unimpaired switching due to shared variance and antagonistic relationships. Extensive research on the 3-factor model indicates that EF is comprised of related (inhibition-common) but separable abilities (updating and switching) (Friedman et al., 2006, 2007, 2008; Miyake et al., 2000; Miyake & Friedman, 2012). The common EF (response inhibition) and switching are often found to demonstrate an antagonistic relationship (Friedman & Miyake, 2016; Friedman, Miyake, Robinson, & Hewitt, 2011; Goschke, 2000; Miyake & Friedman, 2012; Snyder et al., 2015), such that lower inhibition ability may facilitate unimpaired/possibly enhanced switching ability. Trade-offs manifest between response inhibition and switching as they are incompatible demands (Blackwell et al., 2014; Goschke, 2000; Gruber & Goschke, 2004). Inhibition facilitates focus by shielding information from irrelevant distractors in a top down manner (provides stability), while switching requires interference from distractors to consider alternative options and to flexibly adapt to changing demands (mental flexibility) (Gruber & Goschke, 2004). This may be the reason why the present study found impaired inhibition and updating while finding unimpaired switching abilities associated with dyslexia and comorbid dyslexia-ADHD. Operationally defining and measuring EF within the 3-factor latent model (Miyake & Friedman, 2012) allows us to see that EF may operate in a strengths and impairments manner (Snyder et al., 2015).

The common EF (response inhibition) component may be implicated as a transdiagnostic vulnerability factor for both disorders: This is viable as it has been previously proposed as a transdiagnostic factor implicated in a range of psychopathologies at the cognitive (Goschke, 2014; Snyder et al., 2015) and genetic levels operating as an endophenotype (Robbins et al., 2012). Response inhibition has been found to explain how ADHD and OCD overlap at the endophenotype level (Fineberg et al., 2014). Given that previous research suggests neuro-developmental disorders such as dyslexia and ADHD should be collapsed into a general neuro-developmental category due to considerable overlap at the symptom level (Pauc, 2005), this study highlights response inhibition as a potential transdiagnostic explanation of both which may increase in severity with dual diagnoses. To be classified as a cognitive endophenotype implicated in both dyslexia and comorbid dyslexia-ADHD a number of conditions need to be satisfied. To be classified as a transdiagnostic endophenotype EF impairments need to: (a) be associated with each condition; (b) be predictive of each condition; (c) manifest at all stages of condition; (d) be heritable; and (e) be found in unaffected family members to a greater degree than the general population (Crosbie et al., 2008; Gottesman & Gould, 2003). The findings from this study (study 1) suggest that the same EF impairments are associated with each condition and suggest that further research should be conducted to explore whether these EF impairments are predictive of the diagnosed condition.

A central response inhibition impairment in dyslexia alone may be useful for explaining a range of behavioural level manifestations. For instance, reading impairments are a key behavioural characteristic of dyslexia and part of the diagnostic criteria, yet socio-emotional self-regulatory problems (Dahle et al., 2011; Heiervang et al., 2001; Knivsberg & Andreassen, 2008; Mugnaini et al., 2009) are often observed. Viewing these behaviours within an EF framework may enhance understanding of underlying factors involved while also providing some potential explanations for why dyslexia and ADHD so frequently co-occur. Previous research suggests that inhibition is predictive of severity of reading and socio-emotional problems expressed in dyslexia (Wang & Yang, 2014).

In terms of disorder specificity (phoneme) of impairments associated with dyslexia and comorbid dyslexia-ADHD, inhibition impairments were found to manifest in a general way

(not more severe with phoneme content) across groups as reflected by effect size analysis. However, the disorder specificity of updating impairments across groups could not be determined as task difficulty issues resulted in floor effects. Initially results suggested that control participants demonstrated a greater phoneme updating cost relative to dyslexia and comorbid dyslexia-ADHD. Looking at error rate on the phoneme updating task across groups, it appears that the control group may have experienced a drop in performance from the picture updating task where they demonstrated an error rate of approximately 36% to the phoneme updating task where they demonstrated an error rate of approximately 65%. The error rate expressed by control participants in the phoneme updating task is similar to the range in error rate expressed by dyslexia and comorbid dyslexia-ADHD across both updating tasks (47-67%). Additional post hoc tests revealed floor effects in the phoneme 2-back task such that all groups performed significantly below chance (more than 50% error rate) on the phoneme task while performing similar to or better than chance in the picture task.

Therefore, the results do not reflect that dyslexia and comorbid dyslexia-ADHD experience disorder-specific (phoneme) updating costs but instead are reflective of a task difficulty issue experienced across the board. No significant differences were found in the low-level phoneme task; therefore, it is not low-level informational content that groups are struggling with, rather a high-level updating of this information in working memory. Another possibility which was touched on in section 2.10 is that the disorder specific (phoneme) updating task may place additional demands on inhibitory control. For instance, the picture task, although the name of the picture may come to mind there is no interference resolution involved as the picture names are the same and are matched based on visual features. However, with the phoneme updating task rule is based on sounds of pictures which are not visually matched (e.g. bat, ball), therefore the participant may initially attempt to inhibit this response and thus may have to overcome desire to inhibit response due to stimuli not matching visually as well as update this sound information working memory. This may place additional demands on interference control in the phoneme updating task which are not found in the picture updating task and may

be one possible explanation for why floor effects are experienced in the disorder specific (phoneme) updating task.

Previous research suggests that there is a trend for differences in EF in dyslexia depending on domain of task (Booth et al., 2010), and disorder specific (phoneme) updating impairments have been found in dyslexia with under-activation of frontal brain areas (Beneventi et al., 2010a). The findings of Beneventi et al. (2010a) suggest that dyslexia may be associated with a disorder specific EF updating impairment in processing of phoneme content, which is interesting given that phonological impairments in dyslexia appear manifest only on more complex phonological tasks with increasing executive demands (Ramus & Szenkovits, 2008). Although Beneventi et al. (2010a) explored phoneme updating in dyslexia their study did not include a picture control task, so in addition to not being able to address whether updating impairments manifest with all types of content in dyslexia, this study also could not explore differences between dyslexia and control participants in phoneme versus visual updating tasks. Beneventi et al. (2010a) found a similar task difficulty pattern with the last phoneme updating task whereby control participants appeared to experience a larger drop in performance from the first phoneme updating task. This task difficulty pattern was not found with the first phoneme updating task in their study. Potential reasons for differences in findings here are (1) task difficulty, and, (2) age range- mean sample in present study is 10 years while mean age in Beneventi et al. (2010a) study was 13 years. Age differences may interfere with performance on EF tasks as EF abilities gradually develop with age (Huizinga et al., 2006; Lehto et al., 2003; van der Sluis et al., 2007). Therefore, the sample employed in Beneventi et al.'s (2010a) study may have had more developed EF skills which may have supported EF processing with a more complex processing rule (i.e. sounding out visually presented images), while the sample in the present study may have less developed EF skills which results in difficulty when attempting to process information with a more complex EF processing rule.

It may also be the case that participants did not have enough time to respond due to the additional demands of naming a picture, parsing and then isolating the first phonemes of the depicted object noun, updating this information in working memory and matching to

the next picture. This process would require more time than matching pictures and letters based on visual aspects alone. Indeed, previous research suggests that there are significant processing speed differences for semantic and phoneme processing of pictures (Schmitt, Münte, & Kutas, 2000), and for categorizing pictures compared to word processing (Smith & Magee, 1980), with the latter requiring significantly more time. This may be one reason why the disorder specific (phoneme) updating task is too difficult to capture any between group differences.

Overall the results of this study (study 1) demonstrate that dyslexia and comorbid dyslexia-ADHD are associated with impaired response inhibition and updating and unimpaired switching. EF and other processing impairments manifest more severely in comorbid dyslexia-ADHD than dyslexia alone as reflected by larger effect sizes and an almost trend for more severe inhibition impairments in comorbid dyslexia-ADHD. Response inhibition impairments manifested in a general way in dyslexia and comorbid dyslexia-ADHD, but the disorder specificity of updating impairments could not be concluded due to task difficulty issues. These findings strengthen EF (specifically response inhibition) as a candidate endophenotype for explaining dyslexia alone and overlap between dyslexia and comorbid dyslexia-ADHD. Further research needs to be carried out on EF to determine if it is predictive of disorder likelihood and symptom severity, as well as whether it meets other criteria of an endophenotype (heritable, manifest in at risk family members) (Crosbie et al., 2008; Gottesman & Gould, 2003).

The current study is not without limitations. Although the research design can address whether the EF profile of dyslexia alone is compounded in comorbid dyslexia-ADHD, it cannot address questions in relation to additive or severity of effects in relation to dyslexia and ADHD alone because an ADHD group was not included. This type of design would be optimal for teasing out source of EF problems in the comorbid group and shared risk factors, however, it could not be implemented in the present study due to difficulties in recruiting ADHD alone and subsequent sample size issues. The present study may also experience inflation of type 1 error rate due to multiple statistical tests conducted. To account for this limitation, a Bonferroni correction was employed ($p<.004$) while also considering trends within the data ($p<.05$) to ensure there was a relative balance between

the chances of increasing type 2 errors due to employing a low alpha level. Another limitation of this study is that it didn't employ EF latent variables in between group comparisons which is outlined as best practice (Miyake & Friedman, 2012; Snyder et al., 2015). This type of analysis could not be performed in the present study due to sample size constraints but EF z-mean composite scores were employed as Snyder et al. (2015) suggests this is the next best thing.

Given that considerable work has been conducted on response inhibition as an endophenotype and underlying neuro-cognitive impairment capable of explaining associated symptoms at a behavioural level (Barkley, 1997; Castellanos & Tannock, 2002; Rommelse et al., 2009), future research should focus on establishing whether EF (specifically response inhibition and updating) is predictive of dyslexia alone diagnosis, and core (reading) and non-core (socio-emotional) issues associated with dyslexia alone while systematically accounting for elevated ADHD.

Chapter 4: Clinically-relevant Predictive Ability of EF for Dyslexia Diagnosis, Reading (Core) and Socio-Emotional (Non-Core) Problems

4.1 Introduction

Findings from the previous chapter suggest that across a broad range of cognitive processes (EF and processing resources), response inhibition (or common EF) and updating impairments manifest more severely than other impairments in dyslexia alone. Exploring the predictive ability of EF (response inhibition, updating and switching) to account for a dyslexia diagnosis (clinical status), and also to explain variances in reading (core) and self-regulatory (non-core) behaviours typically implicated in dyslexia may enhance the understanding of aetiological factors implicated and the development of interventions targeted at improving symptom expression (Goschke, 2014; Snyder et al., 2015). EF is an endophenotype for a range of neuro-developmental conditions, suggesting that it demonstrates sensitivity in detecting prodromal phases in at-risk populations and is also linked to severity of functional outcome (Glahn et al., 2014, 2016; Goschke, 2014; Miller & Rockstroh, 2013; Snyder et al., 2015). EFs are not only distinguishable at the neural (Collette et al., 2005) and cognitive levels (Friedman & Miyake, 2016; Miyake et al., 2000; Miyake & Friedman, 2012), but may also be distinguishable at the behavioural level, as different EF components differentially relate to a range of complex behaviours (Friedman et al., 2008; Friedman & Miyake, 2004). However, as outlined in section 2.8, the predictive relationship between key EFs and core reading and non-core socio-emotional outcomes are unclear from previous research. Variances in underlying EF abilities at the construct (EF z-mean composite) level may predict variances in core and non-core symptoms implicated in dyslexia. By accounting for issues of task impurity by employing EF z-mean composite scores of each key EF construct (response inhibition, updating and switching) this study (study 1) may elucidate which key EF aspects are predictive of dyslexia diagnosis and variance in reading (core) and self-regulatory (non-core) behaviours. This has implications for understanding the range of functional outcomes in dyslexia alone.

Although the previous chapter (3, Study 1) explored if dyslexia alone was associated with EF impairments and whether these impairments overlapped with and manifested more severely in comorbid dyslexia-ADHD, the current chapter (4, Study 1) will focus on developing clinically-relevant predictive models in dyslexia alone and control groups. Although some studies define overlapping impairments as those which are predictive of diagnosis of dyslexia and ADHD (Willcutt et al., 2010) or predictive of reading problems in dyslexia and inattention in ADHD (McGrath et al., 2011); the current study (study 1) is not designed to address whether impairments overlap at the predictive level in dyslexia and ADHD due to a lack of an ADHD alone group within the study design. In addition, it is not clear if EF impairments are important for predicting functional outcomes in dyslexia alone, as some find that although EF is impaired, it is not predictive of dyslexia (Willcutt et al., 2010) while others find that EF is predictive of dyslexia (Booth et al., 2014; Moura et al., 2015). The focus of this PhD is to determine how key EFs are implicated in the aetiology and severity of outcomes in dyslexia alone and to assess whether training targeted at key EFs can improve outcomes in dyslexia alone. The previous chapter (3) found EF impairments in dyslexia alone, even after systematically screening for preclinical and clinical ADHD features. Therefore, the next step is to explore whether these EF impairments are predictive of dyslexia diagnosis (clinical status) and relate to functional outcomes at core and non-core levels.

Exploring how EF is related to behavioural outcomes such as reading and socio-emotional problems across a dimension of severity from typical (control) to atypical (dyslexia) can give insight into the spectrum nature of cognitive in relation to different behavioural domains (Cuthbert, 2014; Cuthbert & Insel, 2013). EF may be modifiable with targeted intervention resulting in improvements in reading ability (core symptom of dyslexia) in control children (Loosli et al., 2012), and underlying neural activity (Berkman et al., 2014; Manuel et al., 2013). Therefore, it is important to explore how common (response inhibition) and specific (updating and switching) aspects of EF (Friedman & Miyake, 2016; Miyake & Friedman, 2012) are predictive of clinical diagnosis of dyslexia, and core/non-core behavioural features with the aim of developing more effective targeted neuro-cognitive interventions.

Core issues in Dyslexia-Reading ability

At one end of the reading distribution in typical samples, EF appears to be important for the development of reading skills (Cartwright, 2012), however it is unclear which key aspects of EF (response inhibition, updating and switching) are predictive of reading ability. Studies differ regarding which components of EF are important for typical reading abilities. Some studies find that working memory updating is predictive of word reading ability (Christopher et al., 2012), others find that response inhibition is predictive of word reading ability (Blair & Razza, 2007) while others still find that switching is predictive of word reading ability (Cartwright, 2012). It may also be the case that a combination of different EFs are important for reading ability, however studies also differ regarding *which combination of EFs* are predictive of reading ability. For instance, van der Sluis et al. (2007) found that updating and switching combined are predictive of word reading ability, while other studies suggest that response inhibition and updating combined are predictive of word reading ability (Arrington et al., 2014; Welsh et al., 2010). Some authors have also found that a combination of EF and processing resources such as speed are predictive of word reading ability in typically developing children (Christopher et al., 2012).

At the other end of the reading distribution in atypical samples (dyslexia), it is unclear if EF is predictive of reading problems as some studies find EF implication while others do not. Those suggesting that EF is implicated in word reading problems find a combination of different EFs to play a role, some studies find that response inhibition and updating combined are predictive of reading problems (Booth et al., 2014; Wang & Yang, 2014), while others find that inhibition and switching combined are predictive of reading problems (Altemeier et al., 2008). However, some studies suggest that EF does not play a role in reading problems and instead a combination of working memory, processing speed and phonological abilities predict reading problems (McGrath et al., 2011) or that only processing speed and phonological abilities predict reading problems (Peterson et al., 2016).

It is also unclear which key EF components are predictive of disorder likelihood (dyslexia diagnosis). Again, there is considerable debate regarding which components of EF are predictive of dyslexia status. For instance, Booth et al. (2014) found that response

inhibition and updating combined are predictive of dyslexia diagnosis, and Moura et al. (2015) found that switching alone is predictive of dyslexia diagnosis. Yet others find that EF is not predictive of dyslexia diagnosis, instead a combination of working memory, phonological awareness, processing speed and verbal reasoning abilities are predictive of dyslexia diagnosis (Willcutt et al., 2010).

Although it is not clear which key EFs are predictive of reading ability and dyslexia diagnosis, evidence of EF predicting reading ability in typical and atypical samples suggests that it may play a role in the aetiology of reading problems. Longitudinal studies typically suggest that EF plays a role in reading development (typical and atypical) but generally stronger predictive effects are found for early pre-reading ages (Gooch, Hulme, Nash, & Snowling, 2014; Kegel & Bus, 2013; Thompson et al., 2015), which suggests that EF may play an important role in the early acquisition of reading skills. Another longitudinal study found that EFs in particular response inhibition and updating are predictive of future growth in word reading abilities (Jerman, Reynolds, & Swanson, 2012). However, other studies find that although EF appears to be predictive of reading ability, it is not predictive of growth in reading outcomes (Walda, van Weerdenburg, Wijnants, & Bosman, 2014). Overall it is unclear whether EF is predictive of reading problems and dyslexia diagnosis.

Non-Core Issues in Dyslexia: Socio-Emotional Control

As outlined in section 2.5, Diamond's (2013) EF framework suggests that response inhibition abilities underlie effective self-regulation and socio-emotional wellbeing. Therefore, compromised response inhibition may underpin non-core behaviours associated with dyslexia such as socio-emotional problems.

EF is important for socio-emotional self-regulatory skills (Diamond, 2013; Vohs & Baumeister, 2011), which are a central feature of ADHD (Barkley, 1997) and often associated with dyslexia (Knivsberg & Andreassen, 2008; Mugnaini et al., 2009). Consistent with Diamond's (2013) EF framework, response inhibition is consistently found to be central for effective regulation of socio-emotional behaviours (Albrecht et al., 2005; Bohlin et al., 2012; Brunnekreef et al., 2007; Carlson & Wang, 2007; Eisenberg et al., 2009;

Kooijmans et al., 2000; Rhoades et al., 2009; Young et al., 2009). Some studies find that response inhibition is associated with internalizing (Kooijmans et al., 2000; Rhoades et al., 2009) and externalizing behaviours (Eisenberg et al., 2009; Young et al., 2009); and may sensitively discriminate type of socio-emotional behavioural problems (e.g. internalizing versus externalizing) (Brunnekreef et al., 2007). In contrast, others suggest that response inhibition is not specifically related to experience of negative emotions but more related to the tendency to express negative emotions (Bridgett, Oddi, Laake, Murdock, & Bachmann, 2013).

Response inhibition appears to a transdiagnostic factor capable of explaining socio-emotional problems across a range of psychopathologies such as ADHD, OCD, CD (Albrecht et al., 2005; Bohlin et al., 2012). As outlined in section 2.8, a wealth of previous research suggests that response inhibition is the key EF underpinning typical and atypical self-regulation and socio-emotional wellbeing. This suggests that response inhibition may predict severity of socio-emotional issues experienced in dyslexia, especially given that the previous chapter (3) and previous research found socio-emotional problems in dyslexia (Knivsberg & Andreassen, 2008; Mugnaini et al., 2009) and the previous chapter (3) found response inhibition impairments in dyslexia. Some studies find that working memory may also be related to socio-emotional problems (Aronen, Vuontela, Steenari, Salmi, & Carlson, 2005). Working memory appears to be a good indicator of risk for socio-emotional problems (Brunnekreef et al., 2007) and severity of socio-emotional problems within ADHD (Tseng & Gau, 2013). One study exploring predictive relationship between socio-emotional problems in dyslexia and EF found that inhibition and updating are predictive of severity of externalizing problems (Wang & Yang, 2014).

Problems Understanding Predictive Relationship

Predictive studies are faced with the same issues discussed in the previous chapter which include problems with: (a) classification of dyslexia alone sample and screening for potential undiagnosed ADHD, (b) profiling approach and task impurity, and (c) not controlling for confounds such as processing speed in predictive studies. These problems

make it difficult to infer which specific aspects of EF are predictive of clinical diagnosis or severity in core and non-core behaviours. As mentioned before, predictive studies often use complex tasks viewing EF as a unified construct or multiple separable abilities with many tasks (Snyder et al., 2015). Complex tasks make it difficult to understand which specific aspects of EF are related to behavioural outcome as measures tap multiple domains and are confounded with non-EF noise (e.g. learning from feedback in WCST) (Miyake et al., 2000; Miyake & Friedman, 2012; Snyder et al., 2015). Viewing EF as a number of separate abilities is problematic because it fails to address the theoretical understanding that these abilities are facilitated by a number of core underlying processes which are both related (common EF: inhibition) and unique (updating and switching) (Snyder et al., 2015). This approach is also not equipped to address potential trade-offs between EF abilities (i.e. response inhibition and switching) (Blackwell et al., 2014; Friedman & Miyake, 2016; Goschke, 2000; Gruber & Goschke, 2004; Miyake & Friedman, 2012; Snyder et al., 2015). These difficulties arise across predictive studies of reading and socio-emotional tasks where studies employ complex tasks (Carlson & Wang, 2007; Rhoades et al., 2009; Walda et al., 2014), view EF as a unitary ability (Kegel & Bus, 2013; Thompson et al., 2015) or as multiple separable processes (Walda et al., 2014). In addition, the socio-emotional literature often employs questionnaire measures of cognitive constructs (Eisenberg et al., 2009). Task impurity and methodological issues limit the fine-grained understanding of how the common and specific aspects of EF relate to different behavioural outcomes, and which EFs should be targeted in interventions aimed at improving functional outcomes in dyslexia alone.

To understand predictive relationships, studies should be informed by well validated models and employ the most sensitive measures to systematically reduce non-EF noise (Goschke, 2014; Snyder et al., 2015).

The present study (Study 1) aims to build on the findings from the previous chapter (3) which report that dyslexia is associated with compromised EF, by exploring the predictive relationship of EF z-mean composites for determining clinical status (dyslexia diagnosis), severity of core (reading) and non-core (socio-emotional) outcomes across the spectrum from typical to atypical functioning. Predictive relationships will be informed by Miyake

and Friedman's (2012) and Diamond's (2013) models of EF (see *Figure 11)*. The predictive relationship will be explored in the same sample of dyslexia and control participants from chapter (3). As outlined in chapter 3, multiple measures of each EF construct were employed (response inhibition, updating, and switching) with different types of content (e.g. picture, phoneme, and alpha-numeric).

Similar to the last chapter, latent variable analysis could not be conducted in the present chapter due to sample size constraints, however, EF z-mean composite scores were created for each construct to provide cleaner measures by filtering out any non-EF noise (Snyder et al., 2015). By systematically accounting for task impurity issues within EF measurement, study 1 (PhD aim 3) should elucidate whether common and specific aspects of EF are predictive of diagnostic category and severity in core (reading) and non-core (socio-emotional) outcomes across groups.

Incorporating and addressing potential reasons for inconsistent findings the present study aims to examine the predictive utility of EF constructs for explaining disorder likelihood (dyslexia) and severity of reading and socio-emotional problems expressed.

4.2 Method

4.2.1 Participants

The same twenty-seven dyslexia and twenty-nine control participants who took part in Study 1 were included in Study 1. See page 84 for participant characteristics.

4.2.2 Procedure

The research study was carried out in the psychology laboratories in the School of Nursing and Human Sciences at Dublin City University. All participants were assessed individually in the presence of their parent or guardian. The testing session took approximately two hours to complete and a break was given half way through. During the testing session children completed a battery of neuro-cognitive (EF), reading, phonological and processing speed measures. Parents or guardians of children completed a measure of

their child's socio- emotional behaviour problems. The order of tasks was counterbalanced for each participant to control for fatigue effects. All neuro-cognitive measures were created with E-Prime Software and responses were recorded on a Cedrus RB-50 response pad.

4.2.3 Measures

Symptom Outcomes

Social and emotional behaviour problems: The Parent Child Behaviour Checklist (CBCL) (Achenbach & Rescorla, 2001) was employed as a measure of social and emotional behaviour problems. The following sub-scores were calculated from the CBCL: (1) internalizing problems, (2) externalizing problem, and (3) total problems. The CBCL demonstrates good test retest reliability (competence items= 1; individual items=.95), and consistency (competence items= .69, problem items= .72) (Achenbach & Rescorla, 2001).

Reading ability: Participants completed the Green word reading list from the Wide Range Achievement Test 4 (WRAT-4) (Wilkinson & Robertson, 2006) as a measure of reading ability. The word reading subtest from WRAT-4 requires participants to read from a list of 55 items increasing in difficulty. The assessment was discontinued if participants had 10 consecutive errors. The WRAT-4 word reading subtest demonstrates good test retest reliability (subtest= .86) and consistency (subtest= .87) (Wilkinson & Robertson, 2006).

Executive Functions

Inhibition Composite: An inhibition Z-mean composite score was calculated to provide a cleaner measure of inhibition by filtering out non-EF noise and to increase power due to sample size (Snyder et al., 2015). Z-scores for adapted (Picture Go No-Go and Phoneme Go No-Go commission errors) and classic inhibition tasks (SART commission errors, Stroop error effect) were combined to create an inhibition composite $\left(\frac{ZPicGNGComm+ZPhonGNG+ZSARTComm+ZStroopError}{4}\right)$. The procedures for individual tasks are outlined in chapter 3 (see pages 84-88).

Updating Composite: An updating z-mean composite score was calculated to provide a cleaner measure of updating by filtering out any non-EF noise and to increase power due

to sample size (Snyder et al., 2015). Z-scores for adapted (Picture 2-back and Phoneme 2-back error rate) and classic (Letter 2-back error rate) were combined to create an updating composite score $\left(\frac{ZPic2backerror+ZPhonbackerror+ZLett2backerror}{3}\right)$. The procedures for individual tasks are outlined in chapter 3 (see pages 89-91).

Switching Composite: A switching z-mean composite score was calculated to provide a cleaner measure of switching by filtering out any non-EF noise and to increase power due to sample size (Snyder et al., 2015). Z-score for adapted (Phoneme Switch Error Cost) and classic (Number-Letter Switch Error Cost) tasks were combined to create a switching composite score $\left(\frac{ZNumLettswitcherrorcost+ZPhonswitcherrorcost}{2}\right)$. The procedures for individual tasks are outlined in chapter 3 (see pages 92-94).

Processing Resources

Processing speed: Participants completed a computerized version of the coding task (Wechsler, 2003) as a measure of processing speed. On screen participants viewed a row of letters with a row of numbers directly underneath while a letter was presented centrally. Participants were tasked with searching for the centrally presented letter on the letter row and pressing the number on the keypad which was directly underneath the letter. This task consisted of 30 trials and a practice block of 10 trials where feedback was given. A latent analysis of the coding task revealed that it loads highly (.68) onto general processing speed factor (Keith et al., 2006).

4.3 Data Analyses

To explore the predictive ability of EF z-mean composite scores for clinical status (dyslexia diagnosis) logistic regression and receiver operating characteristic (ROC) curve analyses were performed. To explore whether EF z-mean composites are predictive of core (reading) and non-core (socio-emotional) behavioural features across groups, multiple linear regression analyses were performed. A Bonferroni correction ($p<.004$) was applied to account for inflated type I error rate due to multiple comparisons. Bonferroni correction was calculated based on apriori research questions only to ensure that resulting alpha level would not lead to an increase in type II error rate.

4.4 Results

4.4.1 Preliminary Analysis

Preliminary analyses were conducted to ensure that variables did not violate the assumptions of normality, homogeneity of variance, independence of errors, multicollinearity, linearity, and linearity of logit. All assumptions were met for linear and logistic regression analyses. Normality and homogeneity of variance assumptions were violated for between group comparisons on socio-emotional problem scale, appropriate non-parametric analysis was employed for this measure.

4.4.2 Descriptive Statistics

Descriptive statistics for dyslexia and control group are summarised in Table 9.

Table 9 Means and Standard Deviations for each group on EF, Core and Non-Core Features

	Dyslexia			Control		
Measure	**N**	**M**	**SD**	**N**	**M**	**SD**
EF						
RI Error Comp	27	.135	.499	29	-.391	.546
UP Error Comp	27	.169	.78	29	-.462	.679
SW Error Comp	27	.036	.826	29	-.024	.62
Core Feature						
Reading	27	34.85	8.17	29	50.59	7.48
Non-Core Feature						
Socio-Emotional	27	26.04	15.58	29	10	11.85

Note: RI= response inhibition, UP=updating, SW=switching, Comp=composite score, Reading= reading ability, Socio-emotional= socio-emotional problems

4.4.3 RQ4: Can EF composite scores predict of clinical status (Dyslexia)?

Although dyslexia is associated with response inhibition and updating impairments at the z-mean composite level, the extent to which these impairments can discriminate between groups and therefore predict diagnosis of dyslexia is unclear from previous research.

Results from the binary logistic regression are summarised in Table 10. At step 1, processing speed only was entered into the model to control for its influence on EF. At step 2, in addition to processing speed, response inhibition, updating and switching were entered into the model respectively to reflect the pattern of impaired and unimpaired EF processes associated with dyslexia in chapter 3.

Step 1 (processing speed): demonstrated a trend for predicting dyslexia, the chi square ($X^2(1) = 5.29$, p=.032) and -2Log Likelihood (70.94) statistics demonstrate good model fit. Model 1 correctly classified 65.5% of participants according to presence/absence of dyslexia diagnosis: sensitivity 59.3% (true-positive) and specificity 71.4% (true negative).

The addition of the response inhibition, updating and switching composite scores at step 2, significantly improved model fit (Chi square: Model $X^2(3) = 15.49$, p=.001; -2Log Likelihood: 55.45; R^2_{cs}=.315; $R^2_{N=.}$42). This model correctly classified 78.2% of participants according to presence/absence of dyslexia diagnosis: sensitivity 81.5% (true-positive) and specificity 75% (true-negative). As outlined in Table 10, this model suggests that when accounting for low-level processing speed only response inhibition (Wald: $X^2(1) = 7.06$, p=.008) and updating composite scores (Wald: $X^2(1) = 5.17$, p=.023) demonstrate a trend for predicting dyslexia. The b-values reflect that for every for one-unit change in response inhibition score (errors) there is a corresponding 1.83-unit change in the logit of the outcome variable, while for every one-unit change in updating score (errors) there is a 1.28-unit change in the logit of the outcome variable (*see Figure 25 and Figure 26)*. The proportionate odds values (Exp (B)) are greater than 1 for both predictors suggesting that as error score on each predictor increases the likelihood of the outcome occurring (dyslexia diagnosis) increases.

ROC curve analysis (*see Figure 27*) indicates that the EF predictive model (response inhibition and updating) is a good fit with an area under the curve (AUC) of .835 (95% CI:

.727-.942, p=.000). A randomly selected participant with dyslexia will have a higher error rate on response inhibition and updating composites than a randomly selected control participant approximately 83.5% of the time. According to Swets (1988), criteria for diagnostic accuracy (poor: .5-.7, moderate: .7-.9, high: .9-1.0), response inhibition and updating composites demonstrate moderate accuracy in predicting dyslexia diagnosis.

Table 10 Binary Logistic Regression

	Binary Logistic Regression (Dyslexia Versus Control)			
	β (SE)	**Exp (B)**	**95% CI**	**-2Log Likelihood**
Step 1				70.94
Constant	2.41 (1.18)	11.16		
Processing Speed	-.282 (.131)*	.754	.584-.975	
Step 2				55.45
Constant	.841 (1.42)	2.32		
Processing Speed	-.051 (.168)	.950	.684-1.32	
Response Inhibition	1.83 (.688)*	6.23	1.62-24.00	
Updating	1.28 (.565)*	3.61	1.19-10.92	
Switching	.031 (.468)	1.03	.413-2.58	

Step 1: R^2=.092 (Cox & Snell), .122 (Nagelkerke), Model $X^2(1)$ =5.29, p<.05 **Step 2:** R^2=.315(Cox & Snell), .42 (Nagelkerke), Model $X^2(4)$ =20.77, p<.001. **Note:** Hosmer & Lemeshow (Step 1) $X^2(6)$ =10.13, p=.119, (Step 2) $X^2(7)$ =8.19, p=.316 indicates good model fit. P<.05*, P<.004**.

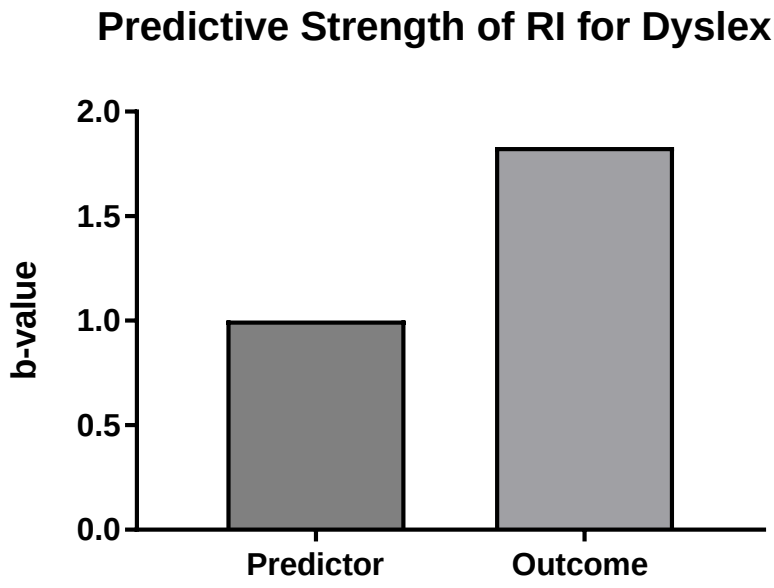


Figure 25 Response inhibition error composite b-values reflecting that for every one-unit increase in scores on error composite there is a corresponding 1.83-unit change in the logit of the outcome (dyslexia diagnosis)

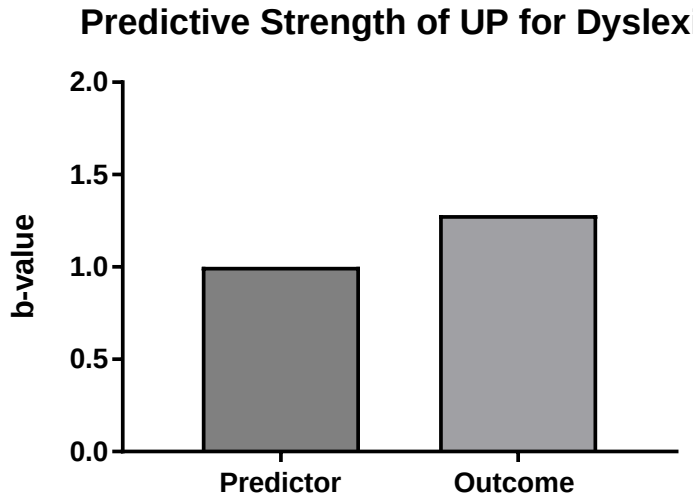


Figure 26 Updating error composite b-values reflecting that for every one-unit increase in scores on error composite there is a corresponding 1.28-unit change in the logit of the outcome (dyslexia diagnosis)

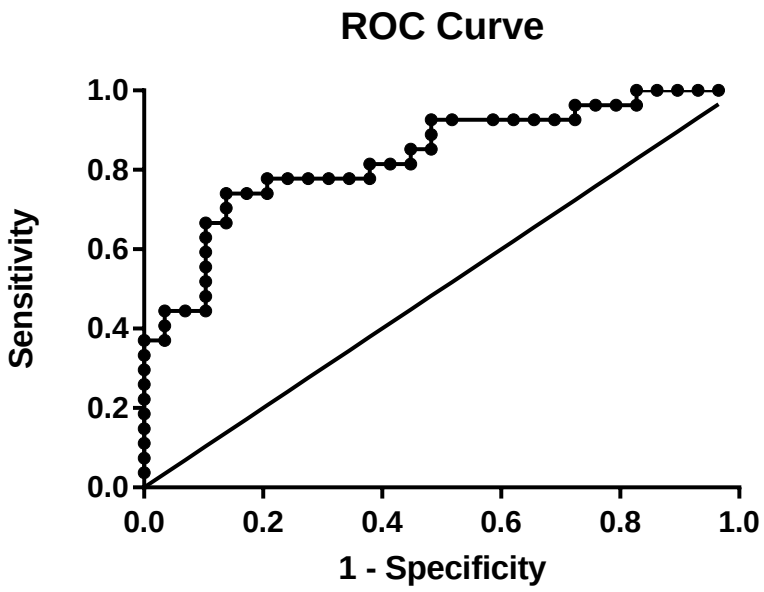


Figure 27 ROC curve of inhibition and updating composite score for predicting likelihood of dyslexia diagnosis

4.4.4 RQ5: Can EF composites predict core behavioural features (reading) associated with dyslexia?

Although dyslexia is associated with response inhibition and updating impairments at the z-mean composite level and these impairments appear to sensitively predict disorder likelihood, it is unclear from previous research whether EF is predictive of outcomes in reading ability. Hierarchical multiple linear regression is explored here with processing speed entered at step 1 and inhibition, updating and switching entered respectively at step 2 to address whether key EFs are predictive of reading ability (see Table 11 for results).

Step 1(processing speed): demonstrated a trend for significantly predicting 11.4% of the variance in reading ability across groups. Step 2 (processing speed and EF): Adding EF composite scores to the model significantly improved the predictive ability (45.9%) and explained an additional 34.5% of the variance in reading ability ($\triangle R^2$=.345, F(3,54)=25.98, p=.000). As outlined in Table 11, the results suggest that after controlling for processing speed abilities response inhibition is the only significant predictor of reading ability.

Although updating demonstrates a trend for predicting some variance in reading ability also. The Beta values for response inhibition reflect that for every 1 standard deviation (SD) increase in response inhibition error composite score there is a corresponding .527 decrease in reading ability score (*see Figure 28).* While the Beta values for updating reflect that for every 1 standard deviation (SD) increase in updating error composite score there is a corresponding .307 decrease in reading ability score (*See Figure 29).* This suggests that response inhibition and updating can predict variance in reading abilities across a trajectory from typical-atypical reading.

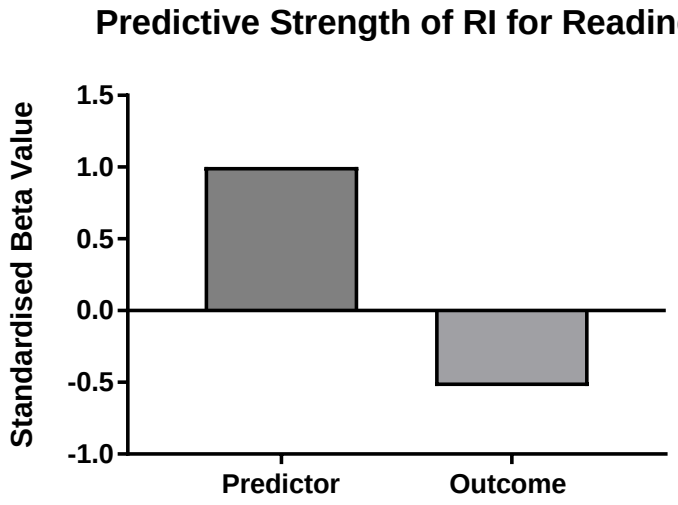


Figure 28 Response inhibition error composite standardised beta values reflecting that for every 1SD in response inhibition errors there is a corresponding .527SD decrease in reading ability

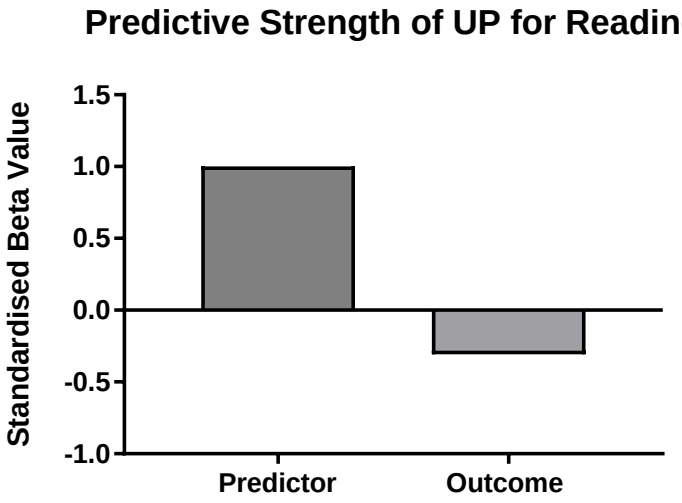


Figure 29 Updating error composite standardised beta values reflecting that for every 1SD in response inhibition errors there is a corresponding .307SD decrease in reading ability

Table 11 Linear Regression Model Predicting Reading Ability Across Groups

	Reading Ability Across Groups				
	B	SEB	β	F/T-Value	P
Step 1				6.83	.012*
Constant	29.30	5.43			
Processing speed	1.58	.61	.338	2.61	.012*
Step 2				10.61	.000**
Constant	39.43	4.79			
Processing speed	-.19	.556	.041	.341	.734
Response inhibition	-10.03	2.14	-.527	-4.68	.000**
Updating	-4.31	1.65	-.307	-.262	.012*
Switching	-1.35	1.7	-.088	-.799	.428

Note Step 1: R^2=.114, ; Step 2: R^2 =.459. *p<.05, **p<.004.

4.4.4 RQ5: Can EF composites predict non-core behavioural features (socio-emotional problems) associated with dyslexia?

Although EF and socio-emotional problems are associated with dyslexia, it is unclear whether EF is predictive of severity of socio-emotional problems which are non-core to dyslexia. Hierarchical multiple linear regression is explored here with processing speed entered at step 1 and inhibition, updating and switching entered respectively at step 2 to address whether key EFs are predictive of socio-emotional problems (see Table 12 for results).

Step 1 (processing speed): did not significantly predict socio-emotional problems across groups (3.2%). Step 2 (processing speed and EF): adding EF composite scores to the model slightly improved variance explained (5.7%), but overall the model was not significantly predictive of variance in socio-emotional problems across groups (See Table 12). This suggests that EF composites are not predictive of variance in socio-emotional problems across groups.

Table 12 Linear Regression Model Predicting Total Socio-Emotional Problems across Groups

	Socio-emotional problems across groups				
	B	SEB	β	F/T-Value	P
Step 1				1.78	.188
Constant	28.18	8.12			
Processing speed	-1.21	.905	-.18	-1.33	.188
Step 2				.752	.562
Constant	24.75	9.06			
Processing speed	-.734	1.05	-.11	-.699	.488
Response inhibition	3.84	4.04	.14	.950	.347
Updating	.945	3.11	.047	.304	.763
Switching	-1.45	3.21	-.065	-.451	.654

Note Model 1: R^2=.032; Model 2: R^2 =.057. *p<.05, **p<.004.

4.4.5 Summary

RQ4: Response inhibition and updating composite scores predict clinical status of dyslexia while controlling for processing speed, such that participants with higher error rates on response inhibition and updating are more likely to have a dyslexia diagnosis.

RQ5: Response inhibition and updating composite scores predict core behavioural features (reading) across groups while controlling for processing speed, such that those with higher error rates on response inhibition and updating are more likely to have lower reading ability.

RQ6: No EF composites were predictive of non-core behavioural features (socio-emotional problems) across groups while controlling for low-level processing speed.

4.5 Discussion

The ability of EF constructs (response inhibition, updating and switching) to predict dyslexia diagnosis and variance across core (reading) and non-core (socio-emotional) behaviours implicated is unclear from previous research.

Across the literature, there is considerable debate regarding which exact EF aspects are predictive of dyslexia (Booth et al., 2014; Moura et al., 2015) and reading ability (Christopher et al., 2012; van der Sluis et al., 2007; Welsh et al., 2010). While the literature concerning socio-emotional problems consistently finds common EF (response inhibition) involvement (Brunnekreef et al., 2007; Albrecht et al., 2005; Kooijmans et al., 2000; Young et al., 2009), very little research has been carried out on socio-emotional problems in dyslexia alone. As mentioned earlier, predictive studies of EF are often confounded by group classification, measurement approach, task impurity (Snyder et al., 2015) and confound control issues. For example, several studies view EF as a unitary ability (Gooch, Thompson, Nash, Snowling, & Hulme, 2016; Thompson et al., 2015), employ complex measures (Carlson & Wang, 2007; Rhoades et al., 2009) and view EF as multiple unrelated abilities (Walda et al., 2014). Despite extensive research establishing that EF is comprised of three key related (common EF: inhibition) but separable abilities (updating and switching) that can be specifically and sensitively measures (Miyake & Friedman, 2012;

Snyder et al., 2015); most EF predictive studies fail to theoretically inform research with well validated EF models and employ the most sensitive measurements (Goschke, 2014; Snyder et al., 2015).

By exploring the predictive ability of EF for dyslexia diagnosis and symptom severity with a method informed by the 3-factor model of EF (Miyake & Friedman, 2012) and employing EF z-mean composite scores to reduce non-EF noise and ensure clean measurement (Snyder et al., 2015) this study (Study 1) could address how common (response inhibition) and unique (updating and switching) EFs are implicated. Response inhibition and updating impairments significantly predicted clinical status of dyslexia diagnosis at the z-mean composite level while accounting for processing speed confounds. Response inhibition and updating composite impairments also predicted core behavioural features (poorer reading ability) across a trajectory from typical to atypical while accounting for processing speed. However, EF composites were not found to be predictive of non-core behavioural features (socio-emotional problems) often found to be associated with dyslexia while controlling for low-level processing speed.

Response inhibition and updating composites significantly predicted likelihood of dyslexia (sensitivity: 81.5%, specificity: 75%) with moderate diagnostic accuracy (.835) according to Swets (1988) criteria (poor:.5-.7; moderate: .7-.9, high: .9-1.0). The accuracy rate suggests that a randomly selected participant with dyslexia will have a higher error rate on response inhibition and updating z-mean composites than a randomly selected control participant approximately 83.5% of the time. The initial model including only speed at step 1 demonstrated a trend for predicting dyslexia diagnosis, however when EF z-mean composite scores were entered into the model at step 2 speed was no longer trending. These findings suggest that response inhibition and updating abilities not only differentiate (chapter 3) dyslexia from control participants but are capable of discriminating dyslexia from control participants. These findings are consistent with work finding inhibition and updating abilities predict dyslexia (Booth et al., 2014) and inconsistent with work finding switching ability predicts dyslexia (Moura et al., 2015). Findings from this study (Study 1) are inconsistent to a certain degree with studies finding that EF is only predictive of dyslexia at early pre-reading stages (Gooch et al., 2016;

Thompson et al., 2015), as this study finds EF composites to predict dyslexia diagnosis in a sample of children aged 10-12 years.

Although findings from the present study (Study 1) are consistent with some previous studies, these studies could not isolate which key EFs are predictive of dyslexia due to methodological and measurement issues (e.g. task impurity) (Friedman & Miyake, 2016; Goschke, 2014; Miyake & Friedman, 2012; Snyder et al., 2015). For instance, Moura et al. (2015) found switching to be the most significant predictor of dyslexia likelihood yet viewed EF as multiple unrelated abilities measured with complex tools, while, models finding EF not to relate to reading at older ages typically measure it with complex tasks and collapse them into a unified EF composite (Gooch et al., 2016; Thompson et al., 2015). By employing EF z-mean composite scores in line with the 3-factor model (Miyake & Friedman, 2012) to systematically reduce non-EF noise and provide cleaner measures of each specific ability (Snyder et al., 2015); this study found response inhibition and updating abilities to be the most important EF constructs for predicting the likelihood of dyslexia diagnosis.

Response inhibition and updating impairments are also predictive of core behavioural features associated with dyslexia (poor reading ability) across a trajectory from typical to atypical while accounting for processing speed confounds. The model produced explained 45.9% of the variance in reading ability. The initial model including only speed at step 1 demonstrated a trend for predicting variance in reading ability (11.4%), however EF z-mean significantly improved the model's predictive ability explaining an additional 34.5% of variance in reading ability. Speed was no longer trending after EFs were entered and the model suggests that response inhibition is the only significant predictor while updating demonstrates a trend ($p<.05$) for predicting reading ability. The relationship was such that those with higher errors on response inhibition and updating z-mean composites had significantly poorer reading ability. This study implemented a cross category (control and dyslexia) approach to understanding how underlying EF abilities may be implicated in reading. The NIMH research domain criteria protocol argues that relationships between cognitive domains rooted in brain systems and behavioural outcomes should be explored across categories (Cuthbert, 2014; Cuthbert & Insel, 2013). This approach can enhance the

understanding of how reading and cognitive abilities fall on a normal distribution (Cuthbert, 2014; Cuthbert & Insel, 2013). Thus, looking at variance within single diagnostic categories (e.g. dyslexia, comorbid dyslexia-ADHD) is akin to looking at one end of the distribution in isolation. The current study (Study 1) employed this cross-category approach to explore the relationship between EF and reading ability while also accounting for task impurity issues in previous work and the confound of low-level processing speed. Current findings suggest that response inhibition and updating are implicated in core reading problems often associated with dyslexia.

These findings are consistent with previous work finding that response inhibition and updating combined are predictive of reading in typical samples (Arrington et al., 2014; Welsh et al., 2010) and are predictive of the severity of reading impairment expressed in atypical samples (dyslexia) (Booth et al., 2014; Wang and Yang 2014). The findings from this study are inconsistent with previous research finding switching is predictive of typical reading abilities (Cartwright, 2012), that processing speed is predictive of both typical (Christopher et al., 2012) and atypical reading (McGrath et al., 2011; Peterson et al., 2016) and that EF is not predictive of reading ability (Peterson et al., 2016). However, interpreting the current findings within the context of previous work is difficult given the methodological and task impurity issues (Friedman & Miyake, 2016; Goschke, 2014; Miyake & Friedman, 2012; Snyder et al., 2015). Employing EF z-mean composite scores to reduce non-EF noise and isolate specific EF processes (Snyder et al., 2015), study 1 found for the first time that response inhibition and updating abilities are predictive of reading ability across the spectrum of typical to atypical reading while controlling for processing speed, indicating that EF -particularly response inhibition- may relate to reading impairments in dyslexia.

This study also found that EF is not implicated in non-core (socio-emotional problems) behaviours associated with dyslexia alone. When speed only was entered into the model 3.2% of the variance in socio-emotional problems was explained, EF composites explained an additional 2.5% of the variance in socio-emotional problems. However, results suggest that neither step of the model nor individual EF construct significantly predicts socio-emotional outcomes. These findings are particularly surprising given that both response

inhibition and socio-emotional impairments are associated with dyslexia alone (chapter 3). Within Diamond's (2013) framework response inhibition is necessary for effective self-regulation and socio-emotional well- being. A wealth of previous literature supports Diamond's (2013) view suggesting that response inhibition is predictive of socio-emotional behaviours in typical samples (Brunnekreef et al., 2007; Bohlin et al., 2012; Carlson & Wang, 2007; Eisenberg et al., 2009; Rhoades et al., 2009) and atypical samples (Brunnekreef et al., 2007; Albrecht et al., 2005; Young et al., 2009). Response inhibition has been found to be sensitive to predicting different types of socio-emotional problems such as internalizing (Kooijmans et al., 2000; Rhoades et al., 2009) and externalizing (Eisenberg et al., 2009; Young et al., 2009), suggesting that it may sensitively predict type of problems experienced (Brunnekreef et al., 2007). Previous work with dyslexia found that response inhibition predicts externalizing socio-emotional problems (Wang & Yang, 2014). This was not reflected in the presented study, however the present study (Study 1) explored total socio-emotional problems expressed and an approach that looks at EF relationship between different types of socio-emotional problems (internalizing and externalizing) may prove more fruitful in future research. Another possibility is that socio-emotional problems in dyslexia may not stem from EF issues, it may be the case that socio-emotional problems stem from other underlying issues such as self-esteem related to reading failure (Terras, Thompson, & Minnis, 2009).

It is difficult to situate findings from the present study within previous research, as a number of studies employ complex EF measures which lack specificity in isolated the specific profile of EFs (response inhibition, updating and switching) (Carlson & Wang, 2007; Rhoades et al., 2009), or implement questionnaire measures of effortful control (majority case in temperament literature) (Blair & Razza, 2007; Eisenberg et al., 2005, 2009). It has been suggested that an integrated (temperament: effortful control; cognitive: executive function) approach to understanding socio-emotional problems may provide more fruitful insights into how each are related (Zhou, Chen, & Main, 2012). Bridgett et al. (2013) explored how both effortful control and executive function overlap and found that effortful control correlated higher with updating and monitoring tasks than other executive skills. However, these findings are not reflected in the current study.

It may be the case that the relationship between socio-emotional problems and EF is non-linear, and, therefore is difficult to model. There is evidence to suggest non-linear relations between socio-emotional outcomes and EF, for instance, Eisenberg's (2005) concept of over-control suggests that those high in effortful control express internalizing problems while those with lower effortful control are under-controlled and tend to express externalizing problems. In support of this view, some studies have found that moderate levels of EF are more conducive to adaptive socio-emotional outcomes, as both reduced and enhanced EF is associated with socio-emotional problems (Carlson & Wang, 2007). In addition, others report that children with enhanced inhibitory control are more likely to have internalizing and those with impaired inhibitory control are more likely to have externalizing problems (Kooijmans et al., 2000). Our approach explored predictive relationship between EF composites and a combined measure of socio-emotional problems, given that EFs may differentially relate to internalizing and externalizing problems, an approach which explores how EF relates to internalizing and externalizing problems in dyslexia with non-linear modelling may help disentangle how EF is related to socio-emotional problems.

Within the current study, the same EF profile associated with dyslexia was predictive of clinical status and core features associated with the condition. Understanding how intermediate neuro-cognitive risk factors relate to conditions and severity of functional outcomes can enhance treatment pathways aimed at improving outcomes (Bishop, 2006; Glahn et al., 2014, 2016; Gottesman & Gould, 2003; Miller & Rockstroh, 2013). Previous research suggests that EF abilities may be modifiable, with interventions resulting in improvements at behavioural (such as increased reading ability and reduced ADHD symptoms) (Johnstone et al., 2010; Loosli et al., 2012), and underlying neural levels (Berkman et al., 2014; Manuel et al., 2013).

Findings from the present study suggest that common EF (response inhibition) abilities should be targeted in an executive function training intervention aimed at improving core features in children with dyslexia. The previous chapter found significant response inhibition impairments and trends for updating impairments in dyslexia, the present study extending these findings to demonstrate that response inhibition ($p<.004$) and updating

(trend, p<.05) predict dyslexia diagnosis and core reading impairments associated with dyslexia. Response inhibition is the common EF and may result in updating impairments due to shared variance (Friedman et al., 2006, 2007, 2008; Miyake et al., 2000; Miyake & Friedman, 2012) and spared switching due to antagonistic relationship with inhibition (Goschke, 2000; Gruber & Goschke, 2004; Snyder et al., 2015). Within predictive models of disorder likelihood and core features response inhibition is always the most significant and heavily weighted predictor. Given shared variance, a response inhibition training intervention may result in improvements in inhibition which facilitate improvements in updating, and transfer to closely related behavioural outcomes such as reading ability.

The current study is not without limitations. One issue is in relation to small sample sizes for within group predictive analysis, as this may result in the inflation of type 1 error rate due to multiple statistical tests. To account for this limitation a Bonferroni correction was employed (p<.004) while also considering trends within the data (p<.05) to ensure there was a relative balance between the chances of increasing type 2 errors due to employing a low alpha level. Another limitation of this study is that it didn't employ EF latent variables for predictive analyses which is outlined as best practice (Miyake & Friedman, 2012; Snyder et al., 2015), this type of analysis could not be performed in the present study due to sample size constraints and EF z-mean composite scores were employed as Snyder et al. (2015) suggests this is the next best thing. In terms of predictive analyses, the present study did not include other measures which may reduce the predictive utility of EF composites, however the aim of the present study was to explore which aspects of EF were most closely related to disorder likelihood and symptom severity to isolate which factors may be targeted for an executive function intervention.

Future research should further focus on validating EF profile and predictive models in a secondary sample of children with dyslexia and explore whether response inhibition training can facilitate improvements of EF and core features of dyslexia.

Chapter 5: Validating EF Profile and Predictive Models for Clinical Status, Core (reading) and Non-Core (socio-emotional) issues in Dyslexia

5.1 Introduction

After addressing issues identified from previous EF profiling and predictive studies such as group classification, poor theoretical approach, task choice, task content and confound control; the work of this PhD thus far indicates that response inhibition and updating are impaired in dyslexia and are predictive of clinical status and core (reading) features of the condition.

Findings from the EF profiling chapter (chapter 3, Study 1) suggest that response inhibition and updating impairments are associated with dyslexia alone. Response inhibition impairments manifest in a general way in dyslexia (across all types of processing rule- phoneme and picture). However, it is unclear whether updating impairments manifest in a general (across all types of processing rule- phoneme and picture) or a disorder specific way (only phoneme processing rule). The disorder specificity of updating impairments in dyslexia could not be concluded due to a task difficulty issue. Previous research found phoneme updating impairments in dyslexia which were underpinned by pre-frontal brain activity differences (Beneventi, et al., 2010a), however this study did not compare disorder specific (phoneme) updating to picture updating to explore whether impairments manifested in a general or disorder specific way. Although chapter 3 attempted to address this issue, it could not be resolved due to floor effects in the phoneme updating task. It may have been the case that participants did not have adequate time to respond in the phoneme updating task due to the additional demands of naming a picture, including parsing the phonemes of the picture name, updating this information in working memory and matching to the next picture. Previous work suggests that there are significant time differences required for semantic versus phoneme processing of pictures (Schmitt et al., 2000), with the later requiring more time. To further explore disorder specific (phoneme) updating abilities this study (study 2) will adapt timing of task to ensure participants have sufficient time to respond.

Overall, findings from Study 1 suggest that at a general level response inhibition and updating abilities not only differentiate dyslexia participants from control participants (Chapter 3) but are capable of discriminating dyslexia from control participants as they are predictive of dyslexia likelihood (Chapter 4). Response inhibition and updating may also be closely related to symptom expression as severity in reading impairment appears to be underpinned by response inhibition and updating impairments. These findings are exciting in relation to the potential for remediation with EF training programmes, however it is important to answer remaining questions from chapter 3 in relation to disorder specificity (phoneme) of updating impairments; and to validate EF predictive models from chapter 4 in a secondary sample, to ensure they are replicable before firm conclusions can be made on how EF is implicated in dyslexia and which aspects of EF to target in a training intervention.

Predictive model validation is crucial to ensure generalisability of the predictive model to the population of interest (Field, 2013; Steyerberg, 2008). A model can be cross validated to ensure generalisability internally with split sample techniques for developing and testing the model, or externally with a new sample of participants (Field, 2013; Steyerberg, 2008). External validation is viewed as a more rigorous approach to model validation and generalisability as it is not biased due to being developed and tested within the same sample (Altman, Vergouwe, Royston, & Moons, 2009; Bleeker et al., 2003; Steyerberg, 2008). Study 2 aims to validate predictive models developed in chapter 4 in a secondary dyslexia sample to test generalisability.

EF profile and predictive models will be further confirmed and validated (Study 2) as part of a large-scale EF training study in dyslexia (Study 2). At baseline (prior to EF training), both dyslexia and control participants will complete pre-training assessment of EF, processing resources and core (reading) and non-core (socio-emotional) behavioural outcomes (similar to Study 1). Study 2 will confirm EF profile and predictive models within pre-intervention data. In order to address the disorder specificity of updating impairments in dyslexia alone, updating tasks employed in study 1 will be adapted to allow participants more time to respond in study 2. Although no amendments were necessary for response

inhibition and switching tasks to address any task difficulty issues, these measures were adapted for EEG recording which will be explored in Study 2 (Chapter 6) which addresses the near transfer effect of EF training to improved ERPs and Study 2 will also explore far transfer of EF training (Chapter 7). Study 2 validation of EF profile and predictive models will be examined at the error composite and reaction time composite levels in case amendments to tasks result in reduced sensitivity at the error level. Due to necessary EEG amendments both response inhibition and switching tasks will also allow participants more time to respond (see Section 5.2.3 for details). The total testing battery from overall study 1 to study 2 will also be reduced to ensure that the testing session is not too long with the addition of EEG recording.

Study 2 validation aims (confirm PhD aims 1,2 and 3 in Dyslexia-alone) to: (a) validate the EF profile found to be associated with dyslexia in Chapter 3, (b) address remaining questions from Study 1 in relation to disorder specificity (phoneme) of updating impairments, and (c) validate the EF predictive models of dyslexia and core-features (reading impairment) developed in Study 1. Validation of Study 1 models are in a different dyslexia-alone sample in Study 2.

5.2 Method

5.2.1 Participants

Fifty-Seven participants aged 10-12 years took part in this research study: 32 (female:14, male:18) participants with dyslexia alone (mean age: 10.78 years), and 25 (female:10, male: 15) with no clinical diagnosis. Participant diagnoses (Dyslexia) was confirmed by parents and a copy of the psychological assessment report was requested. The initial sample included 36 children with dyslexia and 27 control participants. However, 4 participants in the dyslexia group and 2 participants in the control group were removed either due to scoring in the clinical range on the ADHD scales of the Child Behaviour Checklist (Achenbach & Rescorla, 2001) and the Conners 3 Parent form (Conners, 2008) or reporting comorbid dyspraxia. In the final dyslexia group, diagnostic reports were submitted for twenty-three participants and twenty of these assessments were conducted

by an educational psychologist, while three of these assessments were conducted by a clinical psychologist. Twenty-two participants with dyslexia were referred for reading difficulties, while one was referred for reading and attentional difficulties but didn't receive a diagnosis of ADHD. Of these twenty-three participants, two were diagnosed at 6 years of age, one was diagnosed at 7 years of age, ten were diagnosed at 8 years of age and ten were diagnosed at 9 years of age. Nine parents did not submit the diagnosis report but confirmed that their child had received a diagnosis of dyslexia. Twenty-nine of those with dyslexia were enrolled in primary school when they participated and three had transitioned into 1st year of secondary school. Twenty-two participants with dyslexia were right handed and ten were left handed. All participants in the control group were enrolled in primary school when they participated in this study. Twenty participants in the control group were right handed and five were left-handed. Although some participants failed to submit the diagnostic report, all participants were screened for ADHD with the combined-ADHD scale of the child behaviour checklist and reading was assessed with a standardised reading test (Wilkinson & Robertson, 2006). All participants were Caucasian, monolingual English speakers, with normal or corrected vision and hearing. Participants had no additional diagnosis of a psychological disorder. Informed consent and assent were obtained from participating parents and children. Ethical approval for this research project was granted by Dublin City University's Research Ethics Committee (DCUREC/2015/254). Participants were recruited through the Dyslexia Association Ireland, the Centre for Talented Youth Ireland at DCU and local primary schools.

5.2.2 Procedure

The research study was carried out in the psychology laboratories in the School of Nursing and Human Sciences at Dublin City University. All participants were assessed individually in the presence of their parent or guardian. The complete testing session took approximately two hours to complete. During the testing session children completed a battery of neuro-cognitive (EF) and reading measures. Parents/guardians of children completed a measure of their child's socio- emotional behaviours. The order of tasks was counterbalanced for each participant to control for fatigue effects. All neuro-cognitive

measures were created with E-Prime Software and responses were recorded on a Cedrus RB-50 response pad, keyboard or mouse.

5.2.3 Measures

Symptom Expression

Social and emotional behaviour problems: The Parent Child Behaviour Checklist (CBCL) (Achenbach & Rescorla, 2001) was employed as a measure of social and emotional behaviour problems (see page 95 for details).

Reading ability: Participants completed the Green word reading list from the Wide Range Achievement Test 4 (WRAT-4) (Wilkinson & Robertson, 2006) as a measure of reading ability (see page 94 for details).

Executive Function Measures

Inhibition Measures (see pages 84-88 for task details).

Picture Go No-Go task: This task was adapted for electroencephalogram (EEG) recording, such that stimuli appeared on screen for 2,000ms, followed by a blank screen for 1,000ms and a fixation point for 1,000ms. Total stimulus duration was 4,000ms (*see Figure 30 for stimulus timings*).

Phoneme Go No-Go Task: This task was adapted for electroencephalogram (EEG) recording, such that stimuli appeared on screen for 2,000ms, followed by a blank screen for 1,000ms and a fixation point for 1,000ms. Total stimulus duration was 4,000ms (*see Figure 31 for stimulus timings*).

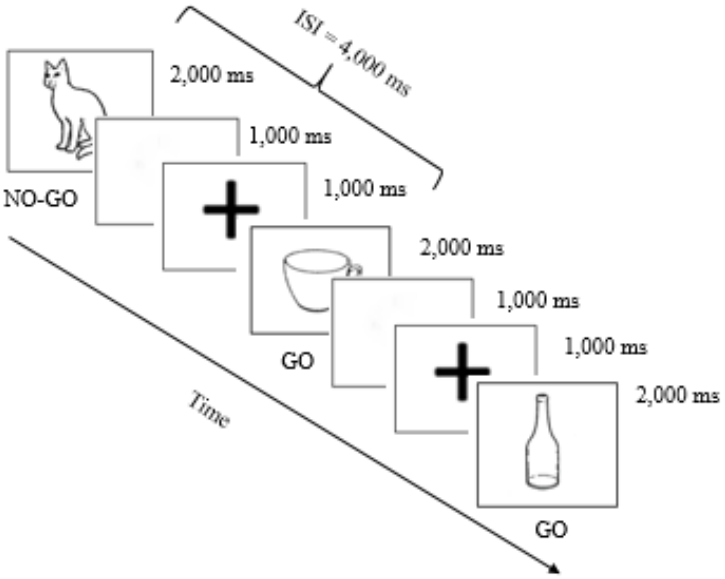


Figure 30 Picture Go No-Go sample stimuli and timings

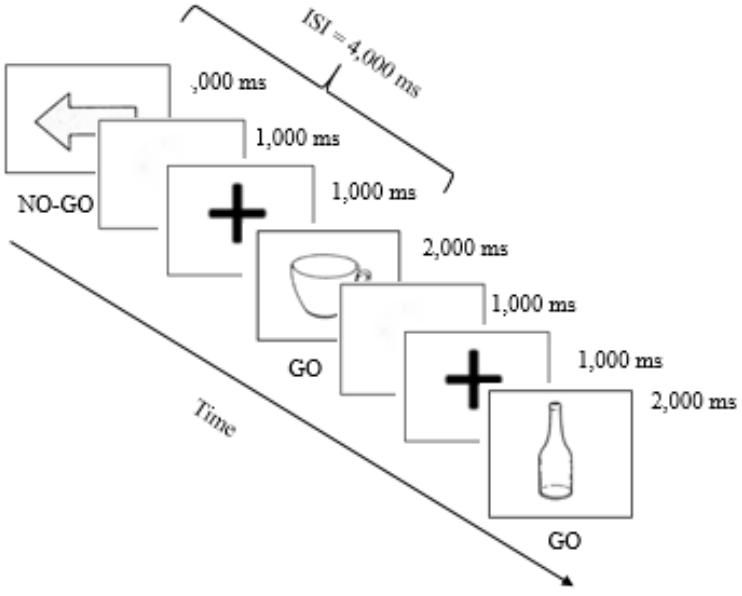


Figure 31 Picture Go No-Go sample stimuli and timings

Updating measures (see pages 89-91 for task details)

Letter 2-Back Task: Timings for this task were adjusted due to ceiling effects in study 1, such that stimuli appeared on screen for 2,000ms and a fixation point appeared on screen for 1,000ms. Total stimulus duration was 3,000ms (*see figure 32 for sample stimuli and timings*).

Picture 2-back Task: Timings for this task were adjusted due to ceiling effects in study 1, such that stimuli appeared on screen for 2,000ms and a fixation point appeared on screen for 1,000ms. Total stimulus duration was 3,000ms (*see figure 33 for sample stimuli and timings*).

Phoneme 2-back Task: Timings for this task were adjusted due to ceiling effects in study 1, such that stimuli appeared on screen for 2,000ms and a fixation point appeared on screen for 1,000ms. Total stimulus duration was 3,000ms (*see figure 34 for sample stimuli and timings*).

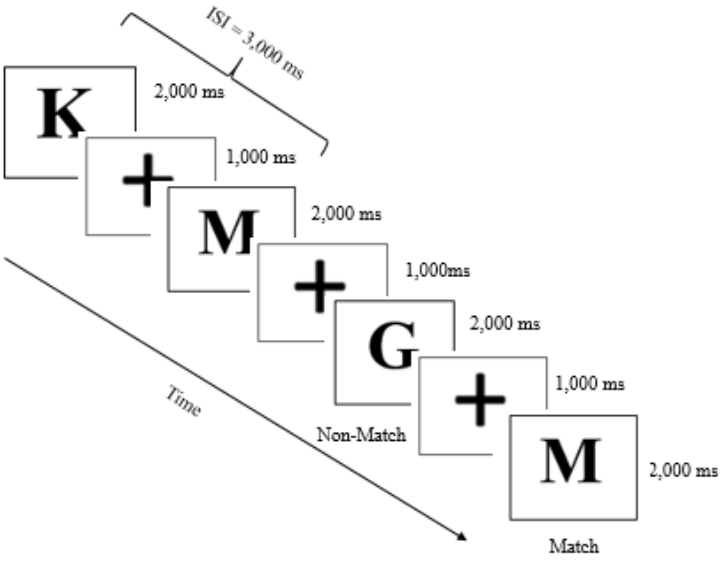


Figure 32 Letter N-back Task sample stimuli and timings

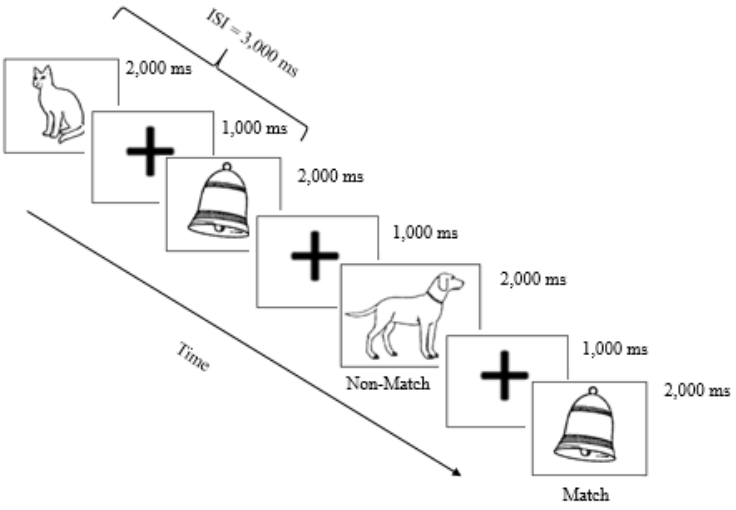


Figure 33 Picture N-back Task sample stimuli and timings

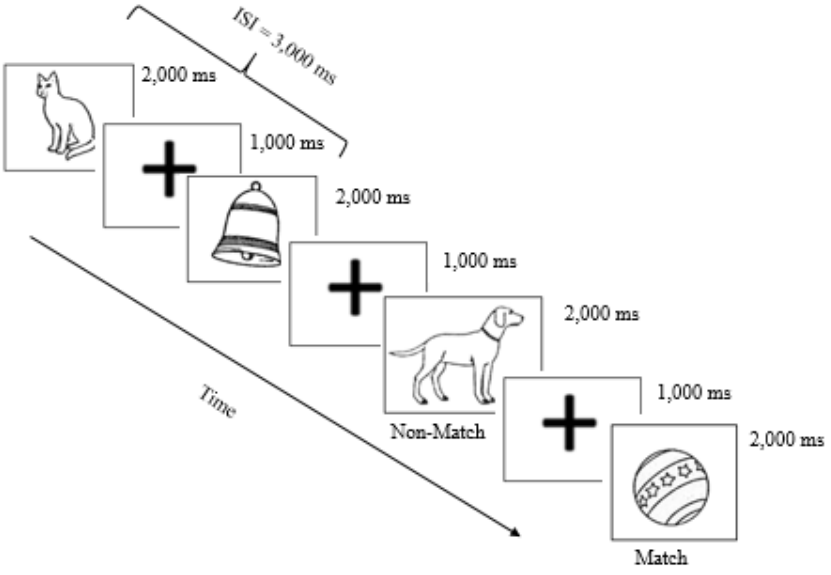


Figure 34 Phoneme 2-back task sample stimuli and timings

Switching Measures (see pages 92-94 for task details)

Number-Letter Switch Task: This task was adapted to electroencephalogram (EEG) recording such that stimuli appeared on screen for 5,000ms, followed by a blank screen for 1,000ms and a fixation point for 150ms. Total stimulus duration was 6,150ms (*see figure 35 for stimulus timings*).

Phoneme Switch Task: This task was not adapted between studies, stimuli appeared on screen for 5,000ms followed by a fixation point for 150ms. Total stimulus was 5,150ms (*see figure 36 for stimulus timings*).

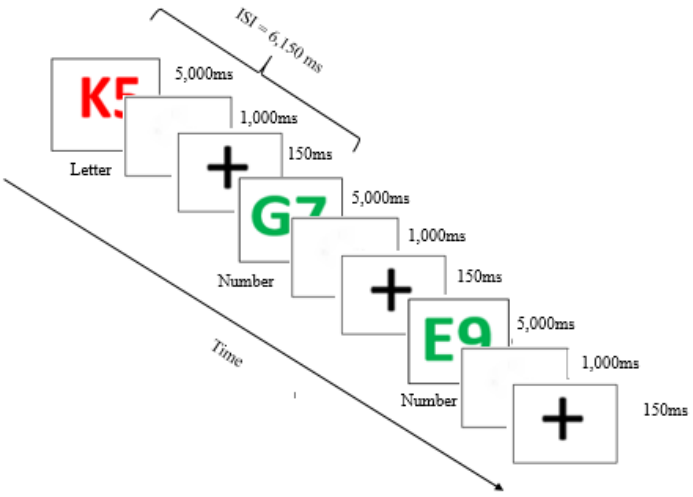


Figure 35 Number-Letter Switch Task Sample Stimuli and Timings

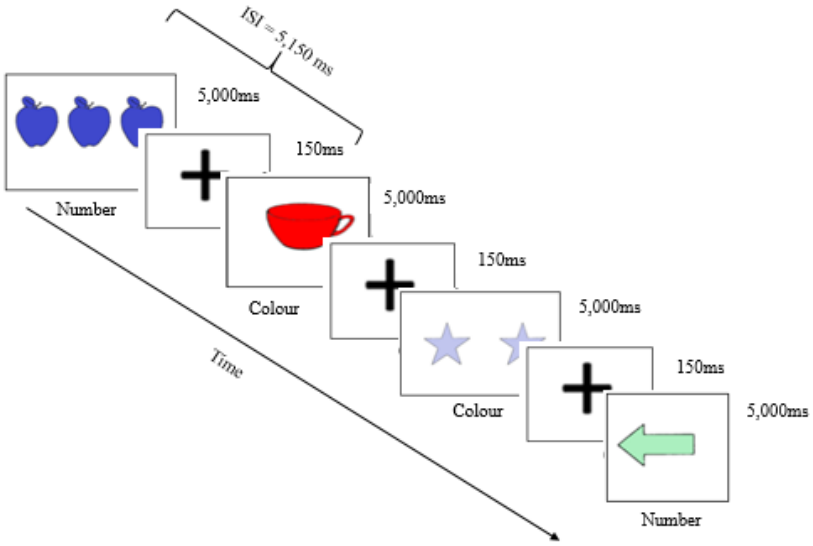


Figure 36 Phoneme Switch Task Sample Stimuli and Timings

Processing Resources

Processing speed: Participants completed a computerized version of the coding task (Wechsler, 2003) as a measure of processing speed. On screen participants viewed a row of letters with a row of numbers directly underneath while a letter was presented centrally. Participants were tasked with searching for the centrally presented letter on the letter row and pressing the number on the keypad which was directly underneath the letter. This task consisted of 30 trials and a practice block of 10 trials where feedback was given. A latent analysis of the coding task revealed that it loads highly (.68) onto general processing speed factor (Keith et al., 2006).

5.3 Results

5.3.1 Preliminary Analysis

Preliminary analyses were conducted to ensure that variables did not violate the assumptions of normality, homogeneity of variance, independence of errors, multicollinearity, linearity, and linearity of logit. All assumptions were met for linear and logistic regression analyses. Homogeneity of variance was violated for Picture 2-back

errors, Picture Go No-Go commission errors, Phoneme Go No-Go commission errors and inhibition error composite score. However, this violation only appears to be a problem for ANOVA when the ratio of groups is greater than 1:5 which is not the case in the present study (1:1.28) (Field, 2013). A Bonferroni correction ($p<.005$) was applied to account for inflated type I error rate due to multiple comparisons. Bonferroni correction was calculated based on apriori research questions only to ensure that resulting alpha level would not lead to an increase in type II error rate.

5.3.2 Descriptive Statistics

Descriptive statistics for dyslexia and control groups are summarised in Table 13.

Table 13 Means and standard deviations for dyslexia and control group

	Dyslexia			Control		
Measure	**N**	**Mean**	**SD**	**N**	**Mean**	**SD**
Age	32	10.87	.15	25	10.68	1.5
Core Issue						
Reading Ability	32	38.09	1.41	25	53.28	1.12
Non-Core Issue						
Total Problems	32	24.81	2.24	24	20.71	4.1
Response Inhibition						
Pic. GNG % Comm.	32	16.65	3.67	23	11.05	1.80
Pic. GNG RT	32	711.97	26.25	23	611.48	34.12
Phon. GNG % Comm.	32	21.55	3.61	23	13.14	1.89
Phon. GNG RT	32	824.24	27.61	23	792.81	28.86
Inhibition Err. Comp	32	.178	.20	23	-.266	.10
Inhibition RT Comp	32	.27	.15	23	-.235	.20
Updating						
Let. 2-back % error	31	30.44	3.90	24	25.56	3.75
Let. 2-back RT	31	934.05	27.27	24	974.93	31.01
Pic. 2-back % error	32	14.97	1.84	25	11.85	1.56
Pic. 2-back RT	32	877.63	19.62	25	890.86	23.21
Phon. 2-back % error	32	44.16	1.94	24	43.45	3.15
Phon. 2-back RT	32	1130.95	35.31	24	1225.73	28.67
Updating Err. Comp	31	.07	.50	24	-.14	.16
Updating RT Comp	31	-.116	.13	24	.174	.12
Switching						
Num-Let SW err. Cost	32	5.36	3.62	23	3.26	2.82
Num-Let SW RT cost	32	1029.29	450.38	23	1085.18	392.28
Phon. SW err. Cost	32	4.27	3.95	23	1.80	2.92
Phon. SW RT cost	32	775.82	811.07	23	1171.11	791.94
Switch Err. Comp.	32	.265	.967	23	-.369	.775
Switch RT Comp.	32	.179	.650	23	-.128	.798

Processing Resources						
Proc. Speed	32	8.63	2.12	23	8.63	2.12

Note. GNG= GoNoGo, Comm= Commission errors, Comp= composite score, Err.=error, RT= reaction time, Num-Let SW error= Number-Letter switch cost in errors, Num-Let SW RT= Number-Letter switch cost in reaction time, Phon SW err.= Phoneme switch cost in errors, Phon SW RT= phoneme switch cost in reaction time, Proc. Speed= processing speed. For between group differences at individual task level see appendix H

5.3.3 Validating EF Profile Associated with Dyslexia

Research question 1 (RQ1) is revisited here to confirm if the same EF profile as developed in Study 1, Chapter 3 (impaired response inhibition and updating, unimpaired switching) is also found in a secondary sample of participants with dyslexia. Due to amendments to tasks, profile will be explored at both EF z-mean error and reaction time levels.

A 2 (Group: Dyslexia, Control) x 3 (EF: Response Inhibition, Updating, Switching) mixed design ANCOVA controlling for speed was conducted to explore whether the EF profile (impaired response inhibition and updating; spared switching) associated with dyslexia in study 1 is confirmed in a secondary sample of children with dyslexia (see Table 14 for results).

For EF z-mean error composite, results suggest no main effect of EF, a near trend main effect of group ($F(1,50)=3.87$, $p<.06$) and no interaction effect. For EF z-mean RT composite, results suggest a trend for a main effect of EF ($F(2,100)=5.24$, $p<.05$), no main effect of group and almost a trend for a group x EF interaction ($F(2,100)=2.98$, $p<.06$).

Separate post hoc 2 (Group: Dyslexia, Control) x 1 (EF: response inhibition, updating, switching) ANCOVAs controlling for speed were conducted with error and RT composite scores to further explore trends for group and interaction effects. For error composite scores (*see Figures 37 – 39*), dyslexia did not significantly differ from control participants on response inhibition or updating. However, there was a trend for a switching impairment associated with dyslexia ($p< .05$). For RT composite scores (*see Figure 40 – 42*), dyslexia did not significantly differ from control participants on response inhibition, updating or switching.

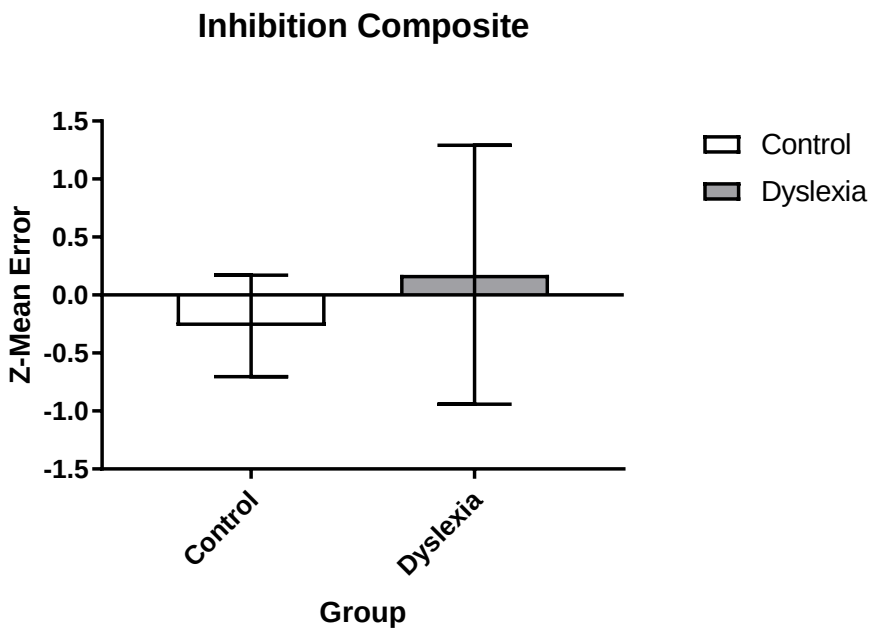


*Figure 37 Dyslexia and Control Response Inhibition Z-Mean Error Composite Score. *P<.05 **p<.004*

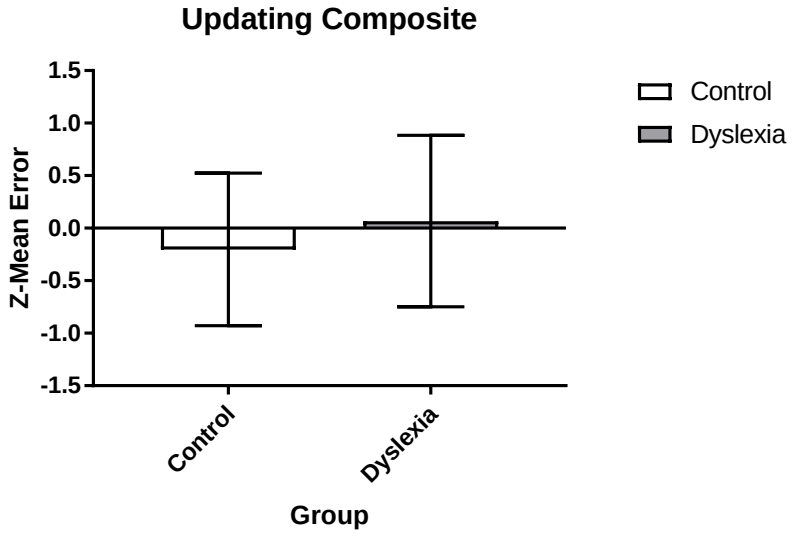


*Figure 38 Dyslexia and Control Updating Z-Mean Error Composite Score. *p<.05 **p<.005*

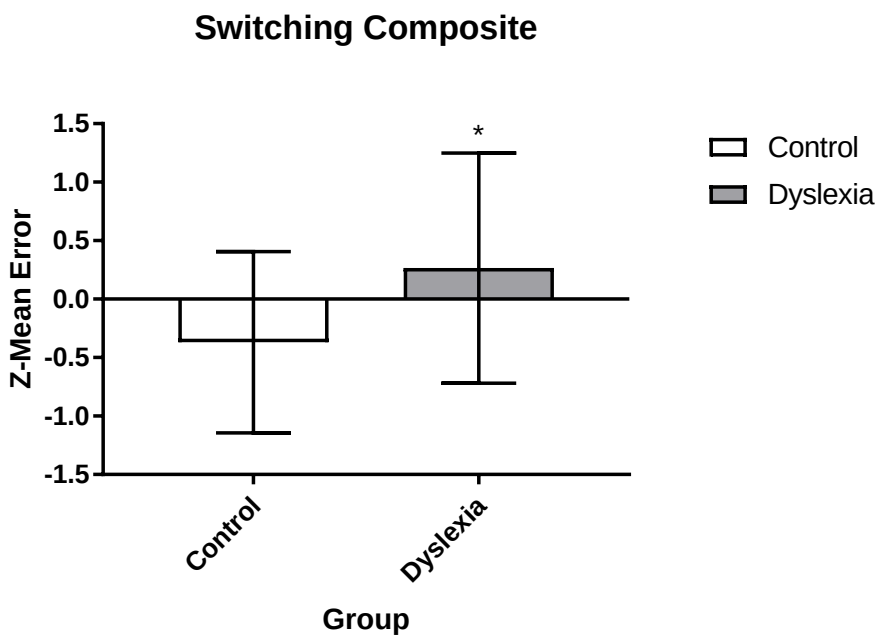


*Figure 39 Dyslexia and Control Switching Z-Mean Error Composite Score. *p<.05 **p<.004*

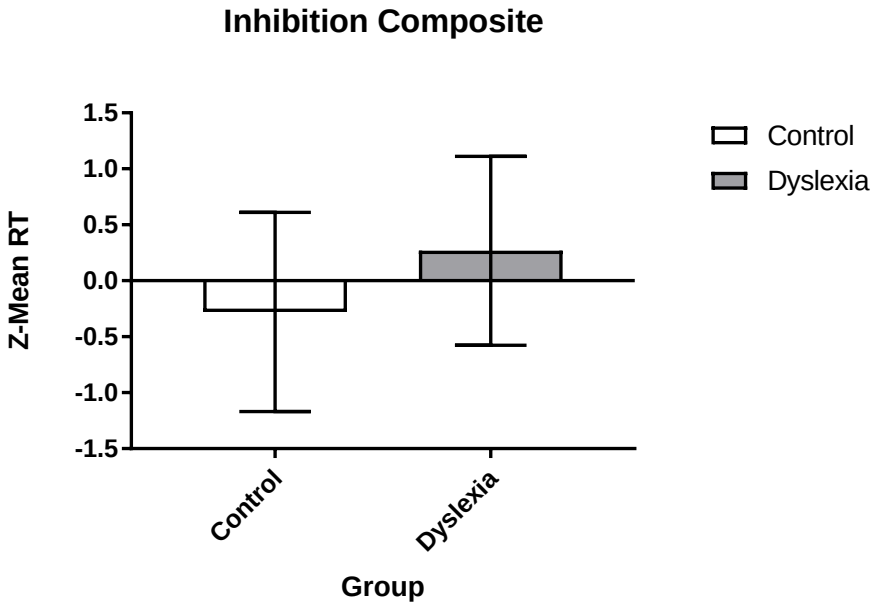


*Figure 40 Dyslexia and Control Response Inhibition Z-Mean RT Composite Score. *p<.05 **p<.004*

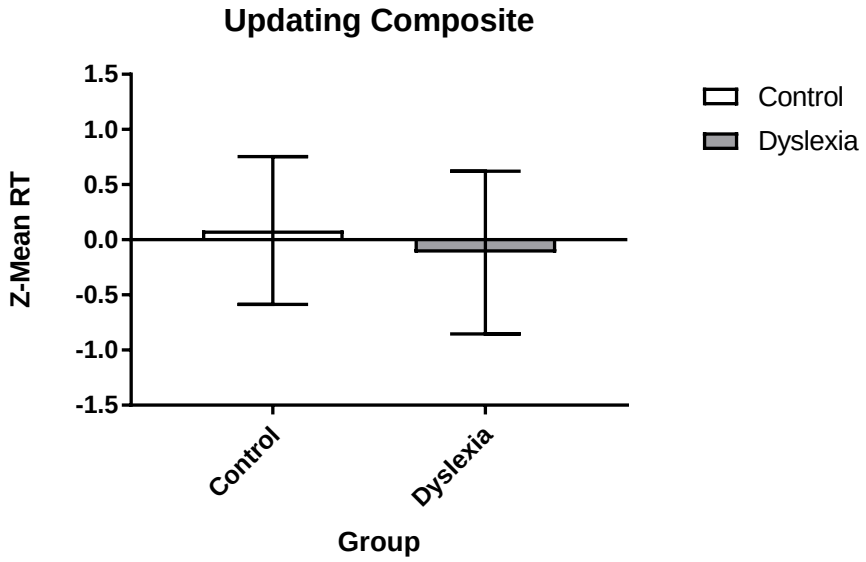


*Figure 41 Dyslexia and Control Updating Z-Mean RT Composite Score. *p<.05 **p<.005*

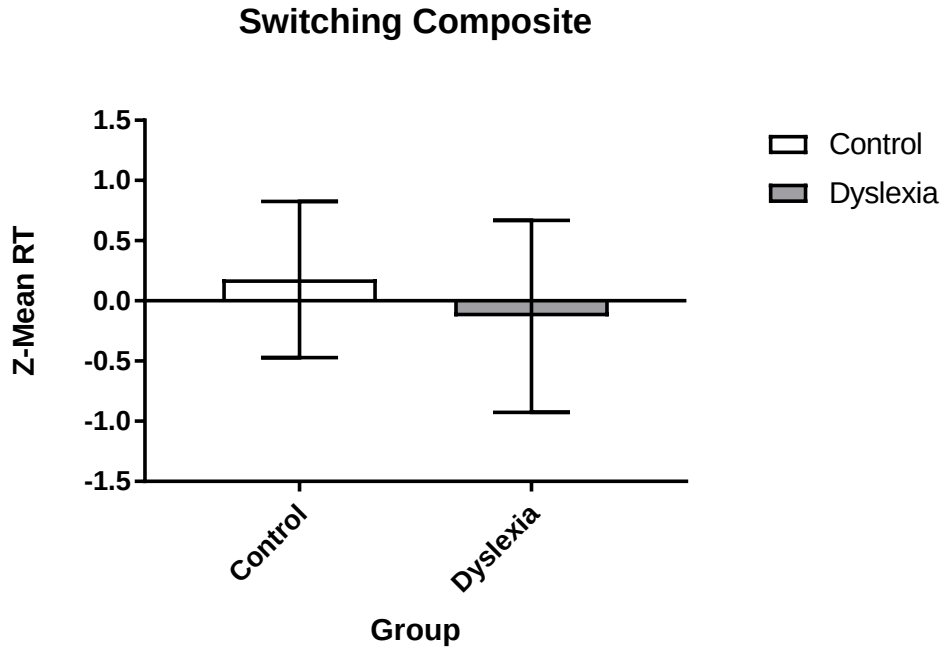


*Figure 42 Dyslexia and Control Switching Z-Mean RT Composite Score. *p<.05 **p<.004*

Summary

The EF profile found to be associated with dyslexia in study 1 (impaired: response inhibition and updating; unimpaired: switching) is not validated in a secondary sample of participants with dyslexia. At the EF z-mean error composite level, there is a trend for a reverse EF profile (impaired: switching; unimpaired response inhibition and updating). At the EF z-mean reaction time composite level, there is no evidence of EF impairments in dyslexia.

Table 14 Validating EF profile associated with Dyslexia while controlling (ANCOVA) for speed

	Chp 3. EF Profile: Err Comp.			**A/R**	**Chp 5. Validating EF Profile: Err. Comp.**			**A/R**	**Chp 5. Validating EF Profile: RT Comp.**			**A/R**
HYP	$\mu_{RI}^{Dys}{}_{/PS} = \mu_{RI}^{Con}{}_{/Ps}$			**R**	$\mu_{RI}^{Dys}{}_{/PS} = \mu_{RI}^{Con}{}_{/Ps}$			**A**	$\mu_{RI}^{Dys}{}_{/PS} = \mu_{RI}^{Con}{}_{/Ps}$			**A**
	$\mu_{UP}^{Dys}{}_{/PS} = \mu_{UP}^{Con}{}_{/Ps}$			**R**	$\mu_{UP}^{Dys}{}_{/PS} = \mu_{UP}^{Con}{}_{/Ps}$			**A**	$\mu_{UP}^{Dys}{}_{/PS} = \mu_{UP}^{Con}{}_{/Ps}$			**A**
	$\mu_{SW}^{Dys}{}_{/PS} = \mu_{SW}^{Con}$			**A**	$\mu_{SW}^{Dys}{}_{/PS} = \mu_{SW}^{Con}$			**R**	$\mu_{SW}^{Dys}{}_{/PS} = \mu_{SW}^{Con}$			**A**
	Profile: Err. Comp				**Profile: Err. Comp.**				**Profile: RT Comp.**			
	F	***Df***	**P**		**F**	***Df***	**P**		**F**	***Df***	**P**	
EF	1.29	2, 104	.281		.46	2, 100	.633		5.24	2, 100	.007	
Group	9.45	1,52	.003**		3.87	1, 50	.055		.012	1, 50	.913	
EF * Group	1.52	2,104	.223		1.08	2, 100	.341		2.98	2, 100	.055	
PS	3.15	1,52	.082		4.65	1, 50	.036		.549	1, 50	.562	
EF * PS	2.01	2,104	.140		.474	2, 100	.624		5.52	2, 100	.005	
P-H	**F**	***Df***	**P**	**P-H**	**F**	***Df***	**P**	**Valid.**	**P-H**	**F**	***Df***	**P**	**Valid.**
RI	9.29	1,52	.004**	RI	1.32	1, 51	.255	**No**	RI	2.32	1,51	.134	**No**
UP	5.68	1,53	.021*	UP	.485	1, 51	.489	**No**	UP	.675	1,51	.415	**No**
SW	.13	1,53	.719	SW	4.87	1,51	.032*	**No**	SW	.764	1, 51	.386	**Yes**

Note: RQ= Research Question, HYP= hypotheses, Comp= composite, Err.=error, RT=reaction time, RI= response inhibition composite, UP= updating composite, SW= Switching composite, Dys= Dyslexia, Con= Control, PS= Processing Speed, A= Accept, R= Reject, , EF= Executive Function, P-H= Post Hoc. * p<.05 (trend), **p<.005 (significant with Bonferroni correction).

5.3.4 Addressing Disorder Specificity of EF Impairments in Dyslexia

Research question 3 is revisited here to further explore whether abilities manifest differently as a function of processing rule across key EFs.

To explore whether the EF profile differed as a function of processing rule (visual based versus phoneme based), separate 2 (Group: dyslexia and control) x 2 (Rule: Visual and Phoneme) mixed ANCOVAs controlling for speed were conducted (see Table 15). Post Hoc between differences on disorder specific (phoneme) cost variables $(PhonemeNbackError/RT - PictureNbackError/RT)$, and one sample t-tests are employed to further explore any significant interaction effects/trends from the ANCOVA analysis.

Response Inhibition

For commission errors, there was no main effect of processing rule, no main effect of group and no interaction effect. For reaction time, there is a trend for a main effect of rule ($F(1,51)=6.59$, $p<.05$), no main effect of group and no interaction effect. When group was collapsed, all participants took significantly longer for the phoneme based rule than for visual based rule.

Updating

For errors, there was a significant main effect for rule ($F(1,52)=18.09$, $p<.004$), no main effect of group and no interaction effect. For reaction time, there was no main effect of rule, no main effect of group and no interaction effect. When group was collapsed, all participants had significantly more errors in the phoneme rule based task than the visual based task.

Switching

For error cost, there was no main effect for rule, a trend for a main effect of group ($F(1,51)=4.91$, $p<.05$) and no interaction effect. For reaction time, there was a trend for a main effect of rule ($F(1,51)=4.31$, $p<.05$) and no interaction effect. When rule was collapsed, participants with dyslexia had a higher error cost of switching than control

participants. When group was collapsed, all participants had a higher reaction time cost in the classic task than the phoneme based task.

Summary

For response inhibition, results from study 1 are confirmed here as there are no differences in severity of profile as a function of processing rule. All participants appear to take longer to inhibit when informational content is phoneme.

For updating, after addressing the task difficulty issue encountered in study 1, there no longer was a trend for a greater phoneme processing cost in control participants. All participants appear to make more errors when processing phoneme content.

For switching, differences by processing rule were not explored in study 1 as there were no group differences at composite level. In a secondary sample, there was no difference in siwthcing ability as a function of processing. However, all participants took longer on the classic alphanumeric task compared to the phoneme task.

Table 15 Does EF profile of Dyslexia differ as a function of processing rule (visual/classic, phoneme)?

Response Inhibition Rule (Phoneme, Visual)		**A/R**	**Updating Rule (Phoneme, Visual)**			**A/R**	**Switching Rule (Phoneme, Classic)**			**A/R**
Hyp	$\mu_{RI\text{-}pic/phon}{}^{Dys}{}_{/PS} = \mu_{RI\text{-}pic/phon}{}^{Con}{}_{/PS}$	**A**	$\mu_{UP\text{-}pic/phon}{}^{Dys}{}_{/PS} = \mu_{UP\text{-}pic/phon}{}^{Con}{}_{/PS}$			**A**	$\mu_{SW\text{-}classic/phon}{}^{Dys}{}_{/PS} = \mu_{SW\text{-}classic/phon}{}^{Con}{}_{/PS}$			**A**
Error	**F**	***Df***	**P**	**Error**	**F**	***Df***	**P**	**Error**	**F**	***Df***	**P**
Group	1.33	1,51	.254	Group	.362	1,52	.550	Group	4.91	1,51	.031*
Rule	.747	1,51	.392	Rule	18.09	1,52	.000**	Rule	3.41	1,51	.07
Group * Rule	.346	1,51	.559	Group * Rule	.034	1,52	.855	Group * Rule	.668	1,51	.418
PS * Rule	.253	1,51	.617	PS * Rule	.606	1,52	.440	PS * Rule	1.08	1,51	.303
PS	3.73	1,51	.06	PS	4.76	1,52	.034*	PS	.672	1,51	.416
RT	**F**	***Df***	**P**	**RT**	**F**	***Df***	**P**	**RT**	**F**	***Df***	**P**
Group	2.32	1,51	.134	Group	.016	1,52	.899	Group	1.02	1,51	.317
Rule	6.59	1,51	.013*	Rule	.214	1,52	.645	Rule	4.31	1,51	.043*
Group * Rule	1.43	1,51	.237	Group * Rule	.363	1,52	.550	Group * Rule	.728	1,51	.397
PS * Rule	.903	1,51	.346	PS * Rule	3.41	1,52	.07	PS * Rule	3.96	1,51	.052
PS	5.49	1,51	.023*	PS	2.29	1,52	.136	PS	2.658	1,51	.109

Note: RQ= Research Question, Hyp= hypothesis, Dys= Dyslexia, Con= Control, PS= Processing Speed, IS=Independent Sample. * p<.05 (trend), **p<.005 (significant with Bonferroni correction). Post-Hoc T-Tests explored only for significant interaction effects.

5.3.5 Validating EF Predictive Model of Dyslexia Diagnosis

Results from predictive models developed in study 1 and validation of predictive models with error and reaction time z-mean composite scores are summarised in Table 16. Although models were developed at the EF z-mean error composite level in Study 1, model validation will be explored at both EF z-mean error and reaction time composite levels in Study 2 in case timing amendments to Study 2 tasks result in less performance sensitivity. For model validation in Study 2, processing speed was entered at step 1, followed by response inhibition, updating and switching respectively (reflecting the developed Study 1 model weights).

As outlined in chapter 4, response inhibition and updating z-mean error composite scores significantly predicted dyslexia diagnosis while controlling for processing speed (Chi square: Model $X^2(3) = 15.49$, p=.001; -2Log Likelihood: 55.45; R^2_{cs}=.315; $R^2_{N=.}$42). The model correctly classified 78.2% of participants according to presence/absence of dyslexia: sensitivity 81.5% (true-positive) and specificity 75% (true-negative). The b-values from this model reflected that for every one-unit change in response inhibition score (errors) there is a corresponding 1.83-unit change in the logit of the outcome variable, while for every one-unit change in updating score (errors) there is a 1.28-unit change in the logit of the outcome variable. The proportionate odds values (Exp (B)) were greater than 1 for both predictors suggesting that as error score on each predictor increased the likelihood of the outcome occurring (dyslexia diagnosis) increased. ROC curve analysis suggested that a randomly selected participant with dyslexia would demonstrate more errors on response inhibition and updating composite scores than a randomly selected control participant 83.5% of the time (AUC= .835, 95% CI: .727-.942, p=.000).

Model Validation

At step 1 for both error and reaction time z-mean composite models, processing speed demonstrated a trend for predicting dyslexia diagnosis, the chi square ($X^2(1) = 6.34$, p<.05= .021) and -2Log Likelihood (65.58) demonstrate good model fit. Step 1 correctly classified

62.3% of participants according to presence/absence of dyslexia diagnosis: sensitivity 83.9% (true-positive) and specificity 31.8% (true negative).

Error Composite model

The addition of EF z-mean error composite scores improved model fit but still only demonstrated a trend for predicting dyslexia (Chi square: $X^2(4) = 12.205$, p=.016; -2Log Likelihood: 59.73; R^2_{cs}=.206; $R^2_{N=.}$277). After controlling for low-level processing speed, the error composite model correctly classified 67.9% of participants according to presence/absence of dyslexia diagnosis: sensitivity 59.1% and specificity 74.2%. As outlined in Table 16, none of the individual composites significantly predicted dyslexia, however switching error composite score almost reached trend level (Wald: $X^2(1) = 3.88$, p=.050). The b-values from this model reflected that for every unit change in switching cost score (errors) there is a corresponding .79-unit change in the logit of the outcome variable (*see Figure 43*). The proportionate odds value (Exp (B)) is greater than 1 suggesting that as switching error score increased the likelihood of the outcome occurring (dyslexia diagnosis) increased. ROC curve analysis (*see Figure 44*) indicates that step 2 of the model is a moderate fit with an area under the curve (AUC) of .757 (95% CI: .682-.885, p=.002): a randomly selected participant with dyslexia will have a higher error cost on switching error composite than a randomly selected control participant approximately 75.7% of the time.

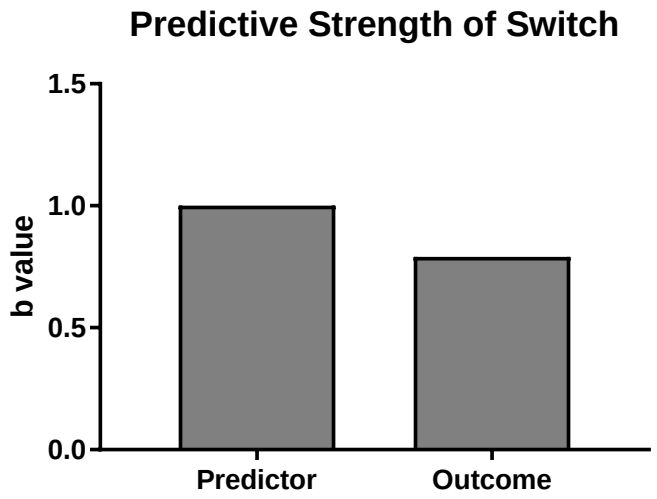


Figure 43 Switching error composite b-values reflecting that for every one-unit increase in scores on error composite there is a corresponding .79-unit change in the logit of the outcome (dyslexia diagnosis)

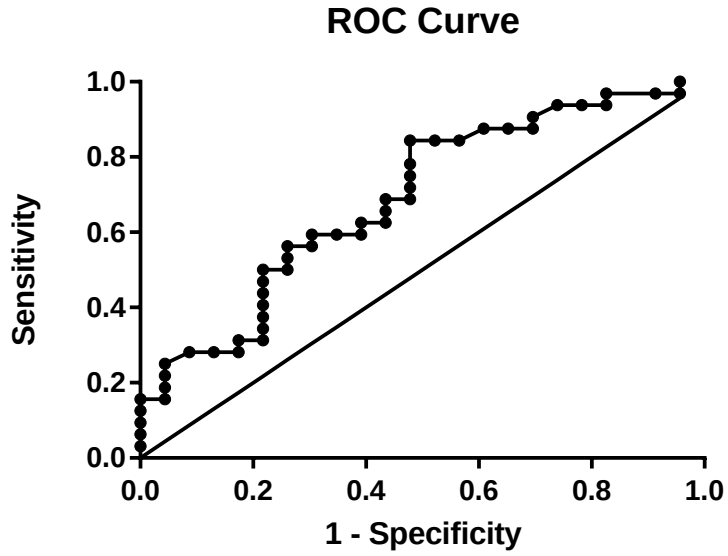


Figure 44 ROC curve of switching error composite score for predicting likelihood of dyslexia diagnosis

Reaction Time Composite model

The addition of EF z-mean reaction time composite scores also improved model fit but still only demonstrated a trend for predicting dyslexia Chi square (Model $X^2(4) = 12.01$, p=.017, -2Log Likelihood= 59.93; R^2_{cs}=.203; $R^2_{N=.}$273). After controlling for low-level processing speed, the reaction time composite model correctly classified 67.9% of participants according to absence/presence of dyslexia: 80.6% sensitivity (true positive) and 50% specificity (true negative). As outlined in Table 16, none of the individual composites significantly predicted dyslexia, however response inhibition reaction time composite almost reached trend level (Wald: $X^2(1) = 3.40$, p=.06). The b-values from this model reflected that for every one-unit change in response inhibition score (reaction time) there is a corresponding .83-unit change in the logit of the outcome variable (*see Figure 45*). The proportionate odds value (Exp (B)) is greater than 1 suggesting that as response inhibition reaction time score increased the likelihood of the outcome occurring (dyslexia diagnosis) increased. ROC curve analysis (*see Figure 46*) indicates that at step 2 the model is a moderate fit with an area under the curve(AUC) of .762 (95% CI: .637-.888, p=.001): a randomly selected participant with dyslexia will have a higher score on response inhibition reaction time composite than a randomly selected control participant approximately 76.2% of the time.

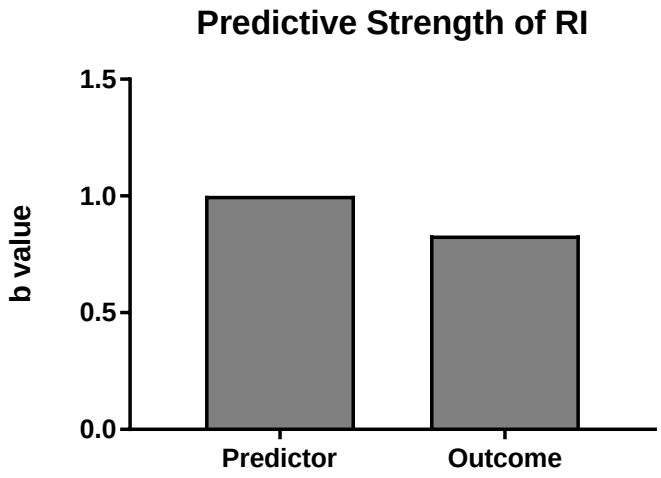


Figure 45 Response inhibition reaction time composite b-values reflecting that for every one-unit increase in scores on error composite there is a corresponding .83-unit change in the logit of the outcome (dyslexia diagnosis)

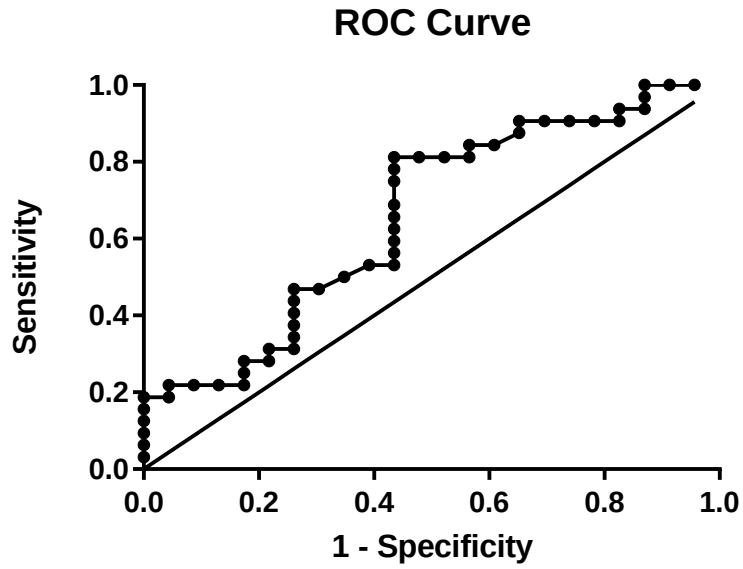


Figure 46 ROC curve of response inhibition reaction time composite score for predicting likelihood of dyslexia diagnosis

Summary

The clinical status model developed in study 1 (Chapter 4) is not validated in study 2 at the EF z-mean *error composite* level. The Study 2 confirmatory model demonstrates almost a trend for switching predicting clinical status. However, the clinical status model developed in study 1 is partially validated in study 2 at the EF z-mean *reaction time composite level* for response inhibition (almost trend). The reaction time model is more sensitive to detect dyslexia cases (80.6%) than the error model (59.1%), however the error model is more specific to detecting non-dyslexia cases (74.2%) than the reaction time model (50%).

Table 16 Validating EF predictive model of clinical status (dyslexia diagnosis)

Chp 4. Model Development (Error Composites)					**Chp 5. Model Validation (Error Composites)**					**Chp 5. Model Validation (RT Composites)**				
	β (SE)	**Exp (B)**	**95% CI**	**-2LL**		**β (SE)**	**Exp (B)**	**95% CI**	**-2LL**		**β (SE)**	**Exp (B)**	**95% CI**	**-2LL**
Step 1				70.94	**Step 1**				65.58	**Step 1**				65.58
Constant	2.41 (1.18)	11.16			Constant	3.85 (1.58)	46.86			Constant	3.85 (1.58)	46.86		
PS	-.28 (.13)*	.75	.58- .98		PS	-.38 (.17)*	.68	.49-.95		PS	-.38 (.17)*	.68	.49-.95	
Step 2				55.45	**Step 2**				59.73	**Step 2**				59.93
Constant	.84 (1.42)	2.32			Constant	3.40 (1.75)	30.08			Constant	2.57 (1.77)	13.06		
PS	-.05 (.17)	.95	.68-1.32		PS	-.32 (.19)	.72	.50-1.05		PS	-.24 (.19)	.78	.54-1.13	
RI	1.83 (.69)*	6.23	1.62-24.00		RI	.30 (.42)	1.35	.60-3.07		RI	.83 (.45)*	2.29	.95-5.52	
UP	1.28 (.57)*	3.61	1.19-10.92		UP	-.08 (.44)	.92	.39-2.18		UP	-.82 (.52)	.44	.161-1.21	
SW	.031 (.47)	1.03	.41-2.58		SW	.79 (.40)*	2.2	1.01-4.82		SW	-.22 (.48)	.78	.31-2.06	
Step 1: R^2=.092 (Cox & Snell), .122 (Nagelkerke), Model $X^2(1)$ =5.29, p<.05 **Step 2:** R^2=.315(Cox & Snell), .42 (Nagelkerke), Model $X^2(4)$ =20.77, p<.001. **Note:** Hosmer & Lemeshow (Model1) $X^2(6)$ =10.13, p=.119, (Model 2) $X^2(7)$ =8.19, p=.316 indicates good model fit. P<.05*, P<.004**.					**Step 1:** R^2=.113 (Cox & Snell), .152 (Nagelkerke), Model $X^2(1)$ =6.34, p<.05= .021. **Step 2:** R^2=.206(Cox & Snell), .277 (Nagelkerke), Model $X^2(4)$ =12.205, p<.05=.016. **Note:** Hosmer & Lemeshow (Model1) $X^2(5)$ =2.58, p=.765, (Model 2) $X^2(8)$ =11.04, p=.200 indicates good model fit. P<.05*, P<.004**.					**Step 1:** R^2=.113 (Cox & Snell), .152 (Nagelkerke), Model $X^2(1)$ =6.34, p<.05= .021 **Step 2:** R^2=.203 (Cox & Snell), .273 (Nagelkerke), Model $X^2(4)$ =12.01, p<.05=.017. **Note:** Hosmer & Lemeshow (Model1) $X^2(5)$ =2.58, p=.765, (Model 2) $X^2(8)$ =6.46, p=.596 indicates good model fit. P<.05*, P<.004**.				

Table 17 Validating EF involvement in Core issues (reading)

Chp 4. Model Development (Error Composites)					**Chp 5. Model Validation (Error Composites)**					**Chp 5. Model Validation (RT Composites)**				
	B (SE)	**B**	**F/T-Value**	**P**		**B (SE)**	**B**	**F/T-Value**	**P**		**B (SE)**	**β**	**F/T-Value**	**P**
Step 1			6.83	.012*	**Step 1**			11.70	.001**	**Step 1**			11.70	.001**
Constant	29.30 (5.43)				Constant	25.75 (5.90)				Constant	25.57 (5.9)			
PS	1.58 (.61)	.34	2.61	.012*	PS	2.16 (.63)	.43	3.42	.001**	PS	2.16 (.63)	.43	3.42	.001**
Step 2			10.61	.000**	**Step 2**			7.38	.000**	**Step 2**			7.15	.000**
Constant	39.43 (4.79)				Constant	33.25 (5.72)				Constant	35.80 (5.99)			
PS	-.19 (.57)	.04	.34	.73	PS	1.29 (.62)	.26	2.09	.04*	PS	1.07 (.64)	.21	1.67	.10
RI	-10.03 (3.24)	-.53	-4.68	.000**	RI	-2.47 (1.39)	-.21	-1.78	.08	RI	-5.32 (1.54)	-.45	-3.46	.001**
UP	-4.31 (2.65)	-.31	-.26	.012*	UP	-2.85 (1.66)	-.21	-1.72	.09	UP	1.49 (1.90)	.10	.79	.44
SW	-1.35 (2.7)	-.09	-.80	.43	SW	-2.65 (1.44)	-.24	1.97	.06	SW	2.91 (1.74)	.21	1.66	.10
Note Model 1: R^2=. 114,; Model 2: R^2 =.459. *p<.05, **p<.004					Note Model 1: R^2=. 184; Model 2: R^2 =.376. *p<.05, **p<.004					Note Model 1: R^2=. 184; Model 2: R^2 =.368. *p<.05, **p<.004				

Summary: Error model- almost trend (p=.055) for switching strength predicting reading problems. **RT model**: response inhibition impairment significantly predicts reading problems

Table 18. Validating Non-EF involvement in non-core issues

Chp 4. Model Development (Error Composites)					**Chp 5. Model Validation (Error Composites)**					**Chp 5. Model Validation (RT Composites)**				
	B (SE)	**β**	**F/T-Value**	**P**		**B (SE)**	**B**	**F/T-Value**	**P**		**B (SE)**	**β**	**F/T-Value**	**P**
Step 1			1.78	.19	**Step 1**			1.25	.269	**Step 1**			1.25	.27
Constant	28.18 (8.12)				Constant	33.97 (9.40)				Constant	33.97 (9.40)			
PS	-1.21 (.91)	-.18	-1.33	.19	PS	-1.12 (1.01)	-.15	-1.12	.27	PS	-1.12 (1.01)	-.15	-1.12	.27
Step 2			.75	.56	**Step 2**			1.30	.28	**Step 2**			2.28	.07
Constant	24.75 (9.06)				Constant	30.64 (10.03)				Constant	22.45 (10.08)			
PS	-.73 (1.05)	-.11	-.70	.49	PS	-.73 (1.08)	-.10	-.68	.50	PS	.12 (1.08)	.02	.11	.91
RI	3.84 (4.04)	.14	.95	.35	RI	-1.14 (2.43)	-.07	-.47	.64	RI	5.20 (2.59)	.30	2.01	.05
UP	.95 (3.11)	.05	.31	.76	UP	5.48 (2.91)	.28	1.88	.07	UP	1.35 (3.19)	.06	.42	.68
SW	-1.45 (3.21)	-.07	-.45	.65	SW	-.10 (2.52)	-.01	-.04	.97	SW	-5.68 (2.93)	.28	-1.93	.06
Note Model 1: R^2=.032; Model 2: R^2 =.057. *p<.05, **p<.004					Note Model 1: R^2=.023; Model 2: R^2 =.096. *p<.05, **p<.004					Note Model 1: R^2=.023; Model 2: R^2 =.157. *p<.05, **p<.004				

Summary: Error model- EF composite scores did not significantly predict socio-emotional problems; **RT Model-** almost a trend for response inhibition and switching impairment predicting socio-emotional problems

5.3.6 Validating EF Predictive Model of Core Issues in Dyslexia

The results of EF predictive models of core reading ability developed in Study 1 and validation of the same model with error and reaction time z-mean composite scores in Study 2 are summarised in Table 17. For model validation, processing speed was entered at step 1, followed by response inhibition, updating and switching respectively (reflecting the developed Study 1 model weights).

As outlined in chapter 4, response inhibition and updating explained a significant proportion (34.5%) of the variance in reading ability after controlling for processing speed. Step 2 of the model developed in chapter 4 (see Table 17) suggests that when accounting for processing speed only response inhibition significantly predicts reading and updating demonstrates a trend for predicting reading. The Beta values for model 2 reflect that for every 1 standard deviation increase in response inhibition errors there is a corresponding .527 decrease in reading ability score, and for every 1 standard deviation increase updating errors there is a corresponding .307 decrease in reading ability score.

Model Validation

At step 1 for both error and reaction time composite models, processing speed significantly predicted reading ability (R^2= .184, p<.004).

Error Composite model

The addition of EF z-mean error composite scores significantly improved the model's predictive ability with an additional 37.6% of the variance in reading accounted for by EF composites (R^2=.376, p<.004). However, as outlined in Table 17, when accounting for processing speed none of the EF z-mean error composite scores significantly predict reading ability and processing speed demonstrated a trend for predicting reading (p<.05). Although not significant, switching z-mean error composite almost demonstrates a trend for predicting reading. The beta values reflect that for every 1 standard deviation increase

in switching error composite there is a corresponding .24 decrease in reading ability (*see Figure 47*).

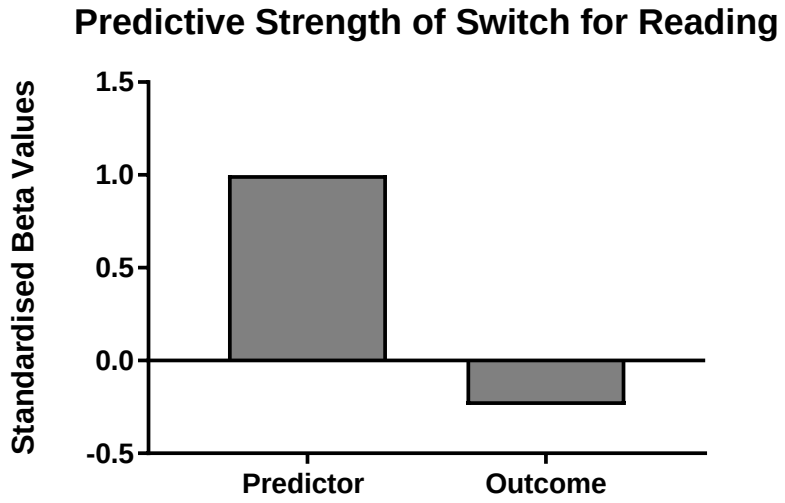


Figure 47 Switching error composite standardised beta values reflecting that for every 1SD increase in switch cost errors there is a corresponding .24 SD decrease in reading ability

Reaction Time Composite Model

The addition of EF z-mean Reaction time composite scores significantly improved the model's predictive ability with an additional 36.8% of the variance in reading accounted for by EF RT composites (R^2=36.8, p<.004). As outlined in Table 17, when accounting for processing speed only inhibition composite reaction time score significantly predicts reading ability. The beta values reflect that for every 1 standard deviation increase in reaction time on response inhibition composite there is a corresponding .45 standard deviation decrease in reading ability (see *Figure 48*). After, including EF reaction time composites processing speed is no longer demonstrating a trend for predicting core issues.

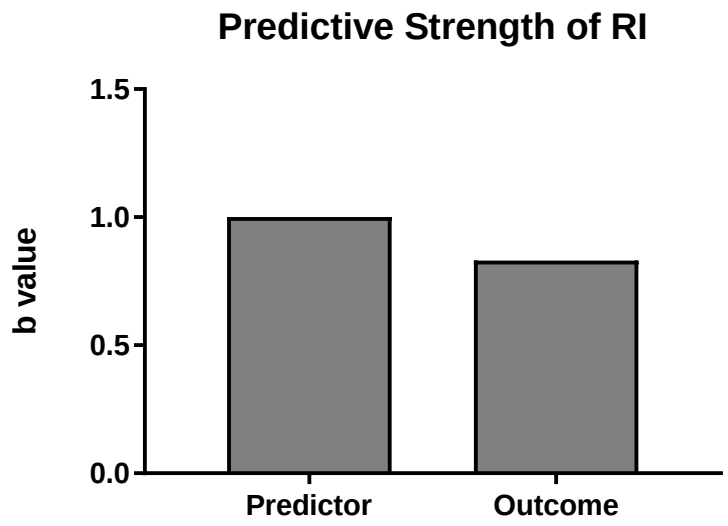


Figure 48 Inhibition reaction time composite standardised beta values reflecting that for every 1SD increase in inhibition reaction time there is a corresponding .45SD decrease in reading ability

Summary

Core issues (reading) model developed in study 1 was not validated in study 2 at the EF z-mean error composite level. However, the predictive relationship between response inhibition and reading ability is confirmed and validated at the EF z-mean reaction time composite level.

5.3.7 Validating Non-EF involvement in non-core issues (socio-emotional problems)

The results of socio-emotional predictive model developed in study 1 and validation of socio-emotional predictive models with error and reaction time z-mean composite scores are summarised in Table 18. For model validation processing speed was entered at step 1, followed by response inhibition, updating and switching respectively (reflecting the developed Study 1 model weights). As outlined in chapter 4, processing speed and EF error composites did not significantly predict variance in socio-emotional problems across groups.

Model Validation

At step 1 for both error and reaction time z-mean models, processing speed did not significantly predict socio-emotional problems.

Error Composite model

The addition of EF z-mean error composite scores did not significantly improve the model's predictive ability, and none of the individual predictors significantly explained socio-emotional problems.

Reaction time composite model

The addition of EF z-mean reaction time composite scores did not significantly improve the model's predictive ability. Although, there was a trend for response inhibition and switching impairments predicting socio-emotional problems.

Summary

Non-EF involvement in Non-Core issues (socio-emotional issues) found in study 1 is further confirmed in a secondary dyslexia sample in study 2.

5.3.8 Results in Summary

Validating EF Profile Associated with Dyslexia: At the composite level, the profile of impairments associated with dyslexia in study 1 (impaired response inhibition and a trend for updating) was not validated in study 2 (a trend for impaired switching).

Addressing Disorder Specificity of EF in Dyslexia: Similar to study 1, response inhibition does not differ as a function of processing rule in study 2. After adapting the updating tasks, the control participants' phoneme updating cost was not found and results suggest that updating does not differ as a function of processing rule. Switching abilities did not differ across groups as a function of processing rule. This suggests that EF profile does not manifest more severely with phoneme content.

Validating EF Predictive Model of Dyslexia Diagnosis: At the EF error z-mean composite level, the clinical model status developed in study 1 (response inhibition and a trend for

updating) was not validated in study 2 (almost a trend for switching) which may be due to changes in tasks that inform the composite scores and also due to EF not differentiating clinical and control groups. However, at the EF reaction time z-mean composite level there was almost a trend for response inhibition predicting clinical status. The reaction time model is more sensitive to detect dyslexia cases (80.6%) than the error model (59.1%), however, the error model is more specific at detecting non-dyslexia cases (74.2%) than the reaction time model (50%).

Validating EF Predictive Model of Reading Ability: The reading model (core issues) developed in study 1 (response inhibition and a trend for updating) was not validated in study 2 at the EF z-mean error composite level, however, response inhibition significantly predicted reading ability across groups at the EF z-mean reaction time level - confirming its predictive role in core issues associated with dyslexia.

Validating Non-EF Involvement in Socio-Emotional Issues: Non-EF involvement in socio-emotional problems (non-core issues) associated with dyslexia in study 1 was validated in study 2.

5.4 Discussion

This chapter aimed to: (a) validate EF profile found to be associated with dyslexia in chapter 3, (b) further explore the disorder specificity (phoneme) of updating impairments associated with dyslexia, and (c) validate EF predictive models of dyslexia diagnosis and core reading issues associated with dyslexia.

The profile of EF (impaired response inhibition and updating, unimpaired switching) associated with dyslexia was not replicated in this secondary sample of participants with dyslexia. There were no significant group differences on any EF z-mean composites, although there was a trend for impaired switching abilities at the error composite level in dyslexia. This finding is of interest as it suggests that a reverse EF profile (impaired switching, unimpaired response inhibition and updating) is associated with dyslexia in a secondary sample. Differences in EF impairments associated with dyslexia across studies 1 and 2 may be related to a lack of generalizability of EF profile to a secondary sample or it

may be related to changes in the measurement of each construct or duration of stimulus presentation which may have reduced the capacity of tasks to detect between group differences. The number of tasks contributing to the response inhibition composite score varied from study 1 to study 2. For example, the response inhibition z-mean composite score in study 1 was comprised of performance indices from the picture Go No-Go task, phoneme Go No-Go task, Stroop task and Sustained Attention to Response task. Whereas the response inhibition z-mean composite score in study 2 was comprised of performance indices from the picture and phoneme Go No-Go tasks. It may be argued that Stroop and SART tasks were driving dyslexia impairment on the response inhibition composite score, however, group differences at the individual task level in study 1 (see appendix F) highlighted Go No-Go tasks as the strongest group differentiator (most severe inhibition impairment in dyslexia alone) while no group differences were found on the Stroop task.

The changes to duration of stimulus presentation and inter-stimulus intervals may have reduced the capacity of the tasks to detect between group differences and therefore reduced the overall predictive utility of EF constructs. The updating tasks were adapted to further explore disorder specificity as the phoneme updating task appeared to suffer from floor effects in error rate across groups; while the inhibition and switching tasks were adapted to ensure they were suitable for EEG recording which will be further explored in Chapter 6. This may particularly be the case for the common EF (response inhibition), where increased time on the task may have facilitated successful inhibition of response on No-Go trials. The passive dissipation model of response inhibition proposed by Simpson et al. (2012) suggests that if more time is given to respond or response is delayed the urge to impulsively respond on No-Go trials will dissolve while the likelihood of successfully inhibiting response will grow. In support of the passive dissipation model, it has been found that if response on Go trials is too quick inhibition of impulsive response fails whereas if response on Go trials is longer inhibition of impulsive response succeeds (Chevalier, Kelsey, Wiebe, & Andrews Espy, 2014). This effect also emerges with varied inter stimulus intervals, when manipulating the duration of inter-stimulus intervals in a Go No-Go task Cragg and Nation (2008) found that more correct responses were made when

the inter-stimulus interval was longer (2,600-3,400ms) than shorter (1,600-2,400ms). The total inter-stimulus interval of Go No-Go tasks in study 1 was 3,000ms while the total inter-stimulus interval here in study 2 is 4,000ms. It may be the case that this change in inter-stimulus interval across studies reduced the percentage of commission errors by allowing dyslexia participants more time to compute the correct answer. In this study, dyslexia and control participants demonstrated a similar percentage of failed inhibitions (dyslexia: 16.65; control: 11.05), however, dyslexia participants required more time to maintain this level than control participants (dyslexia: 711.97; Control: 611.48).

The reduced speed demands in working memory updating tasks may have also reduced their capability for detecting trends for between group differences as they did in study 1. Dyslexia and control participants demonstrated a similar percentage of updating errors (dyslexia: 14.97; control: 11.85), in this case however dyslexia participants did not require more time than control participants (dyslexia: 877.63; control: 890.86). For switching, dyslexia differed from control participants on switch cost as reflected by errors (dyslexia: 4.26; control: 1.80) but also demonstrated a reduced switch cost as reflected by reaction time cost (dyslexia: 775.82; control: 1171.02) which suggests that there may be some degree of speed accuracy trade off in switching in dyslexia.

Another possible reason for not finding the same EF impairments in a secondary sample of children with dyslexia, is that EF as an impairment may variable in children with dyslexia. it was not clear which aspects of EF (if any) were impaired in dyslexia with inconsistent findings emerging for response inhibition (Bental & Tirosh, 2007; Booth et al., 2014; Brosnan et al., 2002; Marzocchi et al., 2008; Wang & Yang, 2014), updating (Beneventi et al., 2010a; Bental & Tirosh, 2007; Peng et al., 2013) and switching (Bental & Tirosh, 2007; De Lima et al., 2012; Poljac et al., 2010). Even though this PhD identified and addressed possible reasons for inconsistencies in previous research by excluding elevated ADHD from dyslexia alone samples, controlling for processing speed, employing sensitive composite measurements of EF constructs and exploring disorder specific EF processing. Inconsistencies in impairments associated with dyslexia still emerged from study 1 to

study 2. This suggests that there may be heterogeneity in type EF impairments (response inhibition, updating and switching) associated with dyslexia.

After adapting the updating tasks, the control phoneme updating cost was not found and results suggest that updating abilities do not differ as a function of processing rule. A similar pattern was observed for response inhibition and switching, suggesting that EF profile associated with dyslexia does not differ with phoneme content. Although previous research suggests that dyslexia is associated with a disorder specific (phoneme) updating (Beneventi et al., 2010), and that phoneme impairments only manifest on tasks with high-level EF demands (Ramus & Szenkovits, 2008). Beneventi et al. (2010a) explored phoneme updating in dyslexia their study but did not include a picture control task, so their experiment could not address whether updating abilities manifested in a general or disorder specific way. Studies 1 and 2 included picture control tasks and suggest that dyslexia is not associated with disorder specific EF impairments, instead core EF (response inhibition, updating and switching) abilities manifest in a general way in children with dyslexia.

The common EF (response inhibition) and updating clinical status model developed in chapter 4 was not validated in this secondary sample at the z-mean error composite level. Within this model there was almost a trend for switching predicting clinical status reflecting the EF profile, although this was not significant with the Bonferroni correction or at trend level. Common EF (response inhibition) for predicting clinical status was validated at the EF reaction time z-mean composite as there was a near trend for predicting dyslexia likelihood- although this was still not significant (p=.06). The reaction time model (response inhibition) was more sensitive to detect dyslexia cases (80.6%) than the error model (59.1%), however the error model was more specific at detecting non-dyslexia cases (74.2%) than the reaction time model (50%).

The model developed for clinical status in chapter 4, with response inhibition and updating demonstrated high sensitivity for predicting dyslexia (81.5%), specificity for predicting non-dyslexia cases (75%), and moderate diagnostic accuracy (.835) (Swets, 1988). In the secondary sample, at the z-mean error composite level switching almost

demonstrated a trend for predicting dyslexia. The switching model demonstrated poorer sensitivity for predicting dyslexia (59.1%), similar specificity for predicting non-dyslexia cases (74.2%) and demonstrated moderate diagnostic accuracy (.757) (Swets, 1988). In the secondary sample, at the z-mean reaction time composite level response inhibition also almost demonstrated a trend for predicting dyslexia. The response inhibition model demonstrated high sensitivity for predicting dyslexia (80.6%), similar specificity in predicting non-dyslexia cases (50%), and demonstrated moderate diagnostic accuracy (.762) (Swets, 1988). The RT model with response inhibition demonstrates better ability to predict dyslexia alone, however, neither model is statistically significant for predicting clinical diagnosis, nor do they outperform the accuracy of the initial developed model. This suggest that the model for clinical diagnosis may not be generalizable to a secondary sample, due to a drop in accuracy and predictive utility (Field, 2013).

The common EF (response inhibition) and updating core issues (reading) model developed in chapter 4 was not validated in a secondary sample at the EF z-mean error composite level, however, at the EF z-mean reaction time composite level common EF (response inhibition) involvement in core issues was validated. This suggests that reading impairments in dyslexia may be underpinned by common EF impairments. The model developed for core reading issues in chapter 4, with response inhibition and updating predicted 45.9% of the variance in reading ability. This model was not validated at the EF z-mean error composite level, in this model at step 1 processing speed significantly predicted core reading features (18.4%), adding EF z-mean error composites to the reading model significantly increased the model's predictive ability (additional 19.2% of the variance explained), however none of the individual EF predictors were significant and the trend for processing speed predicting reading ability remained. The RT model validated the role of common EF (response inhibition) in core reading issues, in this model at step 1 processing speed explained 18.4% of the variance in reading ability, adding EF z-mean reaction time composites significantly improved the model's predictive ability (by explaining an additional 18.4% of the variance) for reading. At the level of individual predictors, response inhibition reaction time composite was the only significant predictor

and processing speed was no longer significant, suggesting that all the variance in the model was explained by response inhibition.

Although the validated model does not explain as much variance in reading ability as the model developed in chapter 4, the findings validated common EF implication in core reading issues associated with dyslexia. Even though response inhibition was not clinically impaired in dyslexia, it almost predicted clinical status and is a strong predictor of variance in reading ability. A cognitive ability does not necessarily have to be impaired in dyslexia to be of clinical relevance or an impairment in a cognitive ability does not mean that it is of clinical relevance. For instance, Wang and Yang (2014) did not find significant differences between dyslexia and control participants on their behavioural inhibition measure yet variances in this ability were clinically relevant for predicting socio-emotional problems; and while McGrath et al. (2011) found processing speed, working memory, phonological and naming impairments in dyslexia, only processing speed and phonological abilities were clinically relevant for reading problems.

Differences in EF predictive models may be related to a lack of generalizability to a secondary sample, changes in the measurement of each EF construct, or related to variability in EF profile associated with dyslexia as discussed above. Although the clinically-relevant predictive models did not demonstrate as high accuracy or explain as much variance in core reading issues associated with dyslexia as those developed in Chapter 4, there is still evidence to suggest that the common EF may be the aspect of EF implicated in dyslexia. For instance, the clinical diagnosis model including response inhibition reaction time composite almost demonstrated a trend for predicting absence/presence of dyslexia. Although not significant, this model was more sensitive for detecting correct cases of dyslexia diagnosis (80.6%) than the error switching composite model (59.1%), suggesting that common EF is more sensitive for detecting dyslexia. In addition, the response inhibition reaction time composite was the only significant EF predictor of reading across error and reaction time composite models, further suggesting that the common EF (response inhibition) is the most probable EF implicated in reading problems associated with dyslexia.

Both EF profile and predictive models of dyslexia are categorical approaches to understanding the condition. These categorical approaches to understanding dyslexia are limited as they cannot explain important neuro-cognitive processes underpinning variability in core symptoms (Insel, 2013). Exploring which EF processes underpin core reading ability across the trajectory from typical to atypical is more beneficial to understanding the underlying etiological factors which can be targeted in an intervention aimed at improving reading (Cuthbert & Insel, 2013). The results are consistent across both studies suggesting that response inhibition is predictive of core reading symptoms across the trajectory from typical to atypical reading development and therefore should be targeted in an intervention aimed at improving reading ability.

Although this study 2 found a trend for a switching impairment at the z-mean error composite level in dyslexia which also demonstrates a trend for predicting dyslexia likelihood, switching abilities are not predictive of the severity of outcome in core reading abilities. Response inhibition on the other hand almost demonstrated a trend for predicting dyslexia likelihood and is the only significant predictor of the severity of outcome in core reading abilities. Response inhibition also demonstrated a trend for predicting dyslexia likelihood in and was the only significant predictor of the severity of outcome in core reading abilities in study 1. The role of response inhibition in dyslexia and reading ability was consistent across both studies, which validates the role of response inhibition in dyslexia. The reduced sensitivity of response inhibition error composite for predicting dyslexia likelihood may be due to adaptations to task timings, however the response inhibition reaction time composite picked up reduced response inhibition efficiency as more time was required by children with dyslexia to maintain a similarly low-level of commission errors as control children. On this basis, response inhibition would be the most likely EF to target in a training intervention aimed at improving core reading impairments in dyslexia. Future research should explore the modifiability of response inhibition in dyslexia, how this impacts on other EF processes, and whether this improves core issues (reading) associated with dyslexia.

Chapter 6: Modifiability of Response Inhibition in Dyslexia

6.0 Introduction

The first large scale study of this PhD (Study 1: Chapters 3 and 4) suggests that dyslexia alone is associated with significant response inhibition and a trend for updating impairments, which are also predictive of dyslexia diagnosis and reading outcomes. The second large scale study of this PhD (Study 2: Chapter 5) validated the predictive relationship between response inhibition and clinically-relevant reading outcomes in a secondary sample of children with dyslexia. Response inhibition (Common EF) involvement in core reading outcomes was the only consistent finding across both studies. In both studies, those with more efficient response inhibition skills demonstrated better reading ability while those with poorer response inhibition skills demonstrated poorer reading ability. This suggests that response inhibition is an underlying cognitive process which facilitates reading ability and may partially explain reading problems experienced in dyslexia.

Previous research suggests that response inhibition abilities are modifiable with training, studies have shown behavioural and neural plasticity with improved performance on response inhibition tasks and changes in underlying ERP markers of response inhibition (Benikos et al., 2013; Johnstone et al., 2012, 2010; Manuel, Grivel, Bernasconi, Murray, & Spierer, 2010; Spierer et al., 2013). The effects of response inhibition training do not appear to be isolated as studies have demonstrated transfer to closely related behaviours such as increased self-regulatory capacity (Spierer et al., 2013) and reduced ADHD symptoms (Johnstone et al., 2012). The findings outlined in this PhD thus far suggest that response inhibition underpins reading ability, therefore response inhibition training may be a useful intervention for remediating reading problems in dyslexia. No study to date has explored whether response inhibition is modifiable in dyslexia and whether training induced changes transfer to improved reading outcomes. This study (Study 2, PhD aim 4) aims to explore whether response inhibition training can improve response inhibition abilities and alter N2 and P3 response inhibition-related ERPs in children with dyslexia.

As outlined in section 2.9, ERPs (event related potentials) are measures of electrophysiological brain activity time locked to specific cognitive events (Luck, 2014). The N2 and P3 ERP components are useful biomarkers of response inhibition (Johnstone et al., 2007; Jonkman et al., 2003; Pires et al., 2014) and are evident in children aged 7-12 years (Johnstone, Pleffer, Barry, Clarke, & Smith, 2005). In typical populations, these ERPs are of a larger magnitude for trials requiring inhibition of response compared to trials requiring a response (Johnstone et al., 2007; Jonkman et al., 2003; Pires et al., 2014). Although relatively few studies have explored response inhibition ERPs in children with dyslexia, previous research suggests response inhibition in dyslexia is associated with *differential ERP responses* when compared to those without dyslexia (Liotti et al., 2010; Van der Schoot et al., 2002). For example, Van der Schoot et al. (2002) found reduced No-Go P3 in fronto-central regions during a stop signal task in a subtype of participants with dyslexia (guessers not spellers). However, these abnormalities were also found to be associated with dyslexia regardless of subtype (Liotti et al., 2010). Previous studies in dyslexia mostly find abnormality in No-Go P3 which is a later index than the N2 but is also a sensitive index of inhibition (Wessel & Aron, 2015). Abnormal response inhibition ERPs associated with dyslexia may be modifiable with training as studies in typical populations find increased amplitude of N2 and P3 as well as improved task performance with training (Benikos et al., 2013; Hartmann et al., 2016).

On a theoretical level, response inhibition training as the common-EF factor (Miyake & Friedman, 2012) may facilitate changes in other EFs such as updating and switching due to shared variance and antagonistic relations (Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015). Extensive research supports the central role of response inhibition as the common-EF which can explain a proportion of variance in other distinct EFs of updating and switching at the behavioural (Friedman et al., 2006, 2008; Huizinga et al., 2006; Lehto et al., 2003; Miyake et al., 2000; Miyake & Friedman, 2012; van der Sluis et al., 2007) and neural levels (Collette et al., 2005). Consistent with this view, Diamond's (2013) EF framework suggests a strong link between response inhibition and working memory, to effectively inhibit a response one must hold a goal in mind and to hold a goal

in mind one must effectively maintain focus and filter distracting information. On this basis, training induced improvements in response inhibition may be transfer to improvements in aspects of working memory such as updating.

The common EF also appears to demonstrate an antagonistic relationship with switching due to incompatibility of each demand, effective response inhibition requires more controlled focus to filter distracting information, while effective switching requires looser focus to consider alternative response options (Blackwell et al., 2014; Goschke, 2000; Gruber & Goschke, 2004). This antagonistic relationship is not only found in typical samples, as children with self-regulation problems demonstrate poorer response inhibition and updating and better switching than children without self-regulation problems (Friedman et al., 2011). Similarly, adults with depression characterised by switching impairments exhibit better response inhibition abilities (Altamirano, Miyake, & Whitmer, 2010). If response inhibition and switching operate in a trade-off manner, then training induced improvements in response inhibition may transfer to reductions in switching performance. Although most response inhibition training studies do not employ a wide enough battery of EF measures to assess whether this is the case, based on theoretical models of EF this may be a possible outcome.

It is possible that improvements in response inhibition may also facilitate improvements in reading ability in dyslexia due to the predictive relationship found in previous Chapters (4 and 5), and, to facilitate socio-emotional and self-regulation, as previous research suggests response inhibition is a foundational cognitive skill essential for the development of effective self-regulatory capacities and socio-emotional wellbeing in both typical and atypical populations (Diamond, 2013). Although no predictive relationship was found between response inhibition and socio-emotional problems, children with dyslexia were found to demonstrate significantly more socio-emotional problems than children without dyslexia. Also, a wealth of previous research suggests that response inhibition is important for the development of effortful control which is a good indicator of self-regulatory abilities and emotional problems (Bridgett et al., 2013; Carlson & Wang, 2007; Eisenberg et al., 2009; Friedman et al., 2008; Rueda, Posner, & Rothbart, 2005; Snyder et al., 2015).

Abnormalities in response inhibition related ERP components are also associated with socio-emotional and self-regulation difficulties. For instance, abnormal fronto-central N2 during inhibition is found in those with greater socio-emotional problems (Albrecht et al., 2005) and larger No-Go P3 is predictive of effective self-regulation (Nash, Schiller, Gianotti, Baumgartner, & Knoch, 2013). Thus, if these ERP components are modifiable with response inhibition training they may transfer to reduced socio-emotional problems and increased capacity for self-regulation in children with dyslexia. Response inhibition has yet to be explored as a training intervention with potential for improving core reading and non-core socio-emotional problems in children with dyslexia.

Plasticity and EF modifiability

Plasticity refers to the modification of neural and/or cognitive systems in response to environmental conditions such as new skill learning. New skill learning can result in a strengthening of brain networks underpinning the learned skill (Gazzaniga, 2004; Stiles, 2000). The brain appears to be capable of restructuring itself in response to environmental input from childhood into adulthood (Stiles, 2000). EF training can be considered a type environmentally induced plasticity as repeated exposure to demanding and increasingly challenging EF exercises has been shown to not only modify EF abilities but also strengthen underlying brain areas (Astle, Barnes, Baker, Colclough, & Woolrich, 2015; Benikos et al., 2013; Karbach & Kray, 2009; Karbach & Schubert, 2013). EF training comes in many variants and is regarded as a type of process based training because it strengthens the information processing capacities and networks of the brain which facilitate a wide range of behaviours (Karbach & Unger, 2014). Different variants of EF training include response inhibition, working memory (capacity based or executive updating), switching or mixed training where more than one process is trained. Response inhibition training aims to enhance the ability to increasingly focus, resolve interference and inhibit impulsive responses. Training in Go No-Go task paradigms is the most common type of response inhibition training explored thus far. Working memory training comes in two forms which either aim to enhance the amount of information which can be stored in working memory (working memory capacity) or the executive aspects of working memory

responsible for manipulation of information (working memory updating). Working memory capacity is mostly trained with span task paradigms while working memory updating is mostly trained with n-back task paradigms. Switching training aims to enhance the ability to rapidly adapt to changing task demands. Training in dual task paradigms is the most common type of switching training implemented thus far. Mixed EF training involves training on a task that involves two or more of these single EF processes, however, this type of training makes it difficult to infer which specific process is responsible for transfer effects (Karbach & Unger, 2014)

Plasticity of EF has been observed following training in both children and adults (Karbach & Kray, 2009; Karbach & Schubert, 2013). The gradual development of EF from early childhood into adulthood (Huizinga et al., 2006; Lehto et al., 2003; Van der Sluis et al., 2007) provides an opportune window to intervene while this system is already undergoing developmental plastic refinements to reach mature adult levels. Although plasticity of EF has been observed in different age ranges (Karbach & Kray, 2009; Kray et al., 2012), it appears that children or those with impairments in EF impairments benefit more from EF training (Jaeggi et al., 2011; Karbach & Kray, 2009; Karbach et al., 2015; Söderqvist, Nutley, Ottersen, Grill, & Klingberg, 2012; Wass, Scerif, & Johnson, 2012). This is promising as children with dyslexia experience EF impairments which are implicated in core reading outcomes, thus an EF intervention may benefit both trained EF (at neural and cognitive levels) and transfer to related cognitive and symptom outcomes.

Although the degree of transfer from EF training to untrained cognitive and behavioural outcomes is a subject of considerable debate across the literature (further explored in Chapter 7) (Enge et al., 2014; Redick et al., 2013; Shipstead, Hicks, & Engle, 2012a; Shipstead, Redick, & Engle, 2012b), there is more consistent agreement that direct improvements occur on the trained task or untrained tasks that tap the same EF construct (Jaeggi et al., 2011; Johnstone et al., 2010; Karbach & Kray, 2009).

Training of working memory capacity or executive working memory components (updating) appear to be modifiable resulting in direct working memory improvements in adults (Jaeggi et al., 2011) and in children (Alloway, Bibile, & Lau, 2013; Astle et al., 2015;

Holmes et al., 2009; Jaeggi et al., 2011; Karbach & Kray, 2009; Karbach et al., 2015; Loosli et al., 2012). These gains were observed immediately post training and also were sustained at 3 (Karbach et al., 2015) and 8 months follow up in children (Alloway et al., 2013). Direct transfer to improved working memory abilities have also been observed in children with dyslexia (Luo et al., 2013) and special education needs (Dahlin, 2011), as well as in adults with dyslexia (Shiran & Breznitz, 2011). Although little research has been conducted on the neural mechanisms of improved working memory with training, one study with children suggests that Cogmed working memory capacity training can alter underlying neural networks which are important for working memory and attentional control (right fronto-parietal and left lateral occipital) (Astle et al., 2015). Another study exploring neural mechanisms of working memory training improvement in adults with and without dyslexia found that training resulted in changes to P3 working memory ERP latency and significantly larger P3 amplitude post training (Shiran & Breznitz, 2011). These findings suggest that working memory training is capable of directly improving working memory in children, adults and those with dyslexia and there may be some alterations in neural mechanisms associated with working memory as a function of training.

Switching abilities also appear to be modifiable with training resulting in direct switching improvements (Karbach & Kray, 2009; Kray et al., 2012). Although switching training has received less attention than working memory, research suggests that switching abilities are plastic in children, adult and older age populations (Karbach & Kray, 2009). More plasticity was observed in children and older age populations suggesting those with a window for improvement due to development or age related cognitive decline benefit the most from switching training (Karbach & Kray, 2009). This is promising also for clinical conditions which are associated with EF impairments. Kray et al. (2012) explored the application of switching training to children with ADHD and found that the intervention resulted in direct improvement of switching abilities.

It is less clear whether response inhibition abilities are modifiable with training interventions, although improvements are often observed on the training intervention (Spierer et al., 2013). Moreover, the degree to which direct training gains transfer to

measures of the same construct is debated as some studies find transfer but not on all measures of response inhibition (Diamond & Lee, 2011; Enge et al., 2014; Thorell et al., 2009).

At the behavioural level response inhibition training appears to result in direct improvements on the trained task in adults (Benikos et al., 2013; Berkman et al., 2014; Enge et al., 2014; Hartmann et al., 2016; Manuel et al., 2013, 2010) and in children (Liu, Zhu, Ziegler, & Shi, 2015; Thorell et al., 2009; Zhao, Chen, & Maes, 2016).In adults, the response inhibition system appears capable of rapid plastic modifications with short durations of training (1-3 training sessions) resulting in improvements at the reaction time level and transfer to different domains (verbal and visual) of response inhibition (Benikos et al., 2013; Hartmann et al., 2016; Manuel et., 2013, 2010). Training over longer durations appears to produce changes to accuracy of response inhibition (Berkman et al., 2014). Research with children has primarily focused on training over longer durations and relatively few studies have been conducted on single session or short duration training. In pre-school children, response inhibition training appears capable of improving performance on the training game (Liu et al., 2015; Thorell et al., 2009). Here both studies found no transfer of Go No-Go training to Stroop task performance (Liu et al., 2015; Thorell et al., 2009), but one reported transfer to a flanker task (Thorell et al., 2009). Such limited transfer to untrained response inhibition tasks leads researchers to doubt whether response inhibition training can really transfer beyond the trained task (Diamond & Lee, 2011). However, one study with both children aged 10-12 years and adults found that training improved performance on the trained task and transferred to Stroop performance in children but not in adults (Zhao et al., 2016). Zhao et al. (2016) found greater transfer effects in children suggesting that response inhibition is more plastic in children than adults and may produce transfer to non-trained response inhibition tasks. No published study to date has explored exclusive response inhibition training for improving response inhibition in clinical populations such as dyslexia.

Most response inhibition studies have explored the underlying plasticity of neural processes as a function of training, and it appears that short and long durations of training

produce plasticity in underlying neural processes of response inhibition in adults. Studies have reported differences in pre-frontal and parietal brain areas following a single 1-hour training session (Manuel et al., 2013, 2010); and changes to N2 and P3 amplitude post training (Benikos et al., 2013; Hartmann et al., 2016). Few studies explore the neural impacts of isolated response inhibition in children. In one study, N2 amplitude was increased as a function of training in girls but not boys of pre-school age (Liu et al., 2015). These findings suggest that, at least in adults, the response inhibition neural system is capable of plasticity. Given that few studies have explored this in children and clinical populations, training-related changes may be greater than that observed in adult studies as the response inhibition system in children appears more plastic at a behavioural level (Zhao et al., 2016).

Some studies have employed mixed approaches to training targeting two or more EFs with a training intervention. Combined working memory and response inhibition has been found to improve both response inhibition and working memory abilities in children with ADHD (Johnstone et al., 2012, 2010). One study found that although the training targeted both domains, the transfer effects were greater for response inhibition (Johnstone et al., 2012). This combined approach to training resulted in altered EEG beta band activity (Johnstone et al., 2012) and increased N2 response inhibition mean amplitude (Johnstone et al., 2010). However, it is difficult to infer which trained factor facilitated improvements in near and far outcomes with a mixed training like this.

Overall, at the direct level of transfer, EF appears to be modifiable. However, differences observed across studies with regard to type of training (working memory, switching, response inhibition, mixed), duration/intensity of training, type of control group (non-adaptive same EF training, active control non-EF training, passive control, or no control), and samples employed (adults, children, clinical conditions) (Kirk et al., 2015; Melby-Lervaag & Hulme, 2013; Schwaighofer, Fischer, & Bühner, 2015), make it difficult to infer for whom EF training will work and under what training conditions. Meta-analytic studies and systematic reviews suggest that children (Karbach & Unger, 2014; Peng & Miller, 2016; Wass et al., 2012) and those with clinical conditions (Karbach & Unger, 2014; Peng

& Miller, 2016) may benefit the most from training due to compensatory effects. Compensatory effects may occur for children and those with clinical condition because they are not performing at peak levels due to the gradual development of EF or impairments associated with a clinical condition, as such there is more room for EF improvement to occur (Karbach & Unger, 2014). It has been suggested that different training conditions produce more transfer, for instance *adaptive* interventions may produce *more transfer* than non-adaptive (Peng & Miller, 2016); and some report greater transfer for spaced compared to continuous training (Wang, Zhou, & Shah, 2014) , suggesting time for consolidation may be key to promoting transfer. To enhance transfer of training, engagement and motivation should also be targeted by incorporating immediate feedback and scoring into game based designs (Kirk et al., 2015).

Overall, response inhibition holds promise as an intervention targeted at improving response inhibition impairments in dyslexia. Although the degree of transfer to non-trained response inhibition tasks across children and adults is unclear, training consistently results in improvement on the trained task and often the underlying neural processes. The previous Chapters from this PhD argue that response inhibition is impaired and implicated in the core reading outcomes associated with dyslexia. Improved response inhibition with training may be possible in dyslexia through the compensatory effects that are observed for children (Karbach & Unger, 2014; Peng & Miller, 2016; Wass et al., 2012) and those with clinical conditions (Karbach & Unger, 2014; Peng & Miller, 2016). A recent meta-analysis exploring the efficacy of EF training for children with intellectual disabilities suggests that efficacy in these groups cannot be determined due to no over-arching theory informing interventions, thus making it difficult to determine which factor or factors drive changes (Kirk et al., 2015). Despite the developmental nature of EF, the unity (common EF: response inhibition) and diversity (updating and switching) fractioning of EF is found in children (Huizinga et al., 2006; Lehto et al., 2003; Rose, et al., 2011; van der Sluis et al., 2007), adolescence (Huizinga et al., 2006), and adults (Friedman et al., 2006, 2007, 2008; Miyake et al., 2000): making it the most suitable framework for interpreting modification of EF and cross comparability of intervention studies across different ages.

No study to date has explored whether response inhibition training can result in improved response inhibition abilities and modification of underlying neural processes in children with dyslexia. Using a spaced training approach (3 times per week for 6 weeks) the present study 2 aims to determine whether: (1) adaptive compared to non-adaptive response inhibition training results in improved performance on the trained task in children with dyslexia; (2) adaptive compared to non-adaptive response inhibition training transfers to improved performance on non-trained response inhibition tasks in children with dyslexia; and (3) adaptive compared to non-adaptive response inhibition training transfers to increased amplitude of N2 and P3 response inhibition ERPs in children with dyslexia.

6.1 Method

6.1.1 Participants

Thirty of the participants with developmental dyslexia aged 10-12 years who were recruited in the previous chapter (see page 156 for more details) took part in this response inhibition training intervention study. Participants were randomly allocated to low (A) and high (B) dose training conditions with a 4-block randomisation method (AABB, ABAB, ABBA, BAAB, BABA, BBAA) to ensure approximately equal sample sizes (Kim & Shin, 2014; Suresh, 2011). This resulted in 14 participants being allocated to the low-dose training condition (mean age:10.86; Gender: 9 males, 5 females) and 16 participants being allocated to the high-dose training condition (mean age: 11; Gender: 8 males, 8 females). Diagnosis of developmental dyslexia was confirmed via access to psychological assessment reports. Initially, a sample of thirty-three children with dyslexia were recruited, however, three participants were removed from the present analysis due to their scoring in the clinical range on the ADHD scales of the Child Behaviour Checklist (Achenbach & Rescorla, 2001) and the Conners 3 Parent form (Conners, 2008) or reporting comorbid dyspraxia. All remaining participants were monolingual English speakers with normal or corrected vision and hearing. Participants had no additional diagnosis of a psychological disorder. Informed consent and assent were obtained from participating

parents and children. Ethical approval for this research project was granted by Dublin City University's Research Ethics Committee (DCUREC/2015/254). A convenience sample of participants were recruited through Dyslexia Association Ireland and local primary schools.

6.1.2 Procedure

This response inhibition training study (Study 2) was a double-blind, four-block (AABB) randomisation, placebo controlled design consisting of three phases: (a) pre-intervention assessment, (b) a 6-week online response inhibition training intervention where participants were randomly allocated to low (non-adaptive) or high (adaptive) dose conditions, and (c) post-intervention assessment. Randomisation, blinding and later unveiling of training conditions was conducted by the author of the game Dr David Delany who was not actively involved in recruitment or pre-post assessment of participants. Participants were required to complete two (pre-post) on-site testing sessions lasting approximately 2 hours in the psychology laboratories in the School of Nursing and Human Sciences at Dublin City University. Participants were assessed individually in the presence of their parent/guardian. During the testing session, participants completed a battery of neuro-cognitive (EF) and reading measures, while parents/guardians of participants completed assessments of their child's self-regulation and socio-emotional behaviours. The order of tasks was counterbalanced for each participant for pre and post assessments to control for fatigue effects. All neuro-cognitive measures were created with E-Prime Software and responses were recorded with a combination of a Cedrus RB-50 response pad, mouse and keypad. Upon completion of the pre-intervention assessment participants were shown a short 5-minute demonstration of the training game and were given a copy of an instruction sheet to take home. Parents/Guardians were informed that they would soon receive an email with a link to their prescribed training intervention and their child's unique log in details (username, password), it was requested that online training be supervised by parent/guardian for child protection reasons. Participants were instructed to log-in and play the training game 3 times per week for 6 weeks. After completing the 6-week intervention participants returned for post-intervention assessment. Participant

activity on the game was monitored with an interface which displayed the number of days since each participant had trained without displaying their training condition. If a participant had not trained in three days a reminder email was sent as a prompt to ensure continuous engagement. Throughout the course of the entire training intervention eleven participants required prompts to continue training.

6.1.3 Inhibitory Control Training Programme

The Complex Sustained Attention Trainer (CSAT; Delany, 2015), a variant of the go no-go attention control paradigm (Donders, 1969), was used to train inhibitory control. Sustained attention paradigms like the CSAT with high Go and low No-Go probability rely more on inhibitory control than sustained attention (Carter, Russell, & Helton, 2013), therefore are suitable for targeted intervention aimed at enhancing inhibitory control and related behaviours. The CSAT trainer is designed to progressively enhance inhibitory control abilities through training sustained attention under increasing distractor interference and working memory load.

At the start of each training game participants were presented with a specific No-Go target image which could consist of three features (colour, shape, and pattern) for example a No-Go target may be a yellow (colour), trapezoid (shape) with dots (pattern). Once the game commenced participants were presented with a sequence of serially presented images each varying on these three features (colour, shape and pattern), and were instructed to press the space bar for all other images (Go Targets) except for the image they viewed at the start of the game (No-Go Target).

Go and No-Go targets were pseudo-randomly selected from a catalogue of 810 possible images generated from a set of 9 colours, 10 shapes and 6 patterns. Due to Go and No-Go targets consisting of three features (colour, shape, and pattern), target stimuli could be categorised into four classes: one No-Go class (No-Go target only) and three Go classes. For instance, a Go target could overlap with the No-Go target (e.g. a yellow trapezoid with dots) on zero features (0-F) (e.g. a green square with stripes), one feature (1-F) (e.g. a green square with dots) or two features (2-F) (a green trapezoid with dots). The degree of

overlap of Go targets (lures) with No-Go target served as a way of manipulating distractor interference in the game.

Participants in both high and low-dose training conditions were required to complete a training session three times per week for 6 weeks. In both conditions, No-Go target image was randomised within and across training sessions over the 6-week period.

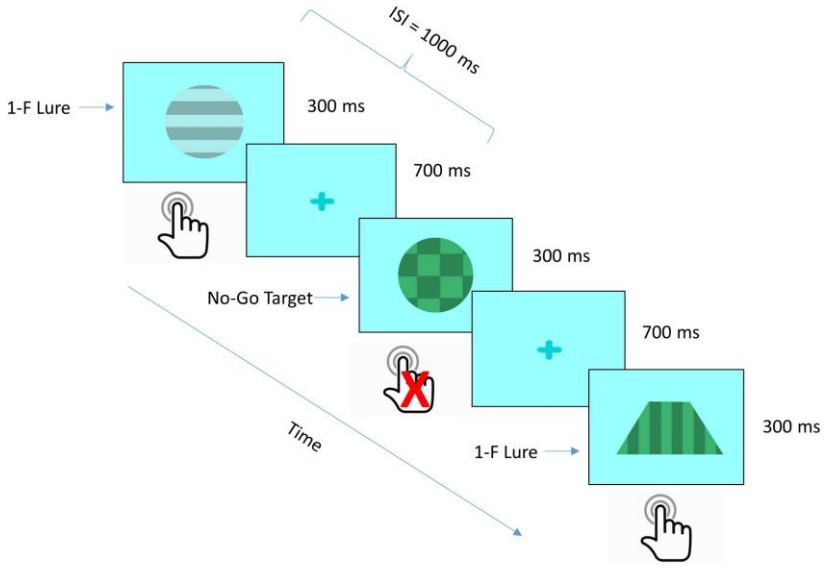
In the high-dose training condition, a training session consisted of 7 games (each lasting 4 minutes) and took approximately 28 minutes to complete. During a game 190 images were presented, Go and No-Go target images were presented centrally for 300ms followed by "+" for 700ms resulting in a total inter-stimulus interval of 1,000ms (*see Figure 49 for schematic diagram of each condition*). Difficulty in the high-dose condition was adaptive based on player's ability to successfully withhold response to No-Go target. Difficulty of the game was manipulated in two ways: reduced probability of encountering a No-Go target and increased overlap of features of the Go Target with No-Go target (1-F and 2-F lures). At first game-play, the probability of No-Go target appearing was set at .45 and the probability of 1-F and 2-F lures was set to zero (only 0-F overlap allowed). As participants successfully withheld response to No-Go target, the task difficulty adapted by systematically increasing the probability of encountering a 1-F lure by 0.01 until it reached a maximum probability of 0.20. When the maximum probability was reached for a 1-F lure, the probability was reset to zero, and the probability of encountering a 2-F lure was increased by 0.01 until it reached a maximum probability of 0.20. When the maximum probability was reached for a 2-F lure the probability was reset to zero, and the probability of encountering a No-Go target was reduced by 0.005. Once No-Go probability was reduced, the lure probability adjustment cycle repeated. If participants did not withhold response to No-Go target the game became easier, such that the probability of encountering a lure was reduced by 0.02 and the probability of encountering a No-Go target was increased by 0.01. Training session was terminated on a given day if a participant reached a No-Go target probability of 0.01.

In the low-dose training condition, a training session consisted of three games (each lasting 2 minutes) and took approximately 6 minutes to complete. During a game 60

images were presented, Go and No-Go target images were presented centrally for 1,100ms followed by "+" for 700ms resulting in a total inter-stimulus interval of 1,800ms (*see Figure 49 for schematic diagram of each condition*). The low-dose training condition did not adapt based on player performance.

Feedback and motivational features were built into both high and low-dose versions of the game. If participants correctly withheld response for a No-Go target or correctly responded to a Go target, a green circle would flash on the right side of the screen and points were added to their score. Additional bonus points were received every time a participant successfully withheld response for a No-Go target. If participants incorrectly responded to a No-Go target and incorrectly withheld response for a Go target, a red circle would flash on the right side of the screen and points were subtracted from their score. On the left-hand side of the screen participants could view their highest score achieved during training. This served to motivate participants to try to beat their high score every time they played the game. A progress bar on the left-hand side of the screen increased every time a participant successfully withheld response to a No-Go target, when the progress bar was full the participant moved on to the next level *(see Figure 50 for CSAT gameplay screenshots of feedback and motivational features*).

CSAT High-dose



CSAT Low-dose

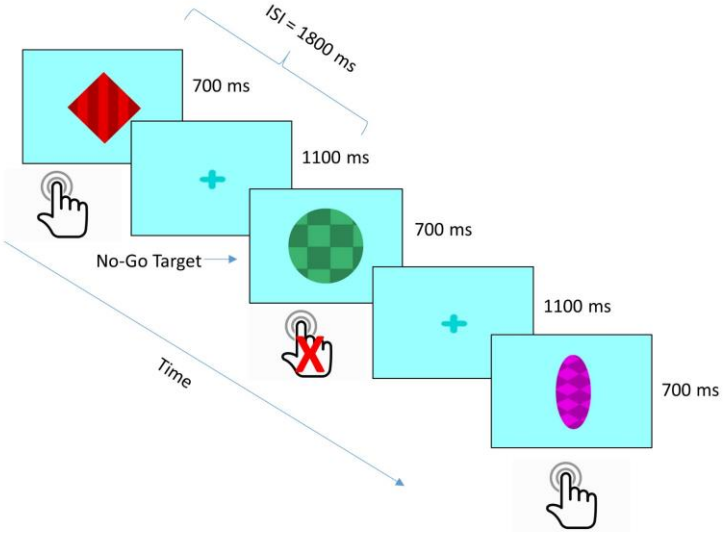
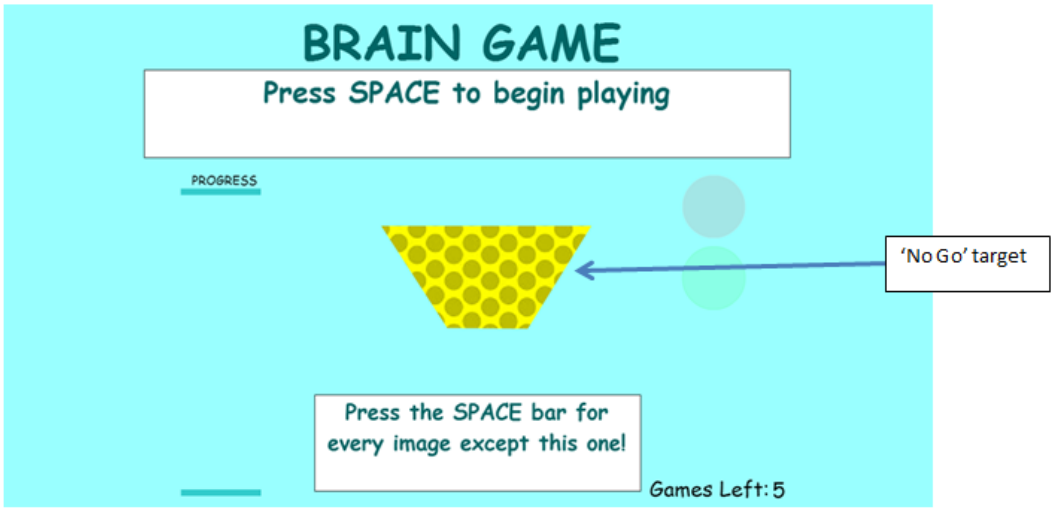
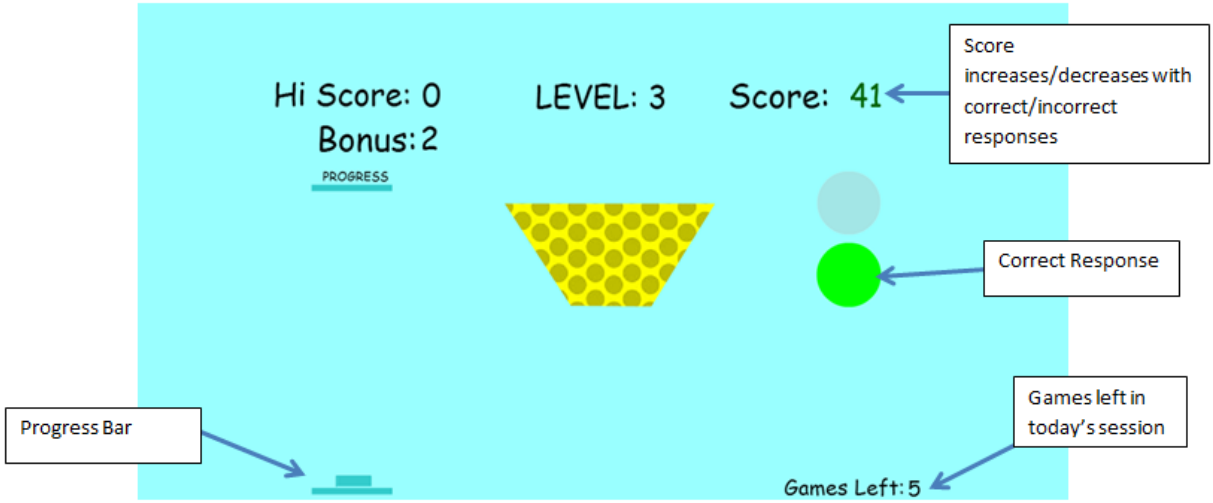


Figure 49 Schematic diagrams of high and low-dose versions of the CSAT



Panel A



Panel B

Figure 50 CSAT gameplay screenshots. Panel A is home page after log in and panel B is gameplay with motivational features.

6.1.4 Pre-Post Assessment Measures

Picture Go No-Go task: See pages 84- 88 for task details. This task was adapted for electroencephalogram (EEG) recording, such that stimuli appeared on screen for 2,000ms, followed by a blank screen for 1,000ms and a fixation point for 1,000ms. Total stimulus duration was 4,000ms (*see Figure 30 for stimulus timings).*

Phoneme Go No-Go Task: See pages 84-88 for task details. This task was adapted for electroencephalogram (EEG) recording, such that stimuli appeared on screen for 2,000ms, followed by a blank screen for 1,000ms and a fixation point for 1,000ms. Total stimulus duration was 4,000ms *(see Figure 31 for stimulus timings).*

6.1.5 EEG Recording, Processing and Analysis

Electroencephalogram (EEG) was recorded during Go No-Go tasks (picture and phoneme versions) using a 32 channel ActiChamp amplifier with electrode placement based on the Internationally recognised 10-20 system. Ocular artifacts were recorded with vertical (VEOG: placed above and below the left eye) and horizontal electrooculogram (HEOG: placed at the outer canthi of both eyes). Recording was carried out in an electrically shielded room and SuperVisc electrolyte gel was applied to all active scalp and EOG electrodes to improve conductance. All recording equipment was based in the School of Nursing and Human Sciences EEG laboratory at Dublin City University and access was granted to Dr Lorraine Boran to use equipment provided by Science Foundation Ireland (via a grant SFI/12/RC/2289 awarded to Prof. Alan Smeaton, Insight Centre Ireland). Data were sampled at the 500Hz rate and a high pass cut off filter of 30Hz and a low pass cut off of 0.15 Hz were applied. All data was recorded in BrainVision recorder and later referenced after acquisition to Cz in BESA.

The effect of ocular artifacts were reduced by applying an automatic dipole modelling algorithm in BESA (Berg & Scherg, 1991), and additional blink, movement or interference related artifacts were removed manually after visual inspection of data in BESA software. Noisy electrodes were defined as bad or interpolated depending on where they were located on the scalp topography in relation to other electrodes (i.e. if an electrode was

surrounded by non-noisy electrodes it was interpolated; if an electrode was near the perimeter of the cap and not surrounded by electrodes it was defined as a bad channel). Across groups and pre-post testing sessions 1.77% of total electrodes were interpolated and 3.28% of total electrodes were defined as bad.

The event related potential (ERP) epoch was set to -200ms to 800ms. A pre-stimulus baseline correction (-200ms-0ms) was applied to all ERP grand averaged data to account for pre-stimulus activity. Time windows for N2 and P3 inhibition-related components were informed by a visual inspection of scalp topography and based on previous literature (Johnstone et al., 2007; Liotti et al., 2010; Smith, Johnstone, & Barry, 2004). Visual inspection of ERP component to select time frames was based on a grand average collapsed across training group (high and low) and time (pre and post). The N2 ERP component was prominent over fronto-central areas (Fz, C3, C4) (*see Figure 51*) and peaked between 130ms-376ms in the picture task and between 148-364ms in the phoneme task. The P3 ERP component was prominent bilaterally over posterior parietal areas (P7, P8) (*see Figure 52*) and peaked between 226-552ms in the picture task and between 218-572 in the phoneme task.

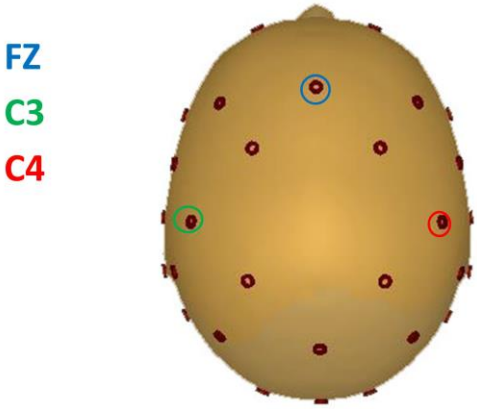


Figure 51 Scalp channels where N2 ERP component was prominent

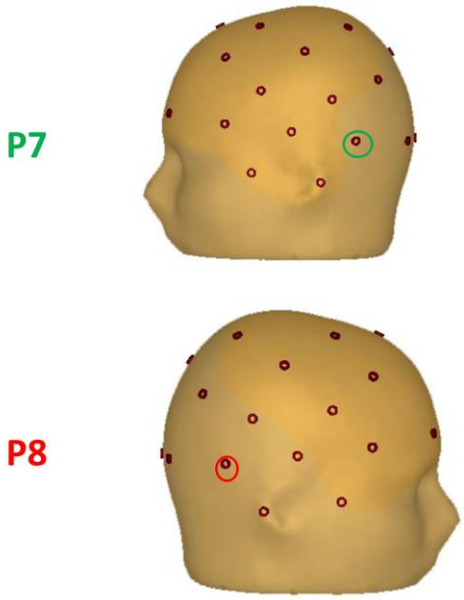


Figure 52 Scalp channels where P3 ERP component was prominent

After defining time windows and electrodes for N2 and P3 response inhibition ERP components, grand average waveforms were calculated separately for each group (high and low-dose) at each time point (pre and post). Mean amplitude of N2 and P3 inhibition-related ERP components were extracted for statistical analysis.

Pre-EEG data were recorded for all thirty participants, however, this was reduced to twenty-four participants for technical reasons. The final grand averaged ERP N2 analysis was based on 24 participants (11 high-dose, 13 low-dose) for the picture task and 21 participants (12 high-dose, 9 low-dose) for the phoneme task; while the final P3 analysis was based 25 participants (12 high-dose, 13 low-dose) for the picture task and 23 participants (12 high-dose, 11 low-dose) for the phoneme task.

For baseline comparison, N2 mean amplitudes were subject to a 2 (dose: high, low) x 2 (trial type: Go, No-Go) mixed design ANOVA. No lateral effects were explored as the scalp topography suggested that this component manifests in right, left and central frontal areas. For baseline comparison, P3 amplitudes were subject to a 2 (dose: high, low) x 2 (trial type: Go, No-Go) x 2 (hemisphere: right- P8, left-P7) mixed design ANOVA. Lateral effects were explored to see if mean amplitude differed between left and right hemisphere as visual inspection suggests no central manifestation of P3 ERP component.

To explore pre-post N2 mean amplitude differences in high and low-dose training conditions, a 2 (dose: high, low) x 2 (trial type: Go, No-Go) x 2 (time: pre, post) mixed design ANOVA was conducted. To address apriori research question, only main effects of time, trial, dose and interactions of time*dose, trial*time, and dose*trial*time are explored.

To explore pre-post P3 mean amplitude differences in high and low-dose training conditions, a 2 (dose: high, low) x 2 (trial type: Go, No-Go) x 2 (time: pre, post) x 2 (hemisphere: right- P8, left-P7) mixed design ANOVA was conducted. To address apriori research questions, only main effects of time, trial, dose, hemisphere, and interactions of time*dose, trial*time, trial*hemisphere, hemisphere*time, time*dose*trial, and time*dose*trial*hemisphere are explored.

Separate analyses were conducted for picture and phoneme versions. Supplementary effect-size analysis (Cohen's d) was used to assess size of transfer effect in high and low-dose training conditions for N2 and P3 amplitudes for both Go and No-Go trials.

6.2 Behavioural Data Analysis

6.2.1 Creating EF Z-mean Composite Measures

Inhibition z-mean composite scores were calculated to provide cleaner general measures by filtering out any non-EF noise and to increases power due to small sample size (Snyder et al., 2015). Composite scores for inhibition were created for error rate and reaction time by summing all standardised z-scores and dividing by the number of tasks. It is necessary to use a common mean and standard deviation when computing standardised scores with two or more time points, as standardised scores at one time point will remove the change in scores across time (Anglim, 2009). To account for this, pre-post standardised scores for each task were calculated with the following equation for time 1 $\left(\frac{T1Errors - Overall\ Mean\ Errors\ (T1\ \&\ T2)}{Overall\ SD\ (T1\ \&\ T2)}\right)$ and time 2 $\left(\frac{T2Errors - Overall\ Mean\ Errors\ (T1\ \&\ T2)}{Overall\ SD\ (T1\ \&\ T2)}\right)$.

6.2.2 Statistical Analysis

Differences between high-dose and low-dose training groups on demographic, response inhibition composites and Go No-Go task performance were assessed at baseline with between group F-Tests. Transfer of training to direct response inhibition outcomes were assessed with 2 (dose: high, low) x 2 (Time: Pre, Post) mixed design ANOVAs. Effect-size analysis (Cohen's d) was used to explore standardised differences between training groups prior to intervention and to assess size of transfer effect in high and low-dose training conditions. Cohen's d for mixed design ANOVA was calculated using the following equation: $(PreScore - PostScore)/(Pooled\ SD)$; which is more suitable for pre-post designs (Dunlap, Cortina, Vaslow, & Burke, 1996). According to Cohen (1988) effects sizes can be classified as small effect (d=.2), medium (d=.5) and large (d=.8).

6.2.3 Preliminary Analysis

Preliminary analyses were conducted to ensure that variables did not violate the assumptions of normality or homogeneity of variance. All variables met the assumptions of normality and homogeneity of variance A Bonferroni correction ($p<.005$) was applied to account for inflated type I error rate due to multiple comparisons. Bonferroni correction was calculated based on *a priori* research questions only to ensure that resulting alpha level would not lead to an increase in type II error rate. Herein, all effects with an alpha level of <.005 will be discussed as significant while all effects with an alpha level of <.05 will be discussed as trend for a significant effect.

6.3 Results

6.3.1 Descriptive Statistics and Baseline Comparisons

Descriptive statistics and baseline comparisons between high and low-dose training conditions are summarised for behavioural measures in Table 19 and for ERP measures in Table 20. Prior to the training intervention participants' age ranged between 10-12 years. At baseline, high and low-dose training conditions did not significantly differ on any measures of response inhibition at the behavioural or ERP (N2 and P3) levels.

In the picture Go No-Go task (see Table 20 for summary), there were no main or interaction effects for the N2 response inhibition-related ERP component over fronto-central areas at baseline. However, for the P3 response inhibition-related component over posterior parietal areas there was a significant main effect of trial type in the picture task ($F(1,23)=44.95$, $p=.000$, $\eta_p^2=.662$). This effect reflects a larger mean amplitude for No-Go ($M=2.72$, $SE=.29$) relative to Go trials ($M=2.09$, $SE=.30$). When mean amplitude was collapsed across both Go and No-Go trials in the picture task, there was a trend for larger P3 mean amplitude ($F(1,23)=5.75$, $p=.025$, $\eta_p^2=.20$) in the right (P8: $M=2.83$ $SE=.34$) compared to the left (P7: $M=1.98$, $SE=.34$) hemisphere.

In the phoneme Go No-Go task (see Table 20 for summary), there were no main or interaction effects for the N2 response inhibition-related ERP component over fronto-

central areas at baseline. However, for the P3 response inhibition-related component over posterior parietal areas there was a trend for a significant main effect of trial type in the phoneme task ($F(1,21)=8.89$, $p=.007$, $\eta_p^2=.319$). This effect reflects a larger mean amplitude for Go (M=2.01, SE=.21) relative to No-Go trials (M=1.48, SE=.240). When mean amplitude was collapsed across both Go and No-Go trials in the phoneme task, there was also a trend for larger P3 mean amplitude ($F(1,21)=4.96$, $p=.037$, $\eta_p^2=.19$) in the right hemisphere (P8: M=2.03, SE=.28) compared to the left hemisphere (P7: phoneme M=1.46, SE=.21). A trend for a significant trial x hemisphere interaction effect was also found in the phoneme Go No-Go task ($F(1,21)=4.78$, $p=.04$, $\eta_p^2=.186$). This effect reflects a greater amplitude difference between Go and No-Go trials in the right hemisphere (P8: Go M=2.42, SE= .27; No-Go M=1.63, SE=.31) compared to the left hemisphere (P7: Go M=1.59, SE=.20; No-Go M=1.34, SE=.27) which is in the direction of larger mean amplitude for Go relative to No-Go trials.

Table 19. Baseline comparisons between high and low- dose training conditions on direct measures of response inhibition

	Low-Dose			High-Dose				
		Mean	SD	N	Mean	SD	F-Value	*p*-value	Cohen's *d*
Age (years)	14	10.86	0.95	16	11.00	.82	.196	.661	-.16
Response Inhibition									
Pic. GNG Comm.	14	16.86	20.10	16	26.44	13.86	.021	.886	.053
Pic. GNG RT	14	671.44	114.38	16	742.51	168.27	1.76	.194	-.49
Phon. GNG Comm.	14	27.14	23.91	16	16.75	14.18	2.16	.153	.52
Phon. GNG RT	14	811.41	140.91	16	854.19	166.90	.862	.361	-.34
Inhibition Error Comp.	14	.099	1.27	15	-.347	.67	1.43	.242	.44
Inhibition RT Comp.	14	.029	.99	15	.414	.96	1.12	.299	-.39

Note: pic=picture, phon=phoneme, comm=commission errors, GNG=go no-go, comp=composite, RT=reaction time. Bonferroni correction p=.005, trend p=.05

Table 20 Baseline comparisons between high and low-dose training conditions for N2 (Fz, C3, C4) and P3 (P7, P8) response inhibition ERPs

	Picture Task					Phoneme Task			
	N2					*N2*			
	F	*df1,df2*	*P value*	η_p^2		*F*	*df1,df2*	*P value*	η_p^2
Trial	2.27	1, 22	.146	.093	Trial	3.15	1,19	.09	.142
Dose	.059	1,22	.811	.003	Dose	.318	1,19	.579	.016
Trial * Dose	1.08	1,22	.310	.047	Trial * Dose	.149	1,19	.704	.008
	P3					*P3*			
	F	*df1,df2*	*P value*	η_p^2		*F*	*df1,df2*	*P value*	η_p^2
Trial	44.95	1, 23	.000**	.662	Trial	8.89	1,21	.007*	.319
Dose	.136	1,23	.715	.006	Dose	1.93	1,21	.179	.081
Hemisphere	5.75	1,23	.025*	.200	Hemisphere	4.96	1,21	.037*	.191
Trial * Dose	.826	1,23	.373	.035	Trial * Dose	.439	1,21	.515	.020
Trial * Hemisphere	1.28	1,23	.269	.053	Trial * Hemisphere	4.78	1,21	.040*	.186
Trial*Dose* Hemisphere	.316	1,23	.579	.014	Trial*Dose* Hemisphere	.417	1,21	.526	.019

Note: ** p<.005 (sig with Bonferroni correction), *p<.05 (trend)

6.3.2 Direct Training Effects (Behavioural)

Results exploring transfer of training to direct measures of response inhibition at a behavioural level are summarised in Table 21.

Direct Training Gain

To explore direct training effects a mixed design ANOVA with time as a within factor (start No-Go probability; end No-Go probability) and dose as a between factor (high-dose, low-dose) was conducted. This analysis revealed a significant time x dose interaction ($F(1,28)=1727.42$, $p=.000$, $\eta_p^2=.984$), a significant main effect of time ($F(1,28)=1351.94$, $p=.000$, $\eta_p^2=.980$) and a significant main effect of dose ($F(1,28)=1006.31$, $p=.000$, $\eta_p^2=.973$).

The low-dose training group experienced a significantly and capped high effect for training loss demonstrating a lower No-Go probability at the start of training (M=.40; SD=.000) than the end of training (M=.42; SD=.009) (Cohen's d=-4.8). This suggests that the low-dose group performed slightly worse from pre to post training. However, it is important to note that the low-dose training game was not equipped to capture any direct training effects or to allow trainers to progress to more difficult levels as the game was non-adaptive.

The high-dose training group experienced a high effect for training gain demonstrating a higher No-Go probability at the start of training (M=.45; SD=.000) than the end of training (M=.052, SD=.037) (Cohen's d= 21.51). This suggests that the high-dose group did improve on the training game as their end No-Go probability of 5% suggests.

Figure 53 presents training gain for both high and low-dose groups. Here it can be seen that the high-dose condition experienced much larger training gains than the low-dose condition as reflected by substantially larger effects sizes in the high-dose.

Response Inhibition Error Composite

To explore near transfer of training to the response inhibition z-mean error composite score a mixed design ANOVA with time as a within factor (pre, post) and dose as a

between group factor (high, low) was conducted. This analysis revealed a non-significant dose x time interaction ($F(1,27)=.042$, $p=.839$, $\eta_p^2=.002$), a non-significant main effect of time ($F(1,27)=1.32$, $p=.261$, $\eta_p^2=.047$), and a non-significant main effect of dose ($F(1,27)=1.79$, $p=.192$, $\eta_p^2=.062$). The low-dose group experienced no effect for error composite from pre (M=.99, SD=1.27) to post (M=.251, SD=1.03), Cohen's d=-.13. The high-dose experimental group experienced a small-medium effect in error composite from pre (M=-.347, SD=.67) to post (M=-.128, SD=.68), Cohen's d=-.32 (*see figure 54 for response inhibition error composite transfer for both high and low- dose groups*).

Response Inhibition Reaction Time Composite

To explore near transfer of training to the response inhibition z-mean reaction time composite score a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (high, low) was conducted. This analysis revealed a non-significant dose x time interaction ($F(1,27)=1.15$, $p=.294$, $\eta_p^2=.041$), a significant main effect of time ($F(1,27)=19.51$, $p=.000$, $\eta_p^2=.425$) and a non-significant main effect of dose ($F(1,27)=.674$, $p=.419$, $\eta_p^2=.024$). The significant main effect of time suggests that both groups experienced a significant reduction in reaction time as a function of training. The low-dose experienced a medium effect for reaction time reduction from pre (M=.029, SD=.99) to post (M=-.396, SD=.66), Cohen's d=.52. The high-dose experimental group experienced a large effect for reaction time reduction from pre (M=.414, SD=.96) to post (M=-.279, SD=.90), Cohen's d=.87. Figure 55 presents transfer for both high and low groups to response inhibition reaction composite.

Picture Go No-Go Task

To explore near transfer to the Picture Go No-Go task a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (high, low) was conducted. For commission errors, the analysis revealed a non-significant dose x time interaction ($F(1,27)=.004$, $p=.569$, $\eta_p^2=.012$), a non-significant main effect of time ($F(1,27)=1.12$, $p=.300$, $\eta_p^2=.040$) and a non-significant main effect of group ($F(1,27)=.333$, $p=.948$, $\eta_p^2=.000$). The low-dose group experienced a small effect for commission errors from pre

(M=16.86, SD=20.10) to post (M=20.86, SD=13.33), Cohen's d=-.24. The high-dose group also experienced a small effect for commission errors from pre (M=13.69, SD=20.33) to post (M=18.13, SD=15.84), Cohen's d=-.25. (*see Figure 56*).

For reaction time, the analysis revealed a non-significant dose x time interaction ($F(1,27)=1.69$, $p=.205$, $\eta_p^2=.059$), a trend for a significant main effect of time ($F(1,27)=6.54$, $p=.011$, $\eta_p^2=.218$) and a non-significant main effect of dose ($F(1,27)=.536$, $p=.470$, $\eta_p^2=.019$). The trend for a main effect of time suggests that both groups experienced a reduction in response inhibition reaction time as a function of training. The low-dose group experienced a small-medium effect for reaction time reduction from pre (M=671.44, SD=114.37) to post (M=638.21, SD=90.56), Cohen's d=.32. The high-dose group experienced medium-large effect for reaction time reduction from pre (M=731.19, SD=167.75) to post (M=638.28, SD=115.92), Cohen's d=.66. (*see Figure 57*).

Phoneme Go No-Go Task

To explore near transfer to the Phoneme Go No-Go task a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (high, low) was conducted. For commission errors, the analysis revealed a non-significant dose x time interaction ($F(1,27)=.083$, $p=.776$, $\eta_p^2=.003$), a non-significant main effect of time ($F(1,27)=.368$, $p=.549$, $\eta_p^2=.013$) and a non-significant main effect of dose ($F(1,27)=3.175$, $p=.086$, $\eta_p^2=.105$). The low-dose group experienced no effect for commission errors from pre (M=27.14, SD=23.91) to post (M=28.00, SD=24.05), Cohen's d=-.04. The high-dose experimental group experienced a small effect for commission errors from pre (M=14.66, SD=11.87) to post (M=17.07, SD=14.06), Cohen's d=-.19 (*see Figure 58*).

For reaction time, the analysis revealed a non-significant dose x time interaction ($F(1,27)=.006$, $p=.940$, $\eta_p^2=.000$), a significant main effect of time ($F(1,27)=12.31$, $p=.002$, $\eta_p^2=.313$) and a non-significant main effect of dose ($F(1,27)=.597$, $p=.446$, $\eta_p^2=.022$). The significant main effect of time suggests that both groups experienced a reduction in response inhibition reaction time as a function of training. The low-dose group experienced a medium-large effect for reaction time reduction from pre (M=811.41,

SD=140.91) to post (M=737.16, SD=80.54), Cohen's d=.67. The high-dose experimental group experienced a medium effect for reaction time reduction from pre (M=845.29, SD=154.00) to post (M=767.76, SD=116.19), Cohen's d=.57. (*see Figure 59*).

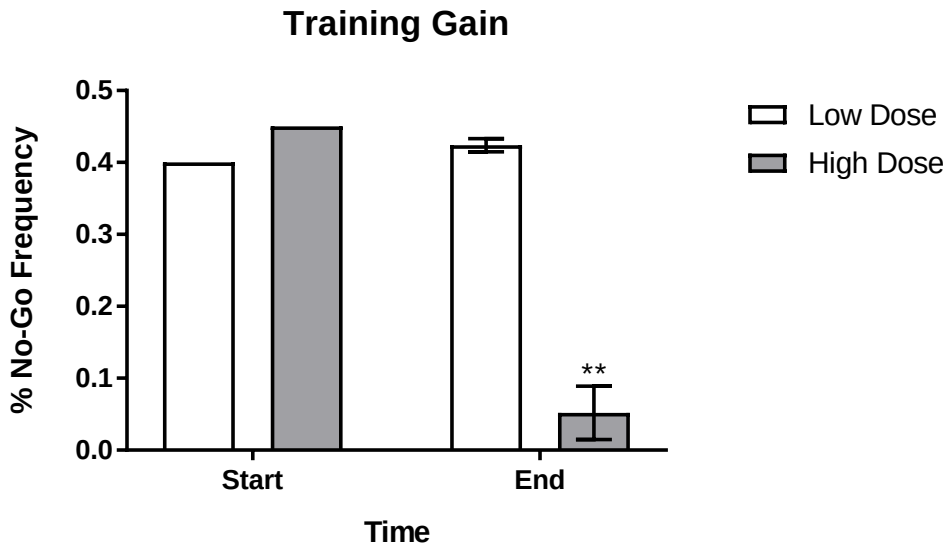


*Figure 53 Direct training gain as indexed by % of No-Go trials for high and low-dose training groups at the start and end of training. *p<.05 **p<.005*

Table 21 Performance on direct measures of response inhibition at a behavioural level as a function of training

	Low-dose			High-dose							ANOVA Time Effect		ANOVA Group Effect		ANOVA Interaction Effect	
Transfer Task	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*F (Time)*	*F (Group)*	*F (Inter-action)*	*df*1, *df*2	*p*-value	η_p^2	*p*-value	η_p^2	*p*-value	η_p^2
Training Gain	.400	.424	-5.33	.45	.052	21.51	1351.94	1727.42	1006.31	1,28	**.000****	.980	**.000****	.973	**.000****	.984
	(.000)	(.009)		(.000)	(.037)											
Pic. GNG Comm.	16.86	20.86	-0.24	13.60	18.13	-0.25	1.12	.333	.004	1,27	.300	.040	.948	.000	.569	.012
	(20.10)	(13.33)		(20.33)	(15.84)											
Pic. GNG RT	671.44	638.21	0.32	731.19	638.28	.066	6.54	.536	1.69	1,27	.011*	.218	.470	.019	.205	.059
	(114.38)	(90.56)		(167.75)	(115.92)											
Phon GNG Comm	27.14	28.00	-0.04	14.66	17.07	-.19	.368	3.175	.083	1,27	.549	.013	.086	.105	.776	.003
	(23.91)	(24.05)		(11.87)	(14.06)											
Phon GNG RT	811.41	737.16	0.67	845.29	767.76	0.57	12.31	.597	.006	1,27	**.002****	.313	.446	.022	.940	.000
	(140.91)	(80.54)		(154.00)	(116.19)											
Inhibition Err. Comp.	.099	.251	-.13	-.347	-.128	-.32	1.32	1.79	.042	1,27	.261	.047	.192	.062	.839	.002
	(1.27)	(1.03)		(.67)	(.68)											
Inhibition RT Comp.	.029	-.396	.52	.414	-.279	-.87	19.51	.674	1.15	1,27	**.000****	.425	.419	.024	.294	.041
	(.99)	(.66)		(.96)	(.90)											

Note. Pic=Picture, Phon=Phoneme, Comm=Commission Errors, GNG= Go No-Go, Comp=Composite, RT=Reaction Time. *p<.05 (trend), **p<.005 (significant with Bonferroni correction

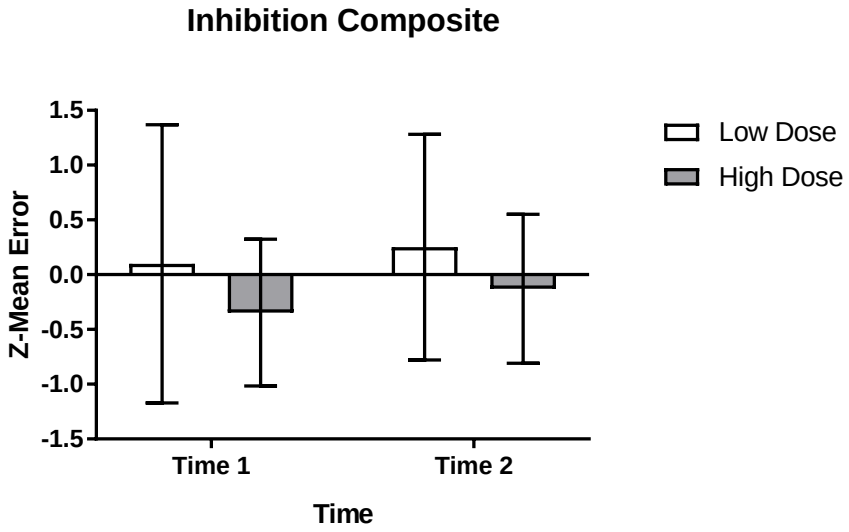


*Figure 54 Response inhibition error composite transfer for high and low-dose training groups at the start and end of training**.** *p<.05 **p<.005*

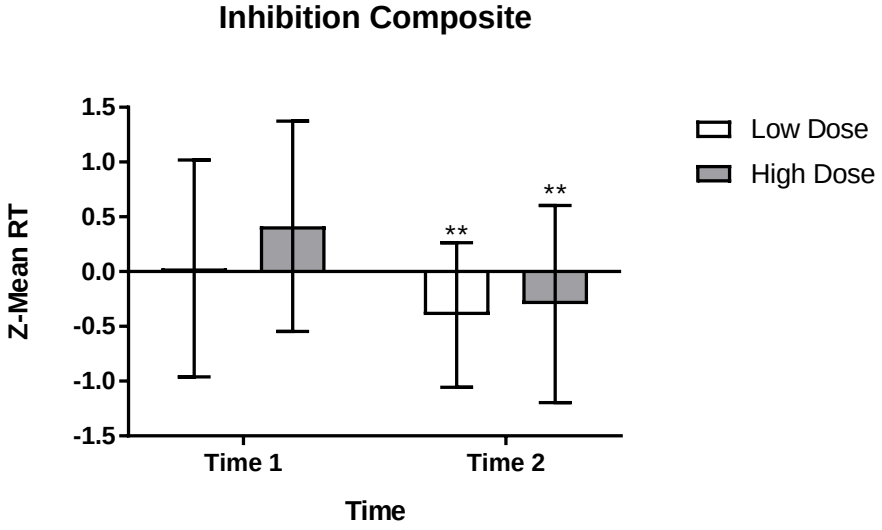


*Figure 55 Response inhibition RT composite transfer for high and low-dose training groups at the start and end of training. *p<.05 **p<.005*

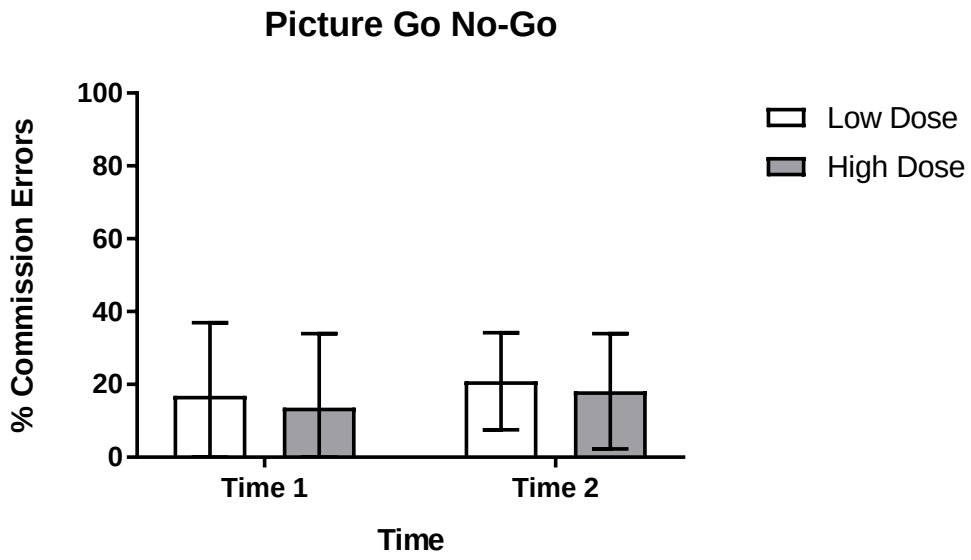


*Figure 56 Picture Go No-Go commission error transfer for high and low-dose training groups at the start and end of training. *p<.05 **p<.005*

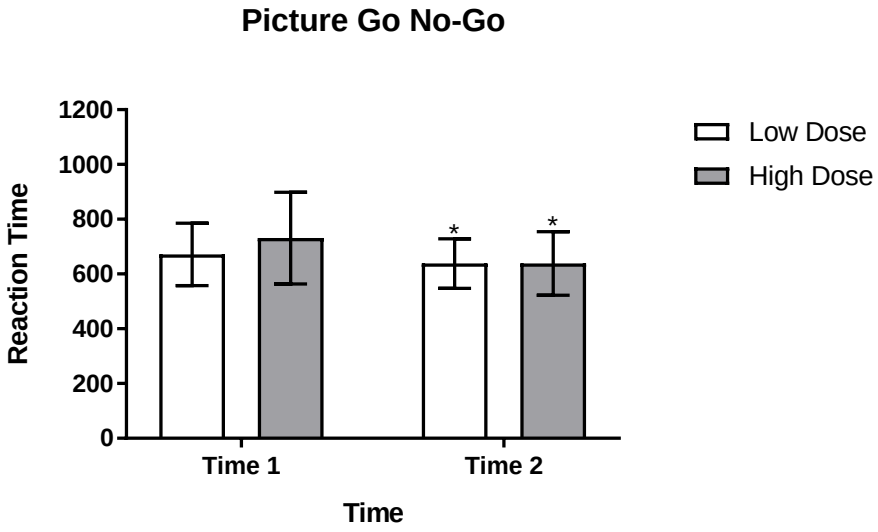


*Figure 57 Picture Go No-Go RT transfer for high and low-dose training groups at the start and end of training. *p<.05 **p<.005*

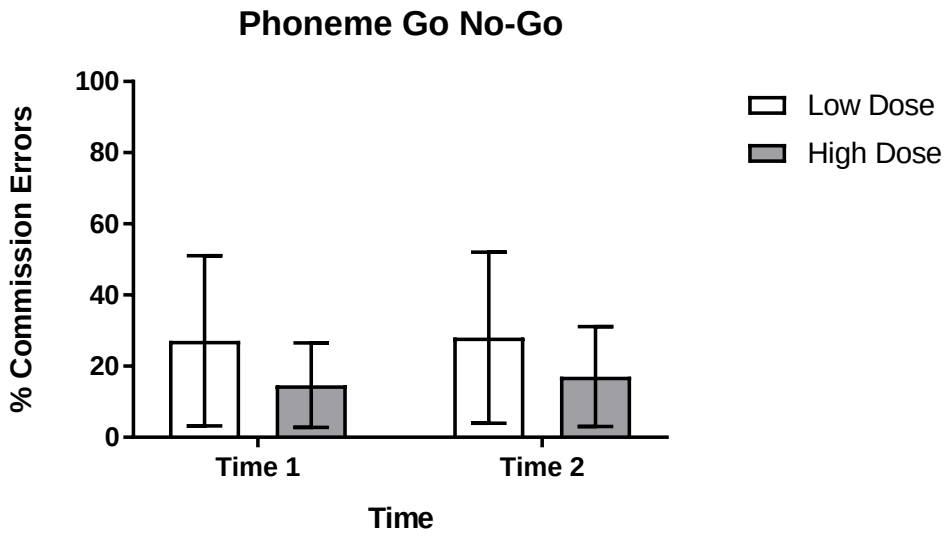


*Figure 58 Phoneme Go No-Go commission error transfer for high and low-dose training groups at the start and end of training. *p<.05 **p<.005*

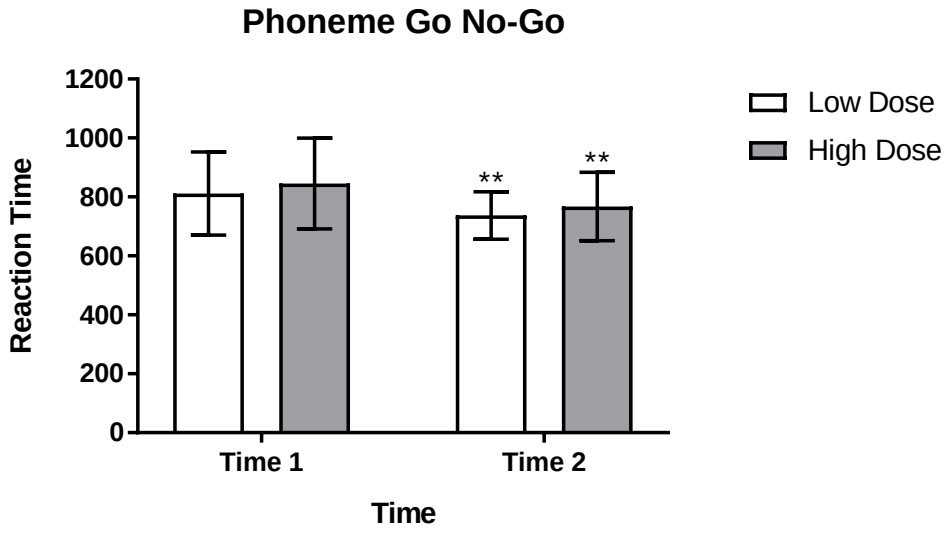


*Figure 59 Phoneme Go No-Go RT transfer for high and low-dose training groups at the start and end of training. *p<.05 **p<.005*

6.3.3 Direct Training Effects (Neural)

Results exploring transfer of training to response inhibition N2 and P3 components are summarised in Table 22 and Table 23. To explore transfer of training to N2 response inhibition ERP component during picture and phoneme Go No-Go tasks two separate 2 (Trial: Go V No-Go) x 2 (Dose: High v Low) x 2 (Time: Pre v Post) mixed design ANOVA's were run at fronto-central sites (Fz, C3, C4) (see Table 22 for summary of results). To explore transfer of training to P3 response inhibition ERP component during picture and phoneme Go No-Go tasks two separate 2 (Trial: Go, No-Go) x 2 (Dose: High, Low) x 2 (Hemisphere: Right, Left) x 2 (Time: Pre, Post) mixed design ANOVA's were run at posterior parietal regions (p7, P8) (see Table 23 for summary of results).

Picture Go No-Go Task

N2 ERP: Analysis revealed no main or interaction effects. No differences in N2 mean amplitude pre-post at fronto-central sites suggests no transfer of training to N2 response inhibition ERP component in the picture task.

P3 ERP: Analysis revealed no main effect of dose, a significant main effect of trial type ($F(1,23)=26.57$, $p=.000$, $\eta_p^2=.536$), a significant main effect of hemisphere ($F(1,23)=16.92$, $p=.000$, $\eta_p^2=.424$), a trend for a main effect of time ($F(1,23)= 5.71$, $p=.026$, $\eta_p^2=.199$), and almost a trend for a hemisphere*trial interaction effect ($F(1,23)=3.65$, $p=.069$, $\eta_p^2=.137$). The significant main effect of trial type suggests there was a larger mean amplitude for No-Go (M=2.87, SE=.273) relative to Go trials (M=2.38, SE=.26). The significant main effect of hemisphere suggests that mean amplitude for both Go and No-Go trials was larger over the right hemisphere (P8: M=3.16, SE=.336) than over the left hemisphere (P7: M=2.085, SE=.242).

The trend for a main effect of time suggests that both groups had a tendency toward larger P3 mean amplitude for Go and No-Go trials at post training (M=2.84, SE=.292) compared to pre-training (M=2.40, SE=.263). The trend for hemisphere*trial type interaction suggests that the No-Go>Go P3 mean amplitude effect was greater at P8 (Go: M=2.81, SE=.363; No-Go: M=3.52, SE=.33) than at P7 (Go: M=1.95, SE=.21; No-Go:

M=2.21, SE=.29). Post-hoc analysis confirms that this No-Go>Go P3 mean amplitude effect demonstrates a trend for significance over the right hemisphere (P8) ($F(1,23)=6.33$, $p=.019$, $\eta_p^2=.21$) but was non-significant over the left hemisphere (P7) ($F(1, 23)=.508$, $p=.483$, $\eta_p^2=.021$). The low-dose group experienced a medium-large effect for larger P3 mean amplitude at P8 to go trials from pre (M=2.63, SD=1.92) to post (M=4.04, SD=2.01), Cohen's d=.72; and a small-medium effect for larger P3 mean amplitude to no-go trials from pre (M=3.71, SD=1.41) to post (M=4.43, SD=2.49), Cohen's d=.36, The high-dose group experienced no effect for P3 mean amplitude at P8 to go trials from pre (M=2.15, SD=2.02) to post (M=2.41, SD=1.70), Cohen's d=.14; and a medium effect for larger P3 mean amplitude at P8 to No-Go trials from pre (M=2.18, SD=1.95) to post (M=3.11, SD=1.60), Cohen's d=.52. Figure 60 presents P3 mean amplitude at P8 for Go and No-Go trials in the picture task at both time points for high and low-dose groups.

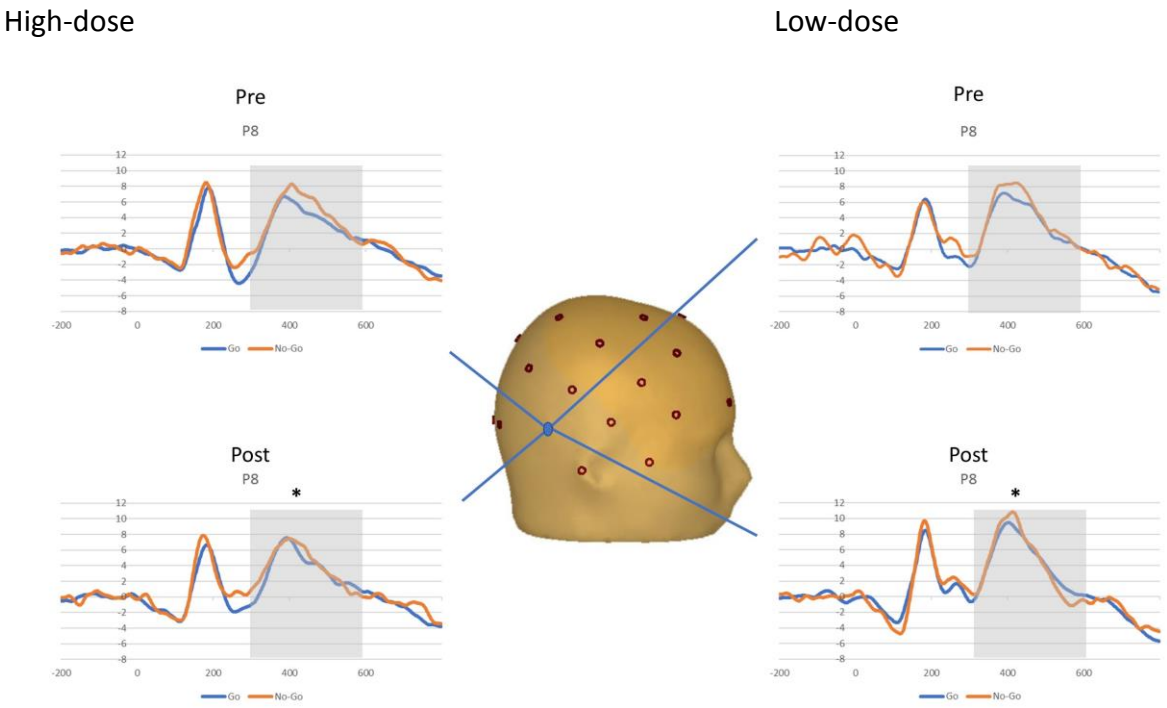


*Figure 60 Pre-Post differences for Go and No-Go P3 mean amplitude in both conditions at P8 for the picture task. *p<.05 **p<.005*

Phoneme Go No-Go Task

N2 ERP: Analysis revealed no main effect of trial or dose, and a non-significant main effect of time ($F(1,19)=3.36$, $p=.083$, $\eta_p^2= .15$). This suggests that both groups had a non-significant but as predicted larger N2 mean amplitude for both types of trials (go and no-go) post training (M=-.515, SE=.133) compared to pre-training (M=-.300, SE=.146). Post Hoc analysis revealed this marginal effect is a trend with Bonferroni correction ($p<.005$) at C3 ($F(1,22)=5.168$, $p=.033$, $\eta_p^2=.190$), but not for Fz ($F(1,23)=1.597$, $p=.219$, $\eta_p^2=.065$) and C4 ($F(1,21)=.289$, $p=.597$, $\eta_p^2=.014$). The low-dose group experienced a small effect for larger N2 mean amplitude at C3 to go trials from pre (M=-.32, SD=.84) to post (-.53, SD=.94), Cohen's d=.24; and a medium-large effect for larger N2 mean amplitude at C3 for No-Go trials from pre (M=-.12, SD=.95) to post (M=-.75, SD=.81), Cohen's d=.72. The high-dose group experienced no effect for N2 mean amplitude change for go trials at C3 from pre (M=-.10, SD=.87) to post (M=-.12, SD=.76), Cohen's d=.02; and a small effect for larger N2 mean amplitude at C3 for No-Go trials from pre (M=.002, SD=1.22) to post (M=-.22, SD=.95), Cohen's d=.21. Figure 61 presents N2 mean amplitude at C3 for Go and No-Go trials in the phoneme task at both time points for high and low-dose groups.

P3 ERP: Analysis revealed no main effect of dose or time, a trend for a main effect of trial type($F (1,21)=7.32$, $p=.013$, $\eta_p^2=.258$), a trend for a main effect of hemisphere ($F(1,21)=8.14$, $p=.008$, $\eta_p^2=.287$), and a trend for a hemisphere*trial*time interaction effect ($F(1,21)=5.97$, $p=.024$, $\eta_p^2=.221$). The trend for a main effect of trial type suggests larger P3 mean amplitude for Go (M=2.02, SE=.19) relative to No-Go trials (M=1.73, SE=.17). The trend for a main effect of hemisphere suggests that P3 mean amplitude for both Go and No-Go trials is larger over the right hemisphere (P8: M=2.19, SE=.22) than over the left hemisphere (P7: M=1.57, SE=.18). The trend for a hemisphere*trial*time interaction was further explored with post hoc separate 2 (time: pre,post) x 2 (trial: Go, No-Go) ANOVAs for right (P8) and left (P7) hemispheres. This analysis revealed a trend for a trial*time effect for right hemisphere (P8: ($F(1, 21)=6.56$, $p=.018$, $\eta_p^2=.24$) but not for left hemisphere (P7: ($F(1,21)=.70$, $p=.412$, $\eta_p^2=.031$). Both high and low-dose conditions

experienced greater pre-post difference for No-Go P3 mean amplitude (Pre: M=1.63, SE=.31; Post: M=2.35, SE=.26) and Go P3 mean amplitude (Pre: M=2.42, SE=.27; Post: M=2.35, SE=.25) at P8. The low-dose group experienced no effect for P3 mean amplitude at P8 to go trials from pre (M=3.03, SD=1.17) to post (M=3.06, SD=1.31), Cohen's d=.02; and a medium-large effect for larger P3 mean amplitude at P8 to No-Go from pre (M=2.04, SD=1.73) to post (M=3.23, SD=1.27), Cohen's d= .78. The high-dose group experienced no effect for P3 mean amplitude at P8 to go trials from pre (M=1.81, SD=1.41) to post (M=1.63, SD=1.05), Cohen's d=.14; and a small effect for larger P3 mean amplitude at P8 for No-Go trails from pre (M=1.22, SD=1.21) to post (M=1.45, SD=1.25), Cohen's d=-.19. Figure 62 presents P3 mean amplitude at P8 for Go and No-Go trials in the phoneme task at both time points for high and low-dose groups.

High-dose Low-dose

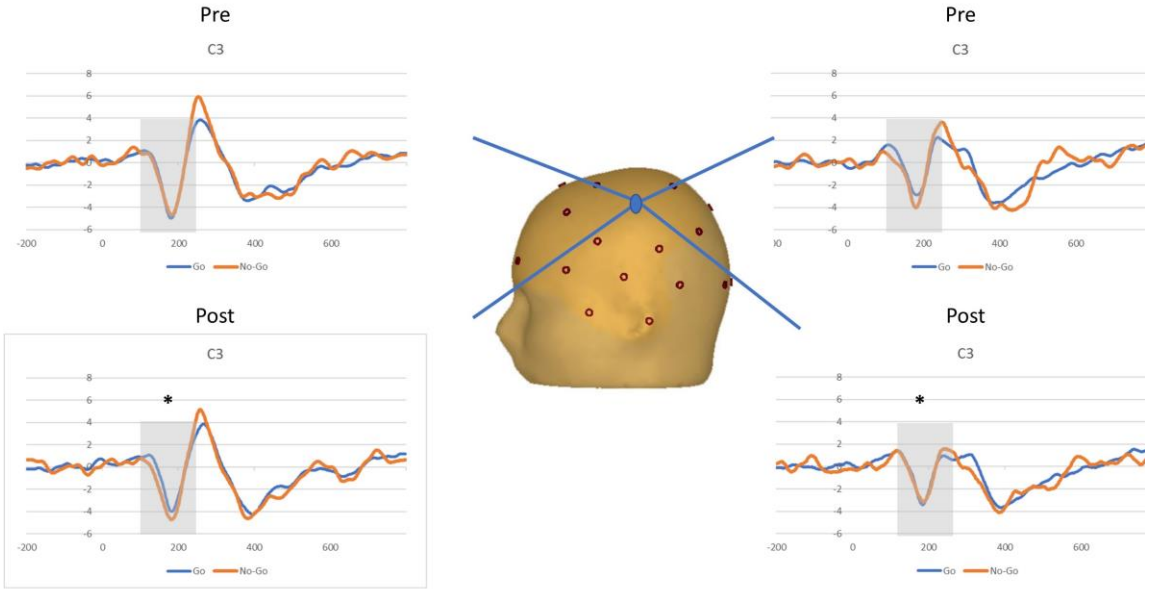


*Figure 61 Pre-Post differences for Go and No-Go N2 mean amplitude in both conditions at C3 for the phoneme task *p<.05 **p<.005*

High-dose Low-dose

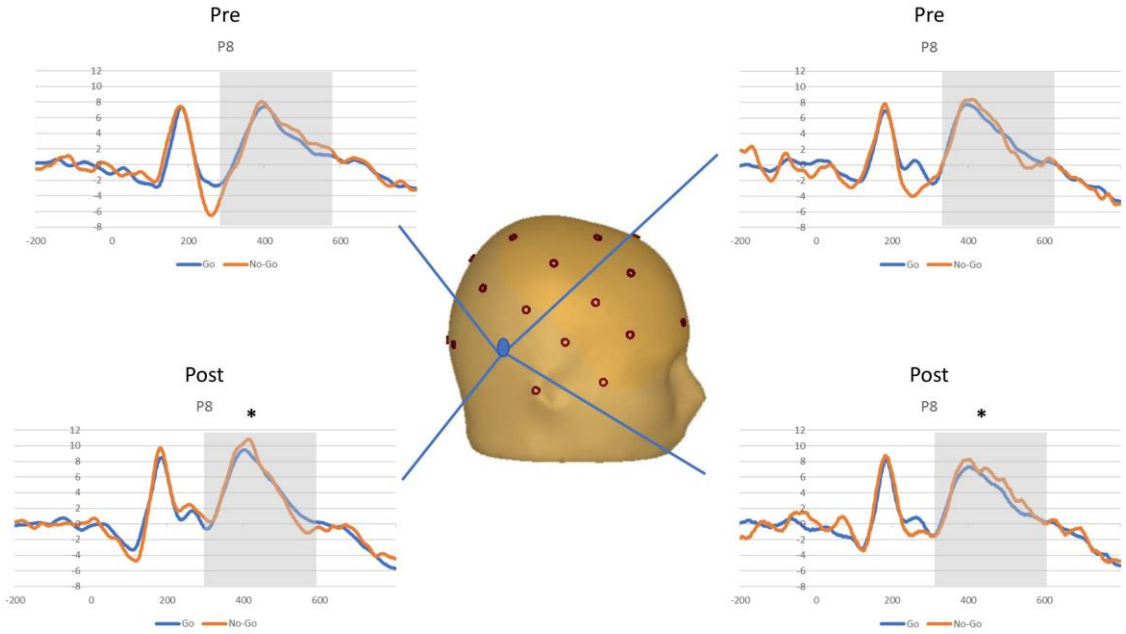


Figure 62 Pre-Post differences for Go and No-Go P3 mean amplitude in both conditions at P8 for the phoneme task. *p<.05 **p<.005

Table 22 Transfer of Training to N2 Response Inhibition ERP Component at Fronto-Central Sites (Fz, C3, C4)

	Picture Task					**Phoneme Task**			
	F	***df1,df2***	***P value***	η_p^2		***F***	***df1,df2***	***P value***	η_p^2
Trial	1.92	1, 22	.18	.08	Trial	2.62	1,19	.122	.121
Dose	.024	1,22	.866	.024	Dose	.939	1,19	.345	.047
Time	.18	1, 22	.676	.008	Time	3.36	1,19	.083	.150
Trial * Dose	.434	1,22	.517	.019	Trial * Dose	.12	1,19	.733	.006
Time * Training	.487	1,22	.493	.022	Time * Training	.479	1,19	.497	.025
Trial * Time	.66	1, 22	.425	.029	Trial * Time	.903	1, 19	.354	.045
Trial * Time * Dose	.695	1, 22	.413	.031	Trial * Time * Dose	.044	1, 19	.836	.002

Note: ** p<.005 (sig with Bonferroni correction), *p<.05 (trend)

Table 23 Transfer of Training to P3 Response Inhibition ERP Component at posterior parietal sites (P7, P8)

	Picture Task					**Phoneme Task**			
	F	***df1,df2***	***P value***	η_p^2		***F***	***df1,df2***	***P value***	η_p^2
Hemisphere	16.92	1,23	.000*	.424	Hemisphere	8.l43	1,21	.008*	.287
Trial	26.57	1,23	.000*	.536	Trial	7.319	1,21	.013*	.258
Dose	1.03	1,23	.321	.043	Dose	4.20	1,21	.053	.167
Time	5.71	1,23	.026*	.199	Time	1.952	1,21	.117	.085
Trial*Hemisphere	3.65	1,23	.069	.137	Trial*Hemisphere	1.45	1,21	.242	.065
Time * Dose	2.99	1,23	.097	.115	Time * Dose	1.16	1,21	.293	.052
Hemisphere * Time	1.19	1,23	.287	.049	Hemisphere * Time	.132	1,21	.720	.006
Trial * Time	1.98	1,23	.173	.079	Trial * Time	3.377	1,21	.08	.139
Trial * Time * Dose	2.40	1,23	.135	.095	Trial * Time * Dose	.491	1,21	.491	.023
Hemisphere* Trial * Time	.035	1,23	.853	.002	Hemisphere * Trial * Time	5.965	1,21	.024*	.221
Hemisphere * Trial *Time * Dose	.047	1,23	.831	.002	Hemisphere* Trial*Time* Dose	2.816	1,21	.154	.094

Note: ** p<.005 (sig with Bonferroni correction), *p<.05 (trend)

6.3.4 Summary of Results

Results of behavioural and ERP analyses suggests that both high-dose (adaptive) and low-dose (non-adaptive) response inhibition training interventions result in pre-post changes at behavioural (reduced response inhibition reaction time $p<.005$) and neural levels (a trend for increased amplitude of ERPs, $p<.05$). The high-dose condition demonstrated direct training gain as measured by reduced No-Go probability at the last training session compared to the first training session. The low-dose did not demonstrate direct training gain on the training game, however the low-dose game was non-adaptive therefore there is no way of assessing direct gain within the low-dose condition. Both high and low-dose conditions had significantly lower reaction times on both picture and phoneme Go No-Go tasks and the response inhibition reaction time score without any significant increases in errors. Neither group demonstrated pre-post reductions in commission errors at the individual task or composite level.

Both groups demonstrated pre-post changes to N2 mean amplitude (larger) for Go and No-Go trials at C3 in the phoneme task, and pre-post changes to P3 mean amplitude (larger) for Go and No-Go trials at P8 in both picture and phoneme tasks. These results indicate that low-dose non-adaptive and high-dose adaptive response inhibition training over a 6-week period may improve response inhibition time at a behavioural and neural level in children with developmental dyslexia.

However, there were no significant interaction effects observed between high and low dose training groups for response inhibition at the cognitive and neural levels. The lack of a time x dose interaction effect makes it difficult to conclude which dose is more effective, and, whether response inhibition training transfers at cognitive and neural levels or findings are due to non-specific placebo effects.

6.4 Discussion

Previous research suggests that response inhibition remains plastic from childhood into late adulthood, with evidence of transfer of response inhibition training to direct cognitive and neural measures (Benikos et al., 2013; Liu et al., 2015; Thorell et al., 2009; Zhao et al., 2016). Response inhibition training is a viable targeted intervention for dyslexia given that dyslexia is associated with abnormal P3 response inhibition ERP (Liotti et al., 2010; Van der Schoot et al., 2002) and previous findings suggest that response inhibition is implicated in reading impairments. No study to date has explored whether response inhibition is modifiable at neural and cognitive levels with targeted training in children with dyslexia.

The present study (Study 2) explored whether high (adaptive) and low (non-adaptive) doses of response inhibition training were capable of improving response inhibition abilities on untrained tasks and may also alter underlying neural processes in children with dyslexia. The results suggest that high and low-dose training interventions improve response inhibition and alter underlying neural processes in dyslexia. The high-dose (adaptive) training group demonstrated direct gain on the trained task as indexed by reduced No-Go probability at the end of training compared to the start of training. Although the low-dose training intervention did not demonstrate direct training gain, this does not reflect that the low-dose condition did not experience improved response inhibition abilities as the low-dose game was non-adaptive and therefore not capable of assessing direct gain on the trained game. Neither training condition experienced transfer to non-trained Go No-Go tasks at the level of commission errors, but both experienced a significant reduction in reaction time on untrained picture and phoneme based Go No-Go tasks and at the z-mean composite level. This highlights that reduced reaction time is not due to a speed-accuracy trade off in performance as both doses experienced reduced reaction time without any significant increases in errors. Changes in reaction time on the response inhibition measures is of interest as this ability was highly predictive of core reading impairments associated with dyslexia in Chapter 4. Both training groups also

experienced marked transfer of response inhibition training at the neural level ($p < .05$), with evidence of larger N2 mean amplitude post training in the phoneme task for Go and No-Go trials, and larger P3 mean amplitude post training in both picture and phoneme tasks for Go and No-Go trials. Overall results suggest that both high and low-dose response inhibition training can result in direct transfer to improved response inhibition efficiency at cognitive (significant at Bonferroni correction $p<.005$) and neural levels (marked change, $p<.05$) in children with dyslexia.

The finding that response inhibition training did not result in a pre-post reduction of commission errors (often the most sensitive index of response inhibition) but a reduction in response inhibition speed (or efficiency improvement) is consistent with previous studies exploring the behavioural impacts of response inhibition training across a range of different ages. Although one study found that response inhibition training can reduce errors of commission in children (Zhao et al., 2016), the majority of studies find that training results in a reduction of the speed of response inhibition but not overall accuracy (Benikos et al., 2013; Berkman et al., 2014; Hartmann et al., 2016; Manuel et al., 2013, 2010). A reduction in speed on Go No-Go tasks is often reflective of improved efficiency in response inhibition mechanisms, as response inhibition mechanisms must strengthen to maintain pre-training performance at the faster rate of Go responding (Benikos et al., 2013; Smith et al., 2006). Smith et al. (2006) found that faster Go-speed was facilitated by strengthening of response inhibition mechanisms at a neural level as indexed by increased P3 amplitude to No-Go trials. A reduction in speed of Go-processing and a marked increase in P3 amplitude (trend, $p<.05$) was found in both of our groups, suggesting that high adaptive and low non-adaptive doses of training can strengthen response inhibition abilities in children with dyslexia. The effect of reduced reaction time on response inhibition composite was large in the high-dose condition (Cohen's $d=.87$) and medium in the low-dose condition (Cohen's $d=.52$), which suggests that unlike working memory training, non-adaptive response inhibition training may be capable of improving performance on untrained tasks. The finding of transfer in both groups is consistent with a

previous study showing transfer to a reduction in response inhibition speed across low, medium and high-doses of training (Benikos et al., 2013).

Response inhibition ERP analysis at baseline indicated an absence of the No-Go>Go amplitude effect for the N2 component across both tasks, even though No-Go>Go amplitude effects for the N2 components are evident in control children in the same age range (Johnstone et al., 2007; Jonkman, 2006). This suggests that children with dyslexia may have abnormal N2 processing compared to control participants, and although this type of analysis was beyond the scope of this PhD thesis, analyses carried out by our colleagues for the same study (Study 2) suggests that children with dyslexia demonstrate reduced N2 and P3 amplitude relative to control participants during the same Go No-Go tasks (Lonergan, 2017). The No-Go > Go amplitude effect was found in dyslexia for P3 in the picture task at baseline which is consistent with previous studies of children in the same age range (Johnstone et al., 2007; Jonkman, 2006). However, in the phoneme task a trial difference was found for P3 at baseline but in the direction of greater amplitude for Go relative to No-Go trials. Although no study has explored specific trial amplitude differences in the phoneme Go No-Go tasks, some studies have explored peak latency differences between semantic Go No-Go and phoneme Go No-Go tasks and it appears as though peak mean latency in the phoneme task is delayed in comparisons to peak mean latency in the semantic task (Rodriguez-Fornells, Schmitt, Kutas, & Münte, 2002; Schmitt et al., 2000).

In the present task, Go-items were pictures that begin with a consonant while No-Go items were pictures that begin with a vowel, thus participants had to consider whether the picture began with one of 5 options for the No-Go trial and one of 21 options for the Go trial. Given the discrepancy between the number of options for No-Go compared to Go trials, increased P3 amplitude to Go trials may be due to stimulus novelty due to less frequent exposure to individual consonants (Friedman, Cycowicz, & Gaeta, 2001). Another reason for increased Go relative to No-Go P3 amplitude in the phoneme task is increased difficulty level compared to the semantic picture task which may dampen the No-Go

amplitude or increase Go amplitude. The P3 No-Go amplitude has been found to decrease as a function of task difficulty (Maguire et al., 2009). If difficulty level in the phoneme task caused a reduction in the P3 amplitude to No-Go trials, it may well explain the Go > No-Go amplitude effect. Another study showed that easier Go No-Go tasks result in greater No-Go relative to Go P3 amplitude while more difficult Go No-Go tasks result in greater Go relative to No-Go P3 amplitude (Comerchero & Polich, 1999). This may be a potential reason for finding the typical No-Go > Go effect in the picture task and the reverse Go>No-Go effect in the phoneme task at baseline.

Regardless of trial type or lack of trial type effects at baseline, response inhibition training resulted in transfer to marked ($p<.05$) increased N2 and P3 amplitude for all trial types in both high and low-dose conditions. Modifiability of neural markers of response inhibition with training is consistent with previous research (Benikos et al., 2013; Berkman et al., 2014; Hartmann et al., 2016; Liu et al., 2015; Manuel et al., 2013). Response inhibition training has been found to increase prefrontal and parietal activity (Manuel et al., 2013, 2010), and increase amplitude of response inhibition ERPs over central and occipital areas (Berkman et al., 2014; Hartmann et al., 2016). However, in pre-school typical children transfer to increased N2 amplitude was found for girls only. No study to date has explored transfer of isolated response inhibition training to ERPs in children aged 10-12 years. However, one study exploring the effectiveness of combined working memory and response inhibition training in children with ADHD found that training increased N2 amplitude (Johnstone et al., 2010). The present study (Study 2) showed transfer to increased N2 and P3 amplitude in high and low-dose conditions. These findings are consistent with other studies reporting transfer to response inhibition neural markers in adults with high, medium and low-doses of response inhibition training (Benikos et al., 2013) and in children with high and low-doses of combined working memory and response inhibition training (Johnstone et al., 2010). This dose independent effect of training suggests that both low and high-doses can result in plastic modifications of underlying response inhibition neural markers.

Transfer of response inhibition to non-trained cognitive and neural indices of response inhibition in both high and low-dose conditions may be due to placebo effects, a low-level of training being sufficient to improve response inhibition, a lack of engagement in the high-dose due to difficulty level, or a higher exposure to the trained construct in the low-dose condition promoting transfer.

It has been argued that to account for the confound of motivation in training, studies should include adaptive (high-dose) and non-adaptive (low-dose) training conditions (Shipstead et al., 2012a). From this viewpoint, direct transfer in adaptive (high-dose) and non-adaptive (low-dose) training conditions could be interpreted as resulting from placebo effects due to the motivational features of the game. However, some authors argue that to completely address whether a cognitive system is modifiable, studies should use active control training which does not tap the target construct (Green, Strobach, & Schubert, 2014). The adaptive (high-dose) and non-adaptive (low-dose) training in this study (2) involved response inhibition, therefore response inhibition as the mechanism of transfer cannot be ruled out. Although it would be difficult to completely partial out response inhibition from an active control intervention as it is a key process underpinning other EFs and a range of high-level cognitive abilities such as planning and reasoning (Diamond, 2013; Miyake & Friedman, 2012). It may also be difficult to completely match the gaming features of the active control task if the demands of each game were fundamentally different. An option for future research may be to adapt the current intervention so that the active control game requires a basic decision on whether each stimulus is for example patterned (i.e. contains stripes or dots) or non-patterned (i.e. bold colour). Although a downside to consider in an active control game such as this may be disengagement due to a lack of challenge in the active control game, which may result in an imbalance in days spent training across groups.

Adaptivity of the training intervention appears to be necessary to induce change in working memory (Holmes et al., 2009; Karbach et al., 2015). However, adaptivity of training may not be necessary to induce change in response inhibition as there is a trend

across previous literature for adaptive and non-adaptive interventions improving response inhibition (Benikos et al., 2013; Enge et al., 2014; Johnstone et al., 2010). Previous studies assessing the efficacy of response inhibition training differ regarding the type of control group employed to assess transfer. For instance, some studies do not include a control group (Hartmann et al., 2016; Manuel et al., 2013, 2010), some include active control training which does not tap the target cognitive process (Liu et al., 2015; Zhao et al., 2016), while others use non-adaptive or low-dose training (Benikos et al., 2013; Enge et al., 2014; Johnstone et al., 2010). The pattern that emerges is in support of direct transfer in low and high-dose conditions: Those employing an active control group not trained on the target process find response inhibition training is effective, whereas those exploring non-adaptive or low-dose training as a control find transfer across conditions. The present study (Study 2) did not include an active control group that trained on a non-inhibition task, therefore it is not clear whether transfer across conditions is driven by improved response inhibition or placebo effect. Although the study design cannot rule out placebo effects, if response inhibition is modifiable by mere suggestion alone then this poses problems for the reliability and validity of the construct as suggested by (Green et al., 2014), as well as problems for its implication in wide range of clinical conditions (Robbins et al., 2012). To confirm response inhibition as the mechanism of transfer in adaptive and non-adaptive conditions, future studies should explore the efficacy of response inhibition training in dyslexia using a combination of passive, active non-inhibition control training and different levels (low, medium, high) of response inhibition training.

Another possibility is that low non-adaptive doses of response inhibition are sufficient to drive neural and cognitive transfer in clinical conditions characterised by response inhibition impairments. Higher rates of transfer have been observed across clinical conditions, children and older adults (Jaeggi et al., 2008; Karbach & Kray, 2009; Karbach et al., 2015; Luo et al., 2013), leading authors to suggest that training transfer may be highest in those with room for compensation due to development, a clinical condition or age-related cognitive decline. Studies exploring mechanisms of transfer within training groups

find that those demonstrating worse performance prior to the intervention experience the most gain from the intervention (Jaeggi et al., 2008; Luo et al., 2013). It may be the case that children with dyslexia demonstrate improved outcomes on response inhibition processing efficiency even with low-doses of training due to compensation effects. It is also possible that transfer of training in both conditions is not due to compensation effects within the clinical group, as short durations of training are capable of producing transfer at cognitive and neural levels in healthy adults also (Hartmann et al., 2016; Manuel et al., 2013, 2010), suggesting that the response inhibition system is capable of rapid plastic modification (Spierer et al., 2013).

Another possibility is that the effect of high-dose training may be masked due to the high difficulty level reducing engagement in children characterised by low-levels of response inhibition. Jaeggi et al. (2011) explored perceived difficulty as a mechanism preventing transfer of working memory training in children and found transfer for children who found the game challenging and engaging, but no transfer for children who found the game too challenging, not engaging and frustrating. This suggests that the game may have been too difficult or the adaptive increments may have been too large to promote optimal engagement across a range of abilities, as such the game could have been outside some children's zone of proximal development (Jaeggi et al., 2011; Vygotsky, 1978). Benikos et al. (2013) found a similar pattern with response inhibition training whereby low-medium doses experienced larger transfer to response inhibition speed than higher doses of training, and high-dose training experienced a significant performance decline under speedier conditions. This suggests that low-moderate levels of training difficulty may be more beneficial than higher levels of difficulty (Benikos et al., 2013).

When the difficulty of a learning activity (such as cognitive training) is just slightly beyond an individual's competence it is within their zone of proximal development. Whereas when the difficulty is too far beyond the individual's competence, it is outside their zone of proximal development (Vygotsky, 1978). A level of challenge appropriately suited to an individual's competence (within their zone of proximal development) will be more

beneficial to learning as there is more engagement, while a level of challenge far beyond an individual's competence will result in less learning due to disengagement and frustration (Vygotsky, 1978). Adaptivity of training essentially serves to continually push the boundaries of an individual's zone of proximal development and many have suggested that it is a pre-requisite for transfer of training (Diamond, 2014; Diamond & Ling, 2016).

Although the high-dose condition of this study gradually adjusted difficulty level based on player performance, jumps in difficulty may have been too high and therefore may have promoted disengagement with the training intervention. Previous response inhibition studies which included an adaptive high-dose condition typically keep No-Go frequency stable and adjust difficulty based on reaction time (Benikos et al., 2013; Berkman et al., 2014; Zhao et al., 2016), with only one study manipulating difficulty based on reaction time and No-Go frequency (Enge et al., 2014). The high-dose adaptive training condition in the present study (Study 2) had increased speed demands relative to the low-dose condition and adjusted difficulty based on No-Go frequency and distracting lures. Therefore, the multi-dimensional increments in the difficulty of the game may have been too large for participants in the high-dose condition to completely benefit from.

Another and most likely explanation for transfer across doses is that the structural differences between high and low-doses may be explaining transfer effects. For instance, the low-dose training condition involved exposure to more frequent No-Go trials which provided more opportunities to exercise and train response inhibition, whereas the high-dose condition involved less frequent exposure to No-Go trials and, exposure became progressively rarer as the task adapted; thus, opportunities to exercise and train response inhibition were rarer. Figure 63 shows a graphical representation of the opportunities to learn across both conditions from the start to the end of training with a sample of 20 trials. Both conditions started training with approximately 45% No-Go trial frequency so out of 20 trials approximately 9 trials were No-Go trials and 11 were Go trials. The number of No-Go trials remained steady in the low-dose condition as the game was non-adaptive so at the end of training approximately 8 out of 20 trials were No-Go trials. However, the

number of No-Go trials declined rapidly for the high-dose condition such that at the end of training approximately 1 out of 20 trials was a No-Go trial. The imbalance in the opportunity to exert response inhibition across conditions may explain transfer effects observed across conditions.

Learning requires exposure to the trained cognitive construct; by design the high-dose has relatively less exposure to No-Go trials and therefore less opportunity for learning to occur. Thorell et al. (2009) explains that a lack of exposure to trials where response inhibition can be exercised may be a possible reason for limited transfer of response inhibition training in children. Similarly, findings of a combined working memory and inhibition training intervention resulted in transfer to increased N2 amplitude for both Go and No-Go trials in the low-dose condition and only Go trials in the high-dose condition (Johnstone et al., 2010). Benikos et al. (2013) also found greater transfer in low-medium doses than a high-dose of training where exposure to No-Go trials was similar (30% No-Go) but speed demands varied (high: 300ms; medium: 500ms; low: 1,000ms). Although the high-dose group in this study experienced a larger transfer effect for reduced speed (Cohen's d=.87) compared to the low-dose training group (Cohen's d=.52), this came at a greater cost to the accuracy of response inhibition in the high-dose (Cohen's d=.32) than in the low-dose (Cohen's d=.13), suggesting that the low-dose condition maintained accuracy at increased speed better than the high-dose condition. Exposure effects are also reflected in transfer to No-Go N2 amplitude in the phoneme task, the low-dose training experienced a larger transfer effect to No-Go N2 amplitude in the phoneme task (Cohen's d=.72) compared to the high-dose training condition (Cohen's d=.21). Both groups experienced medium transfer effects to increased No-Go P3 amplitude in the picture task (Low: Cohen's d=.36; High: Cohen's d=.52), however the low-dose group experienced a larger transfer effect to increased P3 amplitude for No-Go trials in the phoneme task (Cohen's d=.78) compared to the high-dose group (Cohen's d=.19). This suggests that increased exposure to No-Go trials may be a possible reason for increased transfer in the low-dose condition, although further research is needed to determine whether the

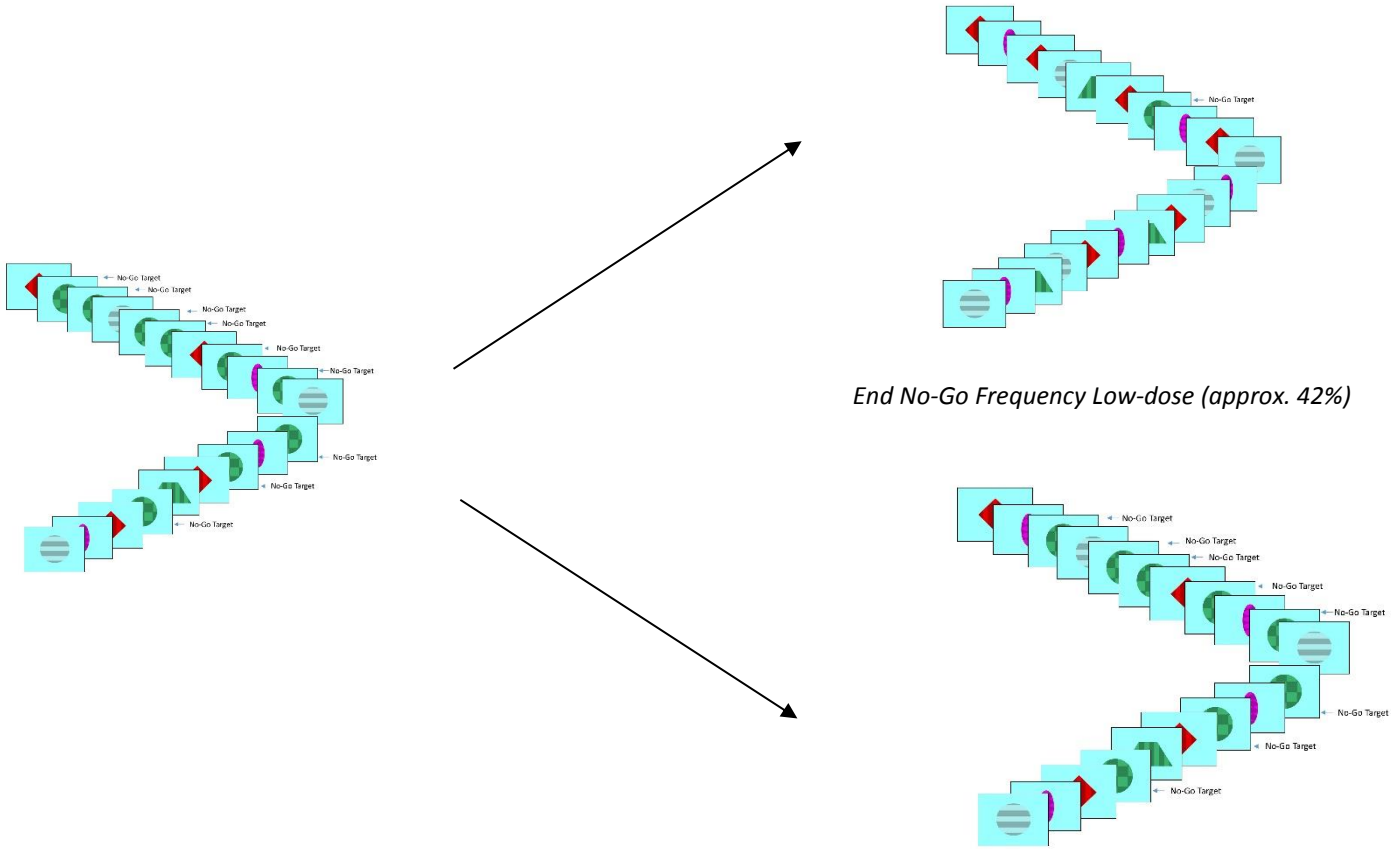
difficulty of the high-dose training reduces engagement and therefore dampens its possible effects relative to the low-dose, or, whether increased exposure to response inhibition trials in the low-dose condition result in greater transfer than the high-dose condition.

Another reason for transfer in the low-dose condition may that there is more similarity between low-dose training and the Go No-Go tests assessing transfer than the high-dose training. For instance, the low-dose group trained at a No-Go frequency of approximately 40% and were assessed on tasks with a No-Go frequency of 25%, while the high-dose group trained at a No-Go frequency of approximately 5 % and were assessed on tasks with a No-Go frequency of 25%. As such, the assessment of training transfer is more similar in design to the low-dose training than the high-dose training. Although no study to date has explored whether varying levels of No-Go frequency during training transfer differentially to varying levels of No-Go frequency at post-test; one possible way of exploring this would be to alter the rate of No-Go frequency in transfer tests from low to high and see whether transfer effects are greater when training No-Go frequency matches post-test No-Go frequency.

The frequency of No-Go trials (approx. 40%) in the low-dose training condition employed in the present study is also more closely matched to the frequency of No-Go trials in previous response inhibition training interventions, indicating that the low-dose condition may be effectively training response inhibition more so than the high-dose training. Across previous training studies No-Go frequency ranges from 50% of trials (Hartmann et al., 2016; Manuel et al., 2010), to 30% (Benikos et al., 2013; Manuel et al., 2013; Zhao et al., 2016) and 25% of trials (Berkman et al., 2014; Enge et al., 2014). This knowledge may contribute to the understanding of optimum conditions for training response inhibition. Although further knowledge is needed to determine the ideal No-Go % frequency for producing the largest response inhibition gains. One way to explore this would be to explore a range of different training conditions with varying increments (e.g. 10%) of No-Go frequency and see whether higher or lower exposure produces more transfer.

Start No-Go Frequency (approx. 45%): Low and High-dose

End No-Go Frequency High-dose (approx. 5%)



End No-Go Frequency Low-dose (approx. 42%)

Figure 63 Rate of exposure to No-Go trials in a set of 20 trials for high and low-dose at the start compared to the end of training

In addition to being exposed to more No-Go trials, another possible explanation for the disparity in the size of transfer effect across conditions is that participants in the low-dose training condition produced less errors because the task was less difficult. The potentially reduced error rate and more positive feedback may have facilitated a greater sense of competence and more engagement which promoted more learning. Techniques whereby the possibility of making errors are minimized or eliminated from other types of interventions appear to promote more memory gains in those with memory problems (Baddeley, 1992; Squires, Hunkin, & Parkin, 1997) and schizophrenia (O'Carroll, Russell, Lawrie, & Johnstone, 1999), and reduce behavioural problems in children with developmental disabilities (Ducharme & Popynick, 1993). Error free/reduced learning aims to increase learning by preventing error making which may result in a conditioned error response (Fillingham, Sage, & Lambon Ralph, 2005). The low-dose condition in the present study may have been exposed to error reduced learning and this may explain why larger effect sizes are observed in the low-dose compared to the high-dose condition.

It is important to note that both high-dose and low-dose conditions experienced significant training induced response inhibition gains. At the start of training, both conditions were exposed to the same higher No-Go frequency rate and error reduced learning. Although No-Go frequency and error reduced learning remained stable in the low-dose condition they both gradually decreased in the high-dose condition. This may explain why significance was found for both groups but larger effect sizes were found (especially for response inhibition-related ERPs) in the low-dose condition. If greater exposure to No-Go learning opportunities and more rewarding learning are optimal conditions for improving response inhibition, then the initial effects could have become diluted in the high-dose condition as they progressed through training.

Although possible mechanisms driving training transfer across conditions are discussed due to larger effect sizes in the low-dose condition, this should be interpreted with caution given that there were no significant time x dose interaction effects observed. Without a significant interaction effect, we cannot conclusively say that the low-dose group experiences more transfer than the high-dose group. In addition, given the absence

of a suitably matched placebo training group (non-inhibition training), the current study cannot rule out placebo mechanisms as a possible explanation for pre-post improvements in response inhibition. The above discussion considers possible reasons for a larger effect size in the low-dose training condition and points to future research avenues which may elucidate whether response inhibition is modifiable. To draw conclusions on the effectiveness of response inhibition training in the absence of a significant dose x time interaction is limited. One possible reason for not finding a significant interaction in the present study is poor power to detect an interaction due to a small sample size. A post-hoc power analysis conducted in G-Power indicates that the present study is underpowered to detect an interaction at the trend ($p<.05$, power $1-\beta=.59$) or corrected level of significance ($p<.004$, power $1-\beta=.24$) across our range of near and far outcome measures (Faul, Erdfelder, Lang, & Buchner, 2007). An additional explanation for no interaction effect is that placebo effects may be explaining pre-post improvements in response inhibition across both conditions. Future research with larger sample sizes and suitable active and passive placebo groups is needed, before we can conclude that response inhibition transfers to improved response inhibition at cognitive and neural levels in children with dyslexia or conclude on the mechanisms driving transfer.

The current study is not without limitations. Although the research design can address whether high adaptive and low non-adaptive doses of response inhibition can improve response inhibition abilities and alter underlying response inhibition-related ERPs in children with dyslexia alone, it cannot address whether response inhibition training is more effective than passive or active control training. A research design incorporating passive and active training control groups as well as different levels of response inhibition training would be ideal for teasing out the optimal training conditions associated with largest transfer. Another limitation of this study is a possible inflation of type 1 error rate due to multiple statistical testing and a small sample of participants. Although a larger sample size is ideal, this is difficult to achieve with clinical populations such as dyslexia and a restricted age range to account for the confound of developmental improvements in EF. Therefore, to account for this limitation, the present study employed a Bonferroni

correction (p<.005) based on *a priori* research questions while also considering trends within the data (p<.05). Reducing the required alpha level while also considering trends within the data allows for a relative balance between the likelihood of both type 1 and type 2 errors.

Overall the results of this study (Study 2) demonstrate that response inhibition is modifiable in children with dyslexia at both cognitive and neural levels. Although the size of transfer effects differed between high and low-dose training conditions, no significant dose by time interactions were found suggesting that overall high and low-dose response inhibition training can significantly reduce the speed of response inhibition and markedly increase amplitude of N2 and P3 neural markers in children with dyslexia. Training induced changes in response inhibition abilities in children with dyslexia may extend to other EFs and reduced severity of core reading and non-core socio-emotional problems. As the common EF, training induced improvements in response inhibition may be mirrored by improvements or reductions in other EFs due to shared variance (updating) and antagonistic trade-offs (switching) (Friedman & Miyake, 2016; Goschke, 2000; Miyake & Friedman, 2012; Snyder et al., 2015). It is possible that these training induced improvements in response inhibition will also be mirrored at the level of symptom expression. Previous Chapters (4 and 5) isolated response inhibition as an important EF cognitive process underpinning reading ability, therefore improvements in response inhibition may transfer to improvements in reading ability in children with dyslexia. Diamond's (2013) EF model and a wealth of previous research indicates that response inhibition is a core cognitive process underpinning the capacity for effective self-regulation with response inhibition failures resulting in increased socio-emotional problems (Bridgett, et al., 2013; Carlson & Wang, 2007; Eisenberg et al., 2009; Friedman et al., 2008; Rueda et al., 2005; Snyder et al., 2015). As such, training induced improvements in response inhibition abilities may transfer to increased self-regulatory capacity and reduced socio-emotional problems in children with dyslexia.

Although some studies have found far transfer of EF training to non-trained cognitive abilities and behavioural outcomes (Jaeggi et al., 2008; Loosli et al., 2012; Spierer et al.,

2013), there is debate regarding the degree of transfer found with some studies suggesting that an improvement only occurs on the trained cognitive process or tasks measuring the same process due to practice effects (Shipstead et al., 2012a), and does not transfer to improved behavioural outcomes (Harrison et al., 2013; Redick et al., 2013). It is unclear whether response inhibition training can transfer to other EFs, reading ability, socio-emotional and self-regulatory outcomes in children with dyslexia. Following on from findings that response inhibition plays a role in other EFs, reading, regulation and socio-emotional problems and appears to be plastic in children with dyslexia; research should explore whether training induced improvements in response inhibition can transfer to other EFs, reading, self-regulation, and socio-emotional outcomes in children with dyslexia. The next chapter of this PhD (Study 2) will explore whether response inhibition training can transfer to other EFs, reading ability, self-regulation and socio-emotional outcomes in children with dyslexia. This research will establish whether response inhibition training is an effective intervention for improving symptom expression in children with dyslexia.

Chapter 7: Far Transfer of Response Inhibition Training in Dyslexia

7.0 Introduction

Findings from the previous Chapter (Chapter 6) suggest that response inhibition training can directly improve response inhibition abilities and alter the underlying amplitude of response inhibition-related ERPs in children with dyslexia. These training induced changes observed in response inhibition may be of clinical importance as they could transfer to a reduction in the severity of core reading and non-core socio-emotional problems experienced by children with dyslexia. A strong predictive relationship between the response inhibition reaction time composite and reading ability was demonstrated in Chapters 4 (Study 1) and confirmed in 5 (Study 2), such that longer reaction times were associated with poorer reading ability while shorter reaction times were associated with better reading ability. Therefore, the training induced reductions in reaction time on response inhibition tasks and composite score experienced by high and low-dose training conditions in Chapter 6, may transfer to significantly improved reading ability. Although response inhibition was not shown to be predictive of socio-emotional problems in Chapter 4 (Study 1) and 5 (Study 2), children with dyslexia did experience significantly more socio-emotional problems than children without dyslexia. Diamond's (2013) EF model posits that response inhibition is crucial for self-regulation and socio-emotional well-being. In support of this view, a wealth of previous research suggests that response inhibition is predictive of socio-emotional problems (Bridgett et al., 2013; Carlson & Wang, 2007; Eisenberg et al., 2009; Friedman et al., 2008; Rueda et al., 2005; Snyder et al., 2015); which is also shown for children with dyslexia (Wang & Yang, 2014). This body of findings suggests that training induced improvements in response inhibition may transfer to significantly reduced socio-emotional problems in children with dyslexia.

In addition to the potential benefits of response inhibition training for reducing the severity of core (reading) and non-core (socio-emotional) symptoms associated with dyslexia, response inhibition training may also transfer to other EF abilities in children with dyslexia. Training induced improvements in response inhibition may also be mirrored by

improvements in other EF abilities such as updating and switching due to response inhibition (as the Common EF) accounting for a proportion of variance in these abilities (*see Figure 6)* (Friedman & Miyake, 2016; Miyake et al., 2000; Miyake & Friedman, 2012). Transfer of response inhibition to improved updating and switching abilities is also consistent with Diamond's (2013) EF framework (*see Figure* 8). Within Diamond's (2013) framework response inhibition and working memory support each other and in combination they contribute to switching skills. As such, training induced improvements in response inhibition may enhance both working memory updating and switching abilities in children with dyslexia. Although this suggests that response inhibition training may facilitate improvements in updating and switching abilities, other research finding antagonistic trade-offs between response inhibition and switching abilities would suggest that response inhibition training may result in reduced switching efficiency (Blackwell et al., 2014; Goschke, 2000; Gruber & Goschke, 2004). Trade-offs between response inhibition and switching are evident in typical (Blackwell et al., 2014; Goschke, 2000; Gruber & Goschke, 2004) and atypical samples (Altamirano et al., 2010; Friedman et al., 2011). Therefore, a possible outcome of training induced improvements in response inhibition is reduced switching ability.

No study to date has explored the efficacy of response inhibition training for reducing the severity of core reading and non-core socio-emotional symptoms associated with dyslexia, or, whether response inhibition training transfers to improved updating and switching in dyslexia. It is important to explore the efficacy of response inhibition training as an intervention for reducing symptom expression in children with dyslexia. The previous Chapter (Chapter 6) demonstrated that response inhibition is modifiable in children with dyslexia at the cognitive and neural levels, suggesting that these improvements may transfer at the symptom level and may induce clinical change.

Although EF training interventions appear to directly improve the trained construct, efficacy of these interventions has been debated as studies do not consistently report transfer of training to untrained cognitive abilities and behavioural outcomes. Some studies report transfer of EF training paradigms to improved reading ability (Karbach et al.,

2015; Loosli et al., 2012), fluid intelligence (Jaeggi, Buschkuehl, Shah, & Jonides, 2014; Karbach & Kray, 2009) and to reduced symptoms in clinical conditions such as ADHD (Johnstone et al., 2012, 2010), suggesting that these cognitive training interventions may be useful for improving a broad range of behaviours and reducing symptoms of clinical conditions (Keshavan et al., 2014). However, these findings have been met with considerable backlash due to a difficulty in replicating transfer effects (Enge et al., 2014; Harrison et al., 2013; Redick et al., 2013; Shipstead et al., 2012a; Shipstead et al., 2012b). Replicability issues have led some authors to argue that direct transfer is due to practice effects (Shipstead et al. 2012b), and EF training does not result in changes to far removed behavioural outcomes (Harrison et al., 2013; Redick et al., 2013). However, even when transfer is found, critics claim that effects may be due to expectation or test re-test effects in the control group (Green et al., 2014). Issues across the training and transfer literature such as not incorporating non-adaptive control groups to account for motivational effects, and, not exploring a range of transfer outcomes that are theoretically informed by linkages between trained constructs and behavioural outcome, may contribute to inconsistent findings (Shipstead et al., 2012a).

Studies exploring working memory training have found transfer of training in adults (Jaeggi et al., 2014) and children (Holmes et al., 2009; Karbach et al., 2015; Loosli et al., 2012). In children, there is evidence that working memory training transfers to improvements in non-trained cognitive abilities such as short-term memory (Astle et al., 2015; Holmes et al., 2009), and interference control (Luo et al., 2013). Working memory training has also been found to transfer to improvements in reading ability (Dahlin, 2011; Karbach et al., 2015; Loosli et al., 2012), maths ability (Holmes et al., 2009), spelling ability (Alloway et al., 2013), verbal IQ (Alloway et al., 2013) and fluid intelligence (Jaeggi et al., 2011). However, there is conflicting evidence for where transfer is observed, as some studies find no evidence of transfer to maths ability (Karbach et al., 2015) or fluid intelligence in children (Dahlin, 2011; Luo et al., 2013).

Although some studies find immediate transfer (Karbach et al., 2015), others find that differences emerge for the adaptive group over time (Holmes et al., 2009; Jaeggi et al.,

2011). Holmes et al. (2009) found that although the adaptive group did not demonstrate transfer to maths ability at post-test, significant transfer to maths ability was observed at 6-month follow-up. Similarly, Jaeggi et al (2011) found that differences emerged more steadily over time with no difference in n-back training performance (as indexed by level achieved) after 3-weeks training and significant differences at 4-6 weeks training. These training effects transferred to improvements in fluid intelligence which were maintained and even enhanced (effect size change analysis) at 3-month follow-up, but only for those with the highest training gain (Jaeggi et al., 2011). These findings suggest that training differences may emerge more steadily over time, with more time required for children to consolidate and implement the trained cognitive mechanism. It is important to note, however, that Jaeggi et al. (2011) had to employ a median split with training gain to detect transfer to fluid intelligence (such that high gain participants reached a mean training level of 3.3 at post-test and low gain participants reached a mean level of 2.55 at post-test). It may also be possible that differences over time are due to general cognitive development or other activities which participants may have engaged in during the interim.

Working memory training can generalise to reduced core reading problems in adults (Shiran & Breznitz, 2011) and children with dyslexia (Luo et al., 2013). Shiran and Breznitz (2011) found that capacity based working memory training (composed of a series of visual, auditory, verbal and spatial forward and backward recall tasks) transferred to significantly improved working memory, word reading and phonemic processing (parsing, segmenting and deleting speech sounds) in Hebrew adults with dyslexia. Although, this study did not include an active control computerised training intervention to account for placebo effects, it did show that working memory training outperformed a self-paced word reading intervention (Shiran & Breznitz, 2011). Lou et al. (2013) found that a combination of capacity based working memory (visual-spatial and verbal) and inhibition (flanker style task) training transferred to improved working memory, inhibition and word reading in Chinese children with dyslexia. These studies suggest that working memory training may transfer to improved reading ability in children with dyslexia; however, one study exploring capacity based working memory training with a series of verbal and

visuospatial tasks in children with special needs and attention problems demonstrated that training transfers to working memory and reading comprehension, but not to word reading, orthographic processing or inhibition (Dahlin, 2011). Although some studies report that working memory training can reduce reading problems in dyslexia, these types of interventions adopt a "kitchen sink" approach to training whereby a broad array of tasks with differing stimuli and working memory demands are trained (Morrison & Chein, 2011, p. 49). On top of employing multiple domains of working memory training tasks, Lou et al. (2013) also train inhibition. Training multiple tasks and different cognitive abilities may produce more transfer as a broad array of diverse tasks are employed, however, a major limitation of this approach is that it is difficult to isolate which elements of the training intervention drive transfer to varying cognitive and behavioural outcomes (Morrison & Chein, 2011).

Less studies have been conducted on the transfer of switching training, transfer has been found for children, adults, and the elderly (Karbach & Kray, 2009). Karbach and Kray (2009) found that switching training transferred to improved interference control, working memory and fluid intelligence across the lifespan when compared to non-switch training. This type of training has also been found to transfer to interference control and working memory but not to fluid intelligence in children with ADHD (Kray et al., 2012).

Despite a range of studies exploring the direct neural and cognitive effects of response inhibition training (Hartmann et al., 2016; Manuel et al., 2013, 2010), relatively few have explored transfer of response inhibition training to non-trained cognitive and behavioural outcomes. Those exploring transfer to behavioural outcomes have typically focussed on addictive behaviours and found transfer of training to over eating, alcohol consumption and gambling (Houben, 2011; Houben, Havermans, Nederkoorn, & Jansen, 2012; Verbruggen, Adams, & Chambers, 2012). In adults, training did not transfer to untrained response inhibition or to fluid intelligence leading some authors to suggest that response inhibition training does not transfer beyond the trained task (Enge et al., 2014). However, there is evidence of training transfer to improved working memory and fluid intelligence in pre-school children (Liu et al., 2015), suggesting that response inhibition training may

be as successful as working memory training. However, another study in pre-school children found no transfer of response inhibition training to working memory or attention (Thorell et al., 2009). One study explored transfer of response inhibition training in older children and adults and found transfer in children to improved interference control, working memory and switching and transfer in adults to improved working memory (Zhao et al., 2016). Transfer was not observed in children or adults to fluid intelligence (Zhao et al., 2016). However, this study did not find immediate transfer effects post training in children; instead working memory and switching transfer were found at 3-month follow-up (Zhao et al., 2016), suggesting that time is needed for transfer effects to emerge. Some authors suggest that the limited success of response inhibition training may be due to a difficulty in understanding how to adapt the difficulty of this type of training (Kirk et al., 2015) or due to less frequent exposure to the trained cognitive construct with less frequent No-Go trials (Thorell et al., 2009).

Some studies have employed mixed approaches to training targeting two or more EFs with a training intervention. One large-scale online study exploring mixed training observed no transfer in adults (Owen et al., 2010). In contrast, other studies suggest that mixed training can actually lead to reductions in symptom expression in children with neurodevelopmental conditions (Horowitz-Kraus, 2015; Johnstone et al., 2012, 2010). Both high and low-doses of combined working memory and inhibitio training transferred to reduced symptoms in children with ADHD (Johnstone et al., 2012, 2010), which were maintained at 6-week follow up (Johnstone et al., 2012). Horowitz-Kraus (2015) explored transfer of combined training (working memory, naming, speed, inhibition, flexibility) in children with ADHD and comorbid dyslexia-ADHD and found differential effects in each subgroup. Training transferred to improved reading ability, speed and spatial abilities in those with comorbid dyslexia-ADHD and improved working memory and speed but not reading ability in those with dyslexia alone (Horowitz-Kraus, 2015). Although these findings are promising for promoting clinical change in neuro-developmental conditions underpinned by EF impairments, it is incredibly difficult to disentangle which aspects of training promote transfer when multiple processes are targeted.

Conditions Underpinning Successful Far Transfer of Training

Executive function training has been proposed as a potential targeted treatment capable of ameliorating symptoms associated with complex neurodevelopmental disorders and affecting clinical change by restoring compromised cognitive processes (Keshavan et al., 2014). However, there are conflicting findings of transfer, which cast doubt as to whether EF training can improve functional outcome. Across the literature, studies differ regarding type of EF training (working memory, switching, response inhibition, mixed), type of comparison control group (non-adaptive same EF training, active control non-EF training, passive control, or no control), range of transfer measures, and samples employed (adults, children, clinical conditions) (Kirk et al., 2015; Melby-Lervaag & Hulme, 2013; Schwaighofer et al., 2015) making it difficult to infer what the necessary conditions underpinning successful transfer of training are.

Meta-analytic and review studies of EF training suggest that several factors may influence transfer. For instance, *room for improvement* may be necessary to observe transfer as greater transfer is typically reported in children (Karbach & Unger, 2014; Peng & Miller, 2016; Wass et al., 2012) or those with neurodevelopmental conditions (Karbach & Unger, 2014; Peng & Miller, 2016). This suggests that windows for improvement due to developmental plasticity of the EF system or an impairment may promote more transfer. Söderqvist et al. (2012) suggests that an *impairment in the trained cognitive process* may be a requirement to observe far transfer of training to untrained cognitive and behavioural outcomes. This is promising for those with clinical conditions, however, rarely do studies explore whether the sample is deficient in the trained cognitive function prior to intervention or develop specialised training interventions to ameliorate cognitive impairments associated with specific clinical conditions.

Other studies suggest that those with *higher baseline abilities* benefit more from adaptive cognitive training due to a higher ability to engage with training (Foster et al., 2017). This may be related to increments in the adaptive game being too large and perceived difficulty preventing far transfer beyond the trained cognitive process in those with low abilities (Jaeggi et al., 2011).

One possibility is that those with low abilities may benefit more from non-adaptive games due to the challenge being more suited to pre-existing abilities and thus facilitating more transfer. This pattern was reflected in the previous chapter (Chapter 6), where low-dose response inhibition resulted in larger effect sizes than high-dose training doses. Low-dose non-adaptive games may be more suited to those with pre-existing impairments in the target cognitive domain as they may be within their zone of proximal development and thus facilitate more learning (Vygotsky, 1978). Some studies also report greater transfer of training when the intervention is adaptive (Peng & Miller, 2016), spaced (Wang et al., 2014), and incorporates motivational game features (Kirk et al., 2015), suggesting that relative challenge, time for consolidation and motivation to play may be necessary for transfer of training. Other non-EF factors such as dose of training, duration of training session, location, and supervision may also moderate effects of training (Melby-Lervag & Hulme, 2013; Schwaighofer et al., 2015).

A major criticism of EF training transfer studies is that transfer to behavioural outcomes does not appear to logically flow from theory underpinning cognitive processes (Shipstead et al., 2012a). This problem has hindered progress in understanding the efficacy of EF interventions for children with intellectual disabilities. For example, a recent meta-analysis concludes that approaches to cognitive training are not rooted in theory which makes it difficult to determine the cognitive processes driving transfer effects (Kirk et al., 2015). Studies exploring transfer should be logically and theoretically informed by the degree of overlap between the trained factor and the target behavioural outcome to be improved (Karbach & Schubert, 2013). In this manner, transfer may emerge as a cascade effect whereby there is a stronger effect for more closely related processes which becomes gradually diluted as the degree of theoretical overlap reduces from near (trained cognitive process) to far transfer (related cognitive and further behavioural outcomes) (Karbach & Kray, 2009). Miyake and Friedman's (2012) 3-factor model of executive function is a good theoretical perspective for exploring transfer to other EF domains. Within this framework, a high degree of transfer to improved updating abilities would be expected due to response inhibition facilitating aspects of updating (Friedman & Miyake, 2016; Miyake &

Friedman, 2012). Although response inhibition and switching abilities appear related (Miyake et al., 2000; Miyake & Friedman, 2012), transfer to reduced switching abilities may emerge due possible antagonistic interactions (Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015).

Training induced improvements in response inhibition may also transfer to improved reading ability, as response inhibition is shown to predict the severity of reading impairment expressed in dyslexia (Chapter 4 and 5) and in other previous studies (Booth et al., 2014; Wang and Yang 2014). Although this effect may be more diluted at the far level of transfer (reading) than the near level (response inhibition) as other non-EF cognitive processes are undoubtedly implicated in reading ability. Training induced improvements in response inhibition may also transfer to reduced socio-emotional problems and increased capacity to self-regulate, as previous research suggests that response inhibition is predictive of the severity of socio-emotional problems in dyslexia (Wang & Yang, 2014) and is crucial for effective self-regulation and socio-emotional wellbeing (Bridgett et al., 2013; Carlson & Wang, 2007; Diamond, 2013; Eisenberg et al., 2009; Friedman et al., 2008; Rueda et al., 2005; Snyder et al., 2015). Again, these effects may be more diluted as response inhibition or other aspects of EF were not predictive of severity of socio-emotional problems expressed in this PhD (Chapter 4 and 5).

Other subsidiary cognitive processes such as speed of processing may also be affected by training due to the speed demands of the training intervention. Transfer effects of response inhibition training to outcomes in children with dyslexia, although theoretically informed, are speculative thus far as no study to date has explored the efficacy of response inhibition training for changing EFs, reading, socio-emotional and self-regulatory processes in children with dyslexia. It is important to explore transfer effects, as response inhibition appears to be modifiable at the cognitive and neural levels in children with dyslexia (Chapter 6), suggesting that these improvements may transfer to improvement at the symptom level which may induce clinical change.

It is not clear whether transfer will emerge differentially between high and low-dose conditions of response inhibition training. The previous chapter (Chapter 6) found that

both high and low-dose training interventions resulted in near transfer to response inhibition improvement at the cognitive and underlying neural levels. However, the pattern of effect sizes suggests that the low-dose condition facilitates greater response inhibition gains than the high-dose condition. As discussed in Chapter 6, more exposure to exercise the trained cognitive process (Thorell et al. 2009) and more positive rewarding feedback due to the low-dose opportunity to learn falling within dyslexic children's zone of proximal development (Jaeggi et al., 2011), may explain larger effect sizes in the low-dose condition. Both conditions were exposed to similar No-Go levels at the beginning and for some period of the training session, it may be the case that the initial effects became more diluted in the high-dose as No-Go frequency gradually reduced. In this regard, the current study (Study 2) may observe transfer effects in both conditions. However, larger transfer may manifest in the low-dose group due to lower levels of difficulty promoting more transfer (Benikos et al., 2013) or in the high-dose group due to adaptivity being necessary to promote transfer in cognitive training (Diamond, 2014; Diamond & Ling, 2016).In this regard, the current study predicts that both conditions will experience significant transfer but it is difficult to state whether the same pattern of larger direct transfer in the low-dose condition will manifest at the level of far transfer.

that the effect sizes for far transfer will be larger in the low-dose compared to the high-dose as larger effect sizes were observed in the low-dose at the near level of transfer.

Another major criticism of EF training transfer studies is that not enough transfer measures are employed to make inferences at the process level and a wide range of behavioural levels (Shipstead et al., 2012a). Sometimes transfer effects will be explored at the single task level which is difficult to generalise due to a range of EF and non-EF processes being implicated at the individual task level (Miyake et al., 2000; Miyake & Friedman, 2012; Snyder et al., 2015). To account for this, the present study (Study 2) will employ a number of sensitive measures and create EF z-mean composite scores to provide cleaner measures by filtering out any non-EF noise (Snyder et al., 2015), which should also enable inferences at the process level. Although, caution is suggested when employing large numbers of transfer tasks. Some authors have suggested that number of

transfer tasks should be based on the minimum necessary to address questions at the process level (whether single or multiple processes) as too many tasks can increase type 1 error rate (Green et al., 2014).

Overall, it is not clear whether EF training can transfer to improved functional outcome on untrained cognitive processes or behavioural measures.

Some studies find that near training induced improvements in response inhibition and working memory can transfer to far improvements in reading ability in children with dyslexia (Luo et al., 2013) and reduced symptoms in children with ADHD (Johnstone et al., 2012, 2010), suggesting that training may be useful for targeting symptoms of complex neurodevelopmental disorders (Keshavan et al., 2014). However, findings of transfer have been met with criticisms due to replicability and methodological issues (Enge et al., 2014; Harrison et al., 2013; Redick et al., 2013; Shipstead et al., 2012a; Shipstead et al., 2012b). Despite these issues, EF training is important to explore as near transfer is found at neural and cognitive levels, which may result in far transfer to related EF, reading, socio-emotional and self-regulatory outcomes. The continuous developmental plasticity of EF abilities from early childhood into adulthood (Huizinga et al., 2006; Lehto et al., 2003; van der Sluis et al., 2007), and findings of increased transfer in children and clinical conditions associated with EF impairment (Jaeggi et al., 2011; Karbach & Kray, 2009; Karbach et al., 2015; Söderqvist et al., 2012; Wass et al., 2012), suggest that response inhibition training effects may transfer to a broad range of improvements in children with dyslexia. The Miyake and Friedman (2012) framework may also be useful for cross comparability across training studies, as the unity (common EF: response inhibition) and diversity (updating and switching) fractioning of EF is found in children (Huizinga et al., 2006; Lehto et al., 2003; Rose et al., 2011; van der Sluis et al., 2007), adolescents (Huizinga et al., 2006), and adults (Friedman et al., 2006, 2007, 2008; Miyake et al., 2000): making it a suitable framework for interpreting modification of EF and cross comparability of intervention studies across different ages.

No study to date has explored whether response inhibition training can result in far transfer to changes in EF, reading, socio-emotional and self-regulatory difficulties in

children with dyslexia. Study 2 (PhD aim 4) aims to explore whether high and low-doses of response inhibition training can transfer to other EF abilities, reading ability, socio-emotional problems and capacity for self-regulation in children with dyslexia.

7.1 Method

7.1.1 Participants

The same thirty participants with developmental dyslexia who took part in Study 2 were included in Study 2. See page 156 and 201 for participant characteristics.

7.1.2 Procedure

This response inhibition training study was a double-blind, four-block (AABB) randomisation, placebo controlled design consisting of three phases: (a) pre-intervention assessment, (b) a 6-week online response inhibition training intervention where participants were randomly allocated to low (non-adaptive) or high (adaptive) dose conditions, and (c) post-intervention assessment. Randomisation, blinding and later unveiling of training conditions was conducted by the author of the game Dr David Delany who was not actively involved in recruitment or pre-post assessment of participants. Participants were required to complete two (pre-post) on-site testing sessions lasting approximately 2 hours in the psychology laboratories in the School of Nursing and Human Sciences at Dublin City University. Participants were assessed individually in the presence of their parent/guardian. During the testing session, participants completed a battery of neuro-cognitive (EF) and reading measures, while parents/guardians of participants completed assessments of their child's self-regulation and socio-emotional behaviours. The order of tasks was counterbalanced for each participant for pre and post assessments to control for fatigue effects. All neuro-cognitive measures were created with E-Prime Software and responses were recorded with a combination of a Cedrus RB-50 response pad, mouse and keypad. Upon completion of the pre-intervention assessment participants were shown a short 5-minute demonstration of the training game and were given a copy of an instruction sheet to take home. Parents/Guardians were informed that they would

soon receive an email with a link to their prescribed training intervention and their child's unique log in details (username, password), it was requested that online training be supervised by parent/guardian for child protection reasons. Participants were instructed to log-in and play the training game 3 times per week for 6 weeks. After completing the 6-week intervention participants returned for post-intervention assessment. Participant activity on the game was monitored with an interface which displayed the number of days since each participant had trained without displaying their training condition. If a participant had not trained in three days a reminder email was sent as a prompt to ensure continuous engagement. Throughout the course of the entire training intervention eleven participants required prompts to continue training.

7.1.3 Inhibitory Control Training Programme

The inhibitory control training programme is outlined in detail in section 6.1.3. To summarise, both high and low-dose training groups completed a 6 week Go No-Go training intervention. The low-dose training condition was non-adaptive with a stable No-Go frequency of approximately 40-45% and an inter-stimulus interval of 1,800ms (*see Figure 49*). The high-dose training condition was adaptive based on player performance, at the start of training the No-Go frequency was approximately 40-45% with an inter stimulus interval of 1,000ms (*see Figure 49*). Difficulty of the high-dose training condition was adapted by incrementally reducing the probability of encountering a No-Go target and increasing the occurrence of distracting lures based on player performance. The high-dose group trained for approximately 28 minutes 3 times per week while the low-dose group trained for approximately 6 minutes 3 times per week.

7.1.4 Pre-Post Far Transfer Measures

Pre-Post measures of far transfer which have previously been used throughout the PhD are outlined in Table 24.

Additional Transfer Measure

Self-Control: Parents of participants completed the revised Early Adolescent Temperament Questionnaire (EAT-Q) (Ellis & Rothbart, 2001). The effortful control super-scale was employed as a measure of children's self-regulation which is based on combining attention (capacity for focusing and shifting attention), inhibitory control (planning, suppression of inappropriate responses) and activation control (ability to perform action when tendency to avoid) subscales. Each subscale demonstrates good reliability (attention=.65 ; inhibitory control=.86; activation control= .66) and factor analyses confirm that each subscale significantly loads onto an effortful control factor (Ellis, 2002; Ellis & Rothbart, 2001).

Table 24 Assessment of Far Transfer of Response Inhibition Training

Non-Trained Cognitive Abilities	**Measure**	**Details and Figures**
Updating	Letter 2-back task	Task procedure is outlined in section 3.2.3, with amendments to timing and task figures displayed in section 5.2.3
	Picture 2-back Task	Task procedure is outlined in section 3.2.3, with amendments to timing and task figures displayed in section 5.2.3
	Phoneme 2-back Task	Task procedure is outlined in section 3.2.3, with amendments to timing and task figures displayed in section 5.2.3
Switching	Number- Letter Switch Task	Task procedure is outlined in section 3.2.3, with amendments to timing and task figures displayed in section 5.2.3
	Phoneme Switch Task	Task procedure is outlined in section 3.2.3, with amendments to timing and task figures displayed in section 5.2.3
Processing Speed	Coding Task	Task procedure is outlined in section 3.2.3.
Behavioural Outcomes		
Reading Ability	WRAT-4 Green Word Reading Test	Task procedure is outlined in section 3.2.3
Socio-Emotional Problems	Parent Child Behaviour Checklist	Task procedure is outlined in section 3.2.3

7.2 Data Analysis

7.2.1 Creating EF Z-mean Composite Measures

Updating and switching z-mean composite scores were calculated to provide cleaner measures by filtering out any non-EF noise and to increases power due to small sample size (Snyder et al., 2015). Composite scores for updating and switching were created for error rate/error cost and reaction time/reaction time cost by summing all standardised z-scores and dividing by the number of tasks for example: $\left(\frac{ZPic2backerror+ZPhonbackerror+ZLett2backerror}{3}\right)$.

It is necessary to use a common mean and standard deviation when computing standardised scores with two or more time points, as standardised scores at one time point will remove the change in scores across time (Anglim, 2009). To account for this, pre-post standardised scores for each task were calculated with the following equation for time 1 $\left(\frac{T1Errors-Overall\ Mean\ Errors\ (T1\ \&\ T2)}{Overall\ SD\ (T1\ \&\ T2)}\right)$ and time 2 $\left(\frac{T2Errors-Overall\ Mean\ Errors\ (T1\ \&\ T2)}{Overall\ SD\ (T1\ \&\ T2)}\right)$.

7.2.2 Preliminary Analysis

Preliminary analyses were conducted to ensure that variables did not violate the assumptions of normality or homogeneity of variance. All variables met the assumptions of normality and homogeneity of variance except for pre letter 2-back error rate, pre updating error composite, and post letter 2-back reaction time which all violated the assumption of homogeneity of variance. However, this violation only appears to be a problem for ANOVA when the ratio of groups is greater than 1:5 which is not the case in the present study (1:1.14) (Field, 2013). A Bonferroni correction ($p<.005$) was applied to account for inflated type I error rate due to multiple comparisons. Bonferroni correction

was calculated based on apriori research questions only to ensure that resulting alpha level would not lead to an increase in type II error rate.

7.2.3 Statistical Analysis

Differences between low-dose and high-dose groups on non-trained cognitive abilities (updating, switching and processing speed) and behavioural outcomes were assessed at baseline (prior to intervention) with between group F-Tests. Training transfer to non-trained cognitive abilities and behavioural outcomes were assessed with 2 (Dose: low-dose, high-dose) x 2 (Time: Pre, post) mixed design ANOVAs. Effect-size analysis (Cohen's d) was used to explore standardised differences between training groups prior to intervention and to assess size of transfer effect in low-dose and high-dose training conditions. Cohen's d for mixed design ANOVA was calculated using the following equation: $(PreScore - PostScore)/(Pooled\ SD)$; which is more suitable for pre-post designs (Dunlap et al., 1996). According to Cohen (1988), effects sizes can be classified as small effect (d=.2), medium (d=.5) and large (d=.8).

7.3 Results

7.3.1 Descriptive Statistics

Descriptive statistics and baseline comparisons between low-dose and high-dose training groups are summarised in Table 25. At baseline, low-dose and high-dose training groups did not significantly differ on any measures of transfer ($p>0.05$).

Table 25 Behavioural and Executive Function descriptive statistic and comparisons between low and high-dose groups at baseline

	Low-dose			High-dose				
		Mean	SD	N	Mean	SD	F-Value	*p*-value	Cohen's *d*
Behavioural Outcomes									
Reading Ability (no. correct)	14	38.29	5.77	16	39.19	.9.16	.101	.754	-.12
Self-Control (effortful control)	14	2.99	.48	16	3.12	.65	.448	.509	-.25
Socio-Emotional Problems (no.)	14	22.64	11.29	16	26.44	13.86	.664	.443	-.30
Executive Function									
Updating									
Letter 2-back % Error	13	21.15	13.60	16	36.72	25.60	3.89	.059	-.76
Letter 2-back RT	13	894.05	158.86	16	960.35	143.52	1.41	.246	-.44
Pic 2-back % Error	14	11.5	7.93	16	16.25	11.69	1.65	.210	**-.47**
Pic 2-back RT	14	865.41	130.06	16	915.49	109.56	1.33	.259	-.42
Phon. 2-back % Error	14	47.79	9.61	16	41.50	11.52	2.59	.119	.59
Phon. 2-back RT	14	1157.95	257.88	16	1118.99	158.93	.255	.617	.18
Updating Error Comp.	14	.063	.55	16	.344	1.13	.713	.406	-.32
Updating RT Comp.	14	.141	.99	16	.627	.80	2.21	.148	-.54

	Low-dose			High-dose					
	N	Mean	SD	N	Mean	SD	F-Value	*p*-value	Cohen's *d*
Switching Cost (Switch- Non-Switch Error/RT)									
Num-Let Sw. Error-Cost	14	5.79	3.52	16	4.59	3.60	.834	.369	.34
Num-Let Sw. RT Cost	14	994.08	597.07	16	1006.34	287.69	.005	.942	-.03
PH-Sw. Error Cost	14	3.57	3.67	16	4.50	4.12	.419	.523	-.24
PH-Sw. RT Cost	14	638.62	918.25	16	872.97	727.48	.608	.442	-.28
Switching Error Comp.	14	-.163	.761	16	-.225	.833	.054	.835	-.08
Switching RT Comp.	14	-.157	.922	16	-.036	.532	.200	.658	-.16
Processing Speed									
Coding (no. items completed)	14	8.64	2.73	16	8.75	1.61	.018	.895	-.04

Note: Alpha=0.005 corrected for eleven comparisons. Pic=Picture, Phon=Phoneme, Comm=Commission Errors, GNG= Go No-Go, Comp=Composite, RT=Reaction Time, SW=switch. Between Group ANOVAs were conducted and *p*-values and effect sizes (Cohen's *d*) based on group mean and SD are reported

7.3.2 Near Transfer of Training to Non-Trained Cognitive Abilities (EF and Speed)

Results exploring transfer of training to non-trained cognitive abilities such as updating, switching and processing speed are summarised in Tables 26 and 27; and size of transfer effects to EFs for low and high-doses are graphed in figure 82.

Transfer of Training to Updating

Updating Error Composite

To explore transfer of training to updating z-mean error composite score a mixed design ANOVA with time as a within factor (pre; post) and dose as a between group factor (Low; High) was conducted. This analysis revealed a non-significant group x time interaction ($F(1,28)=1.14$, $p=.294$, $\eta_p^2=.039$), significant main effect of time ($F(1,28)=21.49$, $p=.000$, $\eta_p^2=.434$), and a non-significant main effect of group ($F(1,28)=1.68$, $p=.205$, $\eta_p^2=.027$). The significant main effect of time suggests that both groups experienced a significant reduction in updating errors at the z-mean composite level as a function of training. The low-dose active control group experienced a large effect for error composite whereby the positive error score at pre-test (M=.063, SD=.55) reduced to a negative error score at post-test (M=-.611, SD=.69), Cohen's d=1.08. The high-dose experimental group experienced a medium effect for error composite whereby the positive error score at pre-test (M=.344, SD=1.13) reduced to a negative error score at post (M=-.077, SD=1.08), Cohen's d=.38. Figure 64 presents transfer for both high and low groups to reduced updating error composite score.

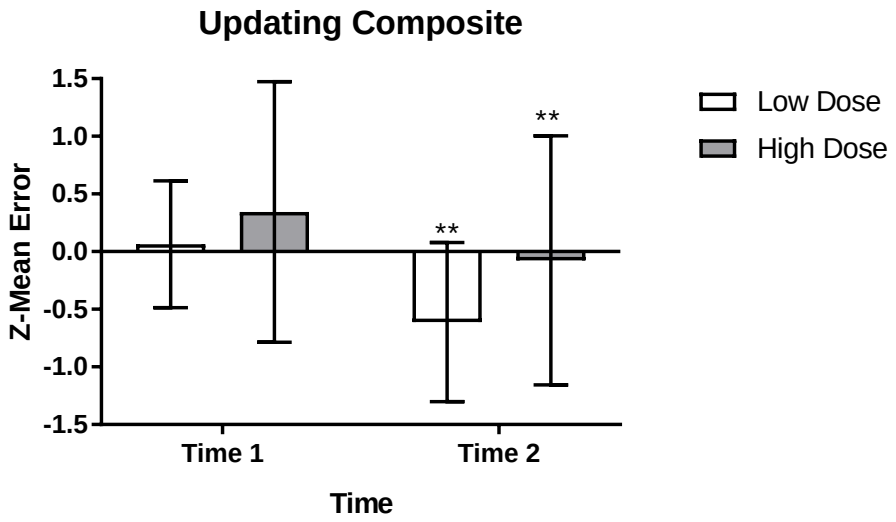


*Figure 64 Near Transfer of Training to Reduced Updating Error Score. *p<.05 **p<.005*

Updating Reaction Time Composite

To explore transfer of training to updating z-mean reaction time composite score a mixed design ANOVA with time as a within factor (pre; post) and dose as a between group factor (Low; High) was conducted. This analysis revealed a non-significant group x time interaction ($F(1,28)=.004$, $p=.951$, $\eta_p^2=.000$), significant main effect of time ($F(1,28)=17.48$, $p=.000$, $\eta_p^2=.384$), and a non-significant main effect of group ($F(1,28)=2.99$, $p=.384$, $\eta_p^2=.095$). The significant main effect of time suggests that both groups experienced a significant reduction in updating reaction time at the z-mean composite level as a function of training. The low-dose active control group experienced a large effect for reaction time composite whereby the positive reaction time score reflecting more time required at pre-test (M=.141, SD=.99) was reduced to a negative reaction time score reflecting less time required at post-test (M=-.748, SD=.72), Cohen's d=1.05. The high-dose experimental group also experienced a large effect for reaction time composite whereby the positive reaction time score reflecting more time required at pre-test (M=.627, SD=.80) was reduced to a negative reaction time score reflecting less time required at post-test (M=-.289, SD=1.20), Cohen's d=.92. Figure 65 presents transfer for both high and low groups to updating reaction time composite.

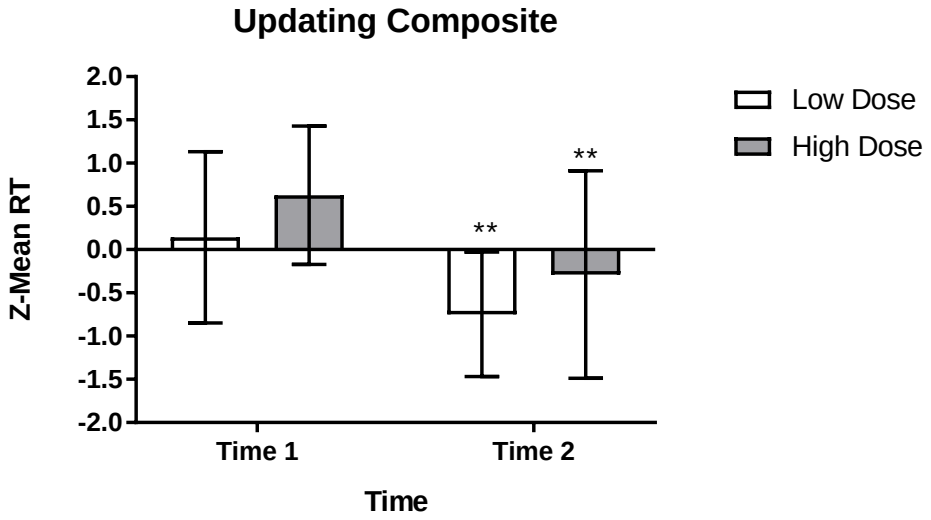


*Figure 65 Near Transfer of Training to Reduced Updating Reaction Time. *p<.05 **p<.005*

Letter 2-back Task

To explore transfer of training to the Letter 2-back Task a mixed design ANOVA with time as a within factor (pre; post) and group as a between group factor (Low; High) was conducted. For errors, the analysis revealed a non-significant group x time interaction ($F(1,28)=2.49$, $p=.126$, $\eta_p^2=.084$), a trend for a significant main effect of time ($F(1,28)=7.47$, $p=.01$, $\eta_p^2=.223$) and a non-significant main effect of group ($F(1,28)=3.328$, $p=.079$, $\eta_p^2=.110$). The trend for a main effect of time suggests that both groups experienced a significant reduction in errors during a letter updating task as a function of training. The low-dose active control group experienced a small effect for reduced errors from pre (M=21.15, SD=13.60) to post (M=18.09, SD=11.47), Cohen's d=.24. The high-dose experimental group experienced a large effect for reduced errors from pre (M=36.72, SD=25.60) to post (M=25.65, SD=17.18), Cohen's d=.85. Figure 66 presents transfer for both high and low groups to letter 2-back reduced error rate.

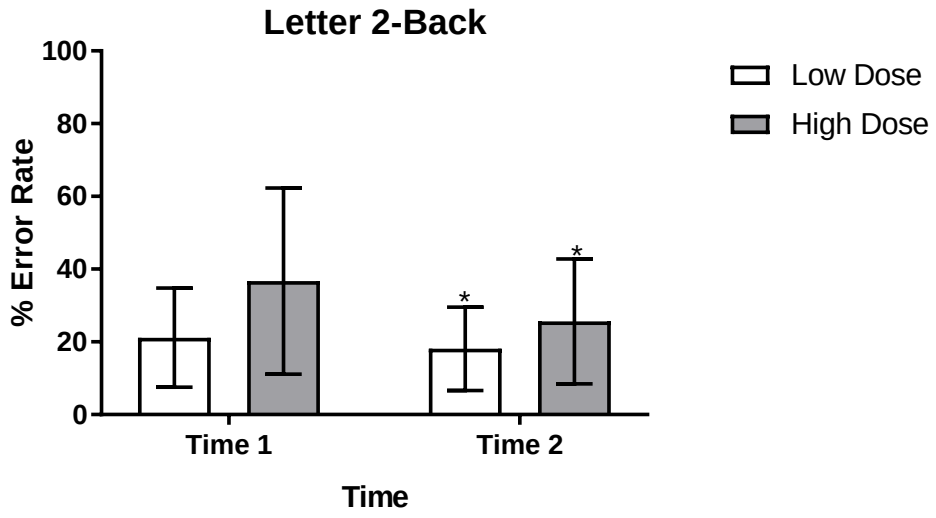


*Figure 66 Near Transfer to reduced errors on the Letter 2-back task. *p<.05 **p<.005*

For reaction time, the analysis revealed a non-significant group x time interaction ($F(1,28)=.140$, $p=.711$, $\eta_p^2=.005$), a trend for a significant main effect of time ($F(1,28)=6.14$, $p=.020$, $\eta_p^2=.185$) and a non-significant main effect of group ($F(1,28)=1.58$, $p=.220$, $\eta_p^2=.055$). The trend for a main effect of time suggests that both groups experienced a significant reduction of reaction time during a letter updating task as a function of training. The low-dose active control group experienced a medium effect for reduced reaction time from pre (M=894.05, SD=156.86) to post (M=819.59, SD=106.97), Cohen's d=.56. The high-dose experimental group experienced a medium-large effect for reduced reaction time from pre (M=960.35, SD=143.52) to post (M=859.35, SD=170.18), Cohen's d=.64. Figure 67 presents transfer for both high and low groups to letter 2-back reaction time.

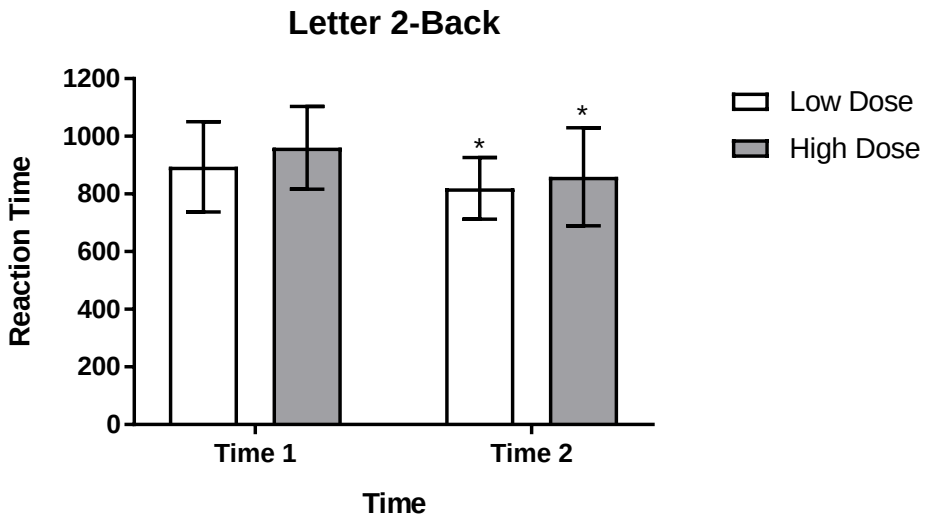


*Figure 67 Near Transfer to Reduced Reaction Time on the Letter 2-back Task. *p<.05 **p<.005*

Picture 2-back Task

To explore transfer of training to the Picture 2-back Task, a mixed design ANOVA with time a within factor (pre; post) and dose as a between group factor (Low; High) was conducted. For errors, the analysis revealed a non-significant group x time interaction ($F(1,28)=.054$, $p=.818$, $\eta_p^2=.002$), a non-significant main effect of time ($F(1,28)=.889$, $p=.351$, $\eta_p^2=.031$) and a non-significant main effect of group ($F(1,28)=2.09$, $p=.160$, $\eta_p^2=.069$). The low-dose active control group experienced a small effect for reduced errors from pre ($M=11.50$, $SD=7.93$) to post ($M=9.64$, $SD=7.24$), Cohen's $d=.25$. The high-dose experimental group no effect for reduced errors from pre ($M=16.52$, $SD=11.69$) to post ($M=15.12$, $SD=13.48$), Cohen's $d=.09$. Figure 68 presents transfer for both high and low groups to picture 2-back reduced errors.

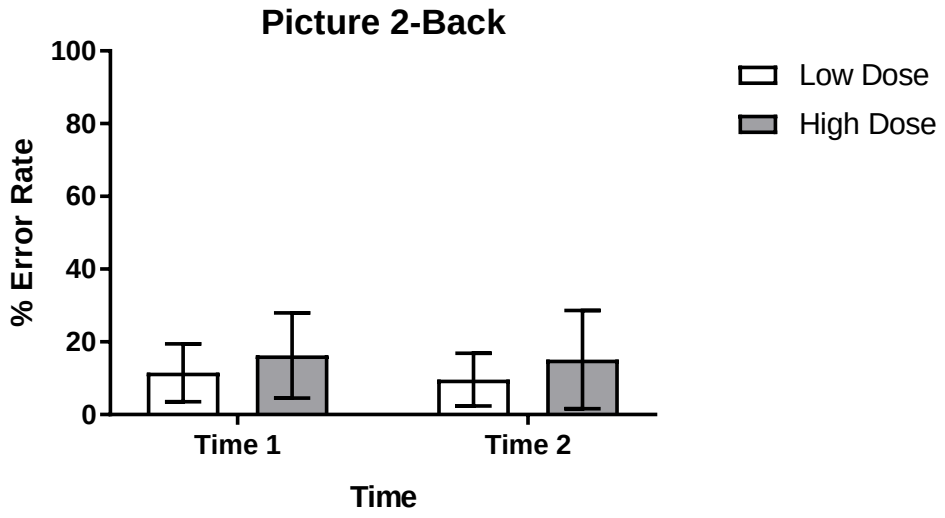


*Figure 68 Near Transfer to Reduced Errors on the Picture 2-back Task. *p<.05 **p<.005*

For reaction time, the analysis revealed a non-significant group x time interaction ($F(1,28)=.439$, $p=.513$, $\eta_p^2=.015$), a significant main effect of time ($F(1,28)=29.32$, $p=.000$, $\eta_p^2=.511$) and a non-significant main effect of group ($F(1,28)=4.17$, $p=.051$, $\eta_p^2=.130$). The significant main effect of time suggests that both groups experienced a significant reduction of reaction time during picture updating task as a function of training. The low-dose active control group experienced a large effect for reduced reaction time from pre (M=865.14, SD=130.06) to post (M=696.22, SD=72.15), Cohen's d=1.67. The high-dose experimental group also experienced a large effect for reduced reaction time from pre (M=915.46, SD=109.56) to post (M=783.38, SD=148.09), Cohen's d=1.03. Figure 69 presents transfer for both high and low groups to picture 2-back reaction time.

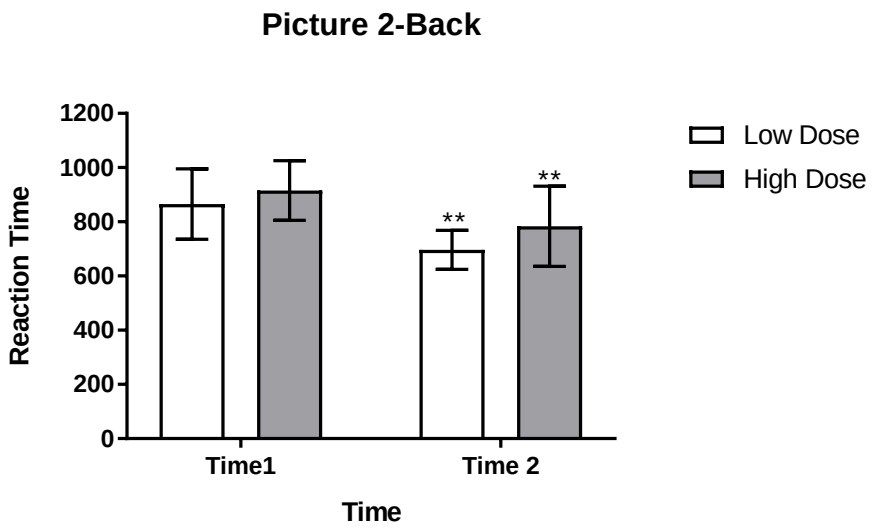


*Figure 69 Near Transfer to Reduced Reaction Time on the Picture 2-back Task. *p<.05 **p<.005*

Phoneme 2-back Task

To explore transfer of training to the Phoneme 2-back Task a mixed design ANOVA with time a within factor (pre; post) and group as a between group factor (Low; High) was conducted. For errors, the analysis revealed a significant group x time interaction ($F(1,28)=10.13$, $p=.004$, $\eta_p^2=.266$), a significant main effect of time ($F(1,28)=34.74$, $p=.000$, $\eta_p^2=.554$) and a non-significant main effect of group ($F(1,28)=.000$, $p=989$, $\eta_p^2=.000$). The significant main effect of time suggests that both groups experienced a significant reduction in errors during the phoneme updating task as a function of training, however, the significant group x time interaction suggests that this reduction was greater in the low-dose compared to the high-dose condition. The low-dose active control group experienced a large effect for reduced errors from pre (M=47.79, SD=9.61) to post (M=30.00, SD=10.91), Cohen's d=1.73. The high-dose experimental group experienced a smaller medium effect for reduced errors from pre (M=41.50, SD=11.52) to post (M=36.19, SD=12.76), Cohen's d=.43. Figure 70 presents transfer for both high and low-dose groups to phoneme 2-back error rate.

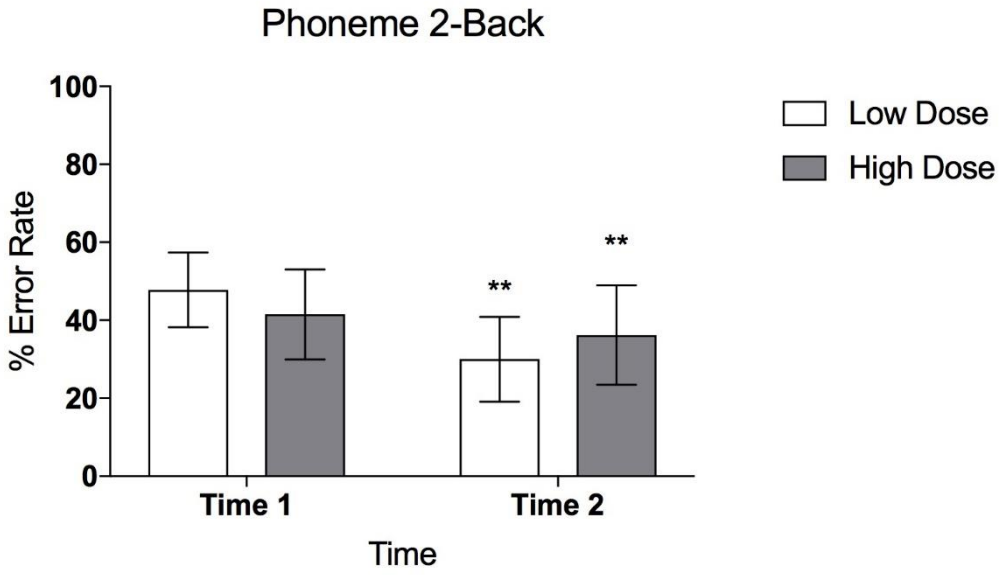


*Figure 70 Near Transfer to Reduced Errors on the Phoneme 2-back Task. *p<.05 **p<.005*

For reaction time, the analysis revealed a non-significant group x time interaction ($F(1,28)=.395$, $p=.535$, $\eta_p^2=.014$), a trend for a significant main effect of time ($F(1,28)=8.85$, $p=.006$, $\eta_p^2=.240$) and a non-significant main effect of group ($F(1,28)=.048$, $p=.826$, $\eta_p^2=.002$). The trend for a significant main effect of time suggests that both groups experienced a reduction in reaction time during the phoneme 2-back task as a function of training. The low-dose active control group experienced a medium-large effect for reduced reaction time from pre (M=1157.95, SD=257.87) to post (M=1020.5, SD=192.92), Cohen's d=.61. The high-dose experimental group experienced a smaller medium effect for reduced reaction time from pre (M=1118.99, SD=158.93) to post (M=1029.47, SD=231.07), Cohen's d=.46. Figure 71 presents transfer for both high and low-dose groups to phoneme 2-back reaction time.

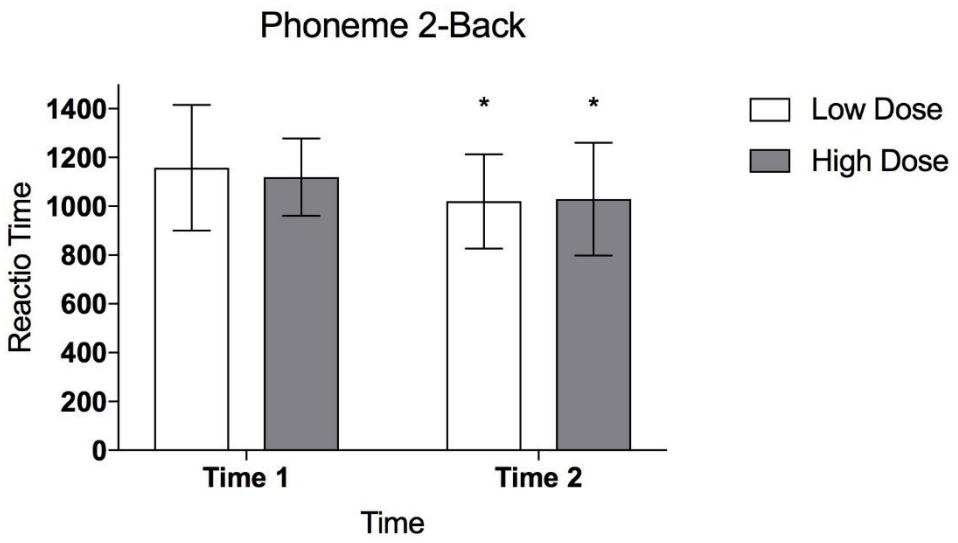


*Figure 71 Near Transfer to Reduced Reaction Time on the Phoneme 2-back Task. *p<.05 **p<.005*

Transfer of Training to Switching

Switch Error Composite

To explore transfer of training to the switching z-mean error cost composite score a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (high, low) was conducted. This analysis revealed a non-significant group x time interaction ($F(1,28)=.121$, $p=.730$, $\eta_p^2=.004$), a non-significant main effect of time ($F(1,28)=2.97$, $p=.096$, $\eta_p^2=.096$) and a non-significant main effect of dose ($F(1,28)=.000$, $p=.984$, $\eta_p^2=.000$).The low-dose active control experienced a medium effect for an increase in switch cost from pre (M=-.163, SD=.76) to post (M=.064, SD=.70), Cohen's d=-.31. The high-dose experienced a medium effect for an increase in switch cost from pre (M=-.225, SD=.83) to post (M=.117, SD=.71), Cohen's d=-.44. Figure 72 presents transfer for both high and low-dose groups to increase switching error cost.

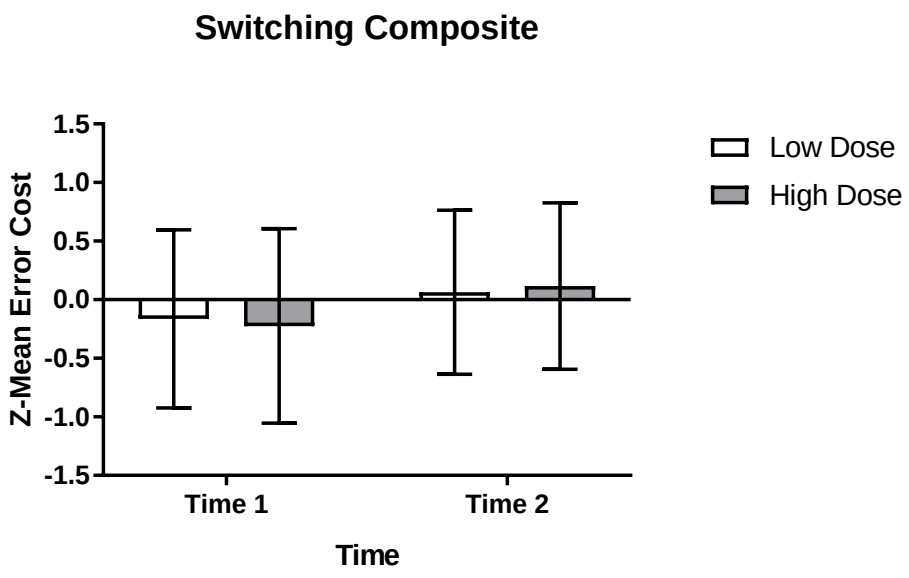


*Figure 72 Near Transfer to Increase Switch Error Cost. *p<.05 **p<.005*

Switch Reaction Time Composite

To explore transfer of training to the switching z-mean RT cost composite score a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (high, low) was conducted. This analysis revealed a non-significant group x time interaction ($F(1,28)=.059$, $p=.810$, $\eta_p^2=.002$), a non-significant main effect of time ($F(1,28)=.786$, $p=.383$, $\eta_p^2=.027$) and a non-significant main effect of dose ($F(1,28)=.301$, $p=.587$, $\eta_p^2=.021$). The low-dose active control experienced a small effect for an increase in switch RT cost from pre (M=-.157, SD=.92) to post (M=-.074, SD=1.03), Cohen's d=-.25. The high-dose experienced a small effect for an increase in switch RT cost from pre (M=-.036, SD=.53) to post (M=.11, SD=.82), Cohen's d=-.21. Figure 73 presents transfer for both high and low-dose groups to increase switching reaction time cost.

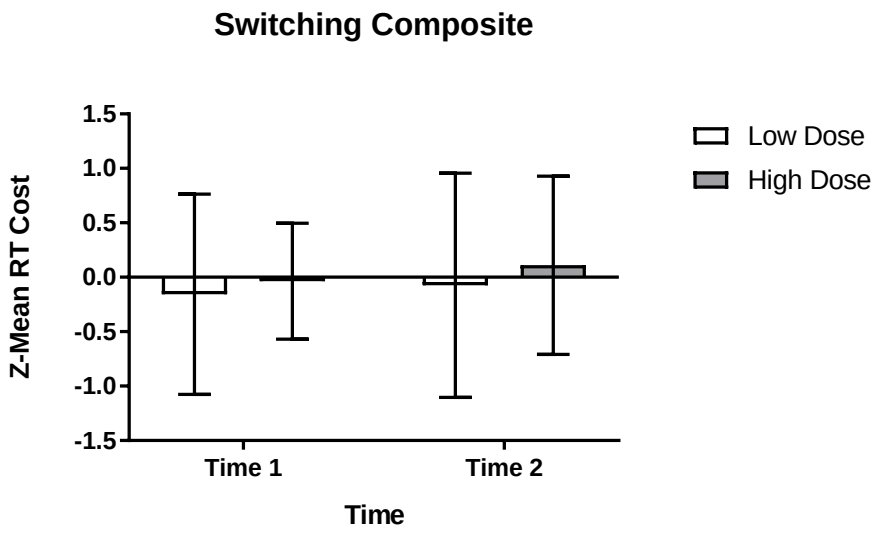


*Figure 73 Near Transfer to Increased Switch Reaction Time Cost. *p<.05 **p<.005*

Number-Letter Switch Task

To explore transfer of training to the Number-Letter Switch task a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (low, high) was conducted. For switch cost in errors, the analysis revealed a non-significant dose x time interaction ($F(1,28)=.036$, $p=.851$, $\eta_p^2=.001$), a non-significant main effect of time ($F(1,28)=.003$, $p=.953$,$b\eta_p^2=.000$) and a non-significant main effect of group ($F(1,28)=1.31$, $p=.263$, , $\eta_p^2=.045$). The low-dose experienced no effect of transfer to number-letter switch cost in errors from pre (M=5.79, SD=3.52) to post (M=5.69, SD=3.86), Cohen's d=.02. The high-dose also experienced no effect of transfer to the number-letter switch cost in errors from pre (M=4.59, SD=3.60) to post (M=4.50, SD=.036), Cohen's d=.02. Figure 74 presents transfer to error cost in the number-letter switch task.

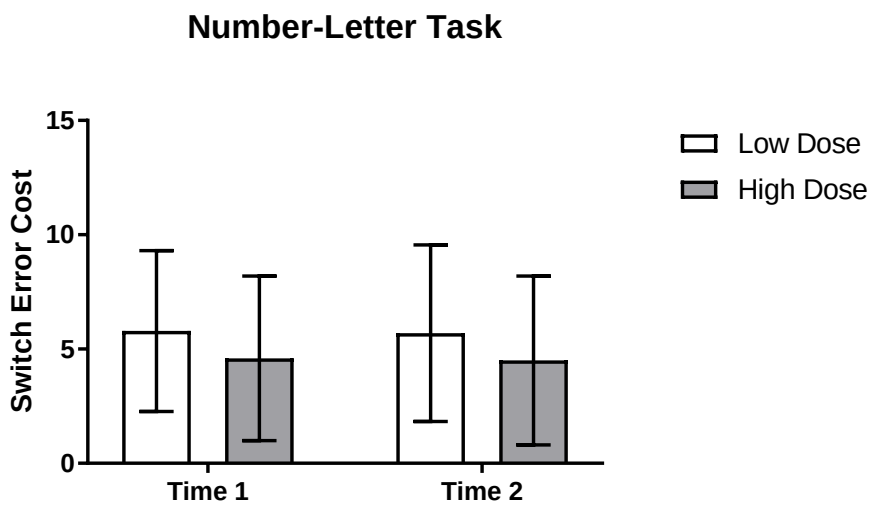


*Figure 74 Near Transfer to Switch Error Cost on the Number-Letter Switch Task. *p<.05 **p<.005*

For switch cost in reaction time, the analysis revealed a non-significant group x time interaction ($F(1,28)=.659$, $p=.424$, $\eta_p^2=.023$), a non-significant main effect of time ($F(1,28)=.465$, $p=.501$, $\eta_p^2=.016$) and a non-significant main effect of dose ($F(1,28)=.197$, $p=.661$, $\eta_p^2=.007$).The low-dose experienced no effect of transfer to switch cost in reaction time from pre (M=994.08, SD=597.7) to post (M=883.74, SD=620.99), Cohen's d=.18. The high-dose also experienced no effect of transfer to switch cost in reaction time from pre (M=1006.34, SD=287.69) to post (M=1015.92, SD=405.32), Cohen's d=-.03. Figure 75 presents near transfer to switch reaction time cost on the number letter switch task.

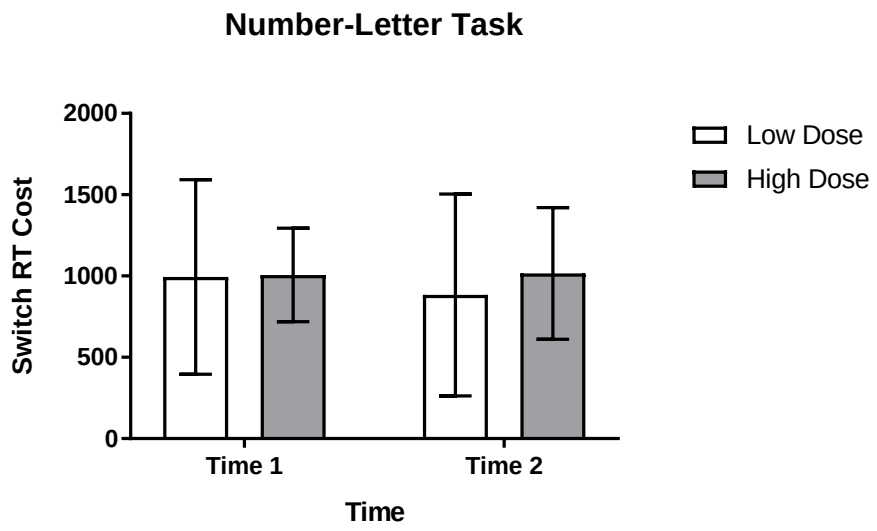


*Figure 75 Near Transfer to Switch Reaction Time Cost in the Number-Letter Switch Task. *p<.05 **p<.005*

Phoneme Switch Task

To explore transfer of training to the phoneme Switch task a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (low, high) was conducted. For switch cost in errors, the analysis revealed a non-significant dose x time interaction ($F(1,28)=.343$, $p=.563$, $\eta_p^2=.012$), a trend for a significant main effect of time ($F(1,28)=4.75$, $p=.032$, $\eta_p^2=.145$) and a non-significant main effect of group ($F(1,28)=1.69$, $p=.204$, $\eta_p^2=.057$). The trend for a main effect of time reflects that both high and low-dose conditions experienced an increase in switch error cost as a function of training. The low-dose experienced a medium effect for increased phoneme error switch cost from pre ($M=3.57$, $SD=3.67$) to post ($M=5.61$, $SD=4.62$), Cohen's $d=-.49$. The high-dose experienced a medium-large effect for increased phoneme error switch cost from pre ($M=4.50$, $SD=4.12$) to post ($M=8.03$, $SD=6.67$), Cohen's $d=-.64$). Figure 76 presents transfer for both high and low-dose groups to phoneme switch error cost.

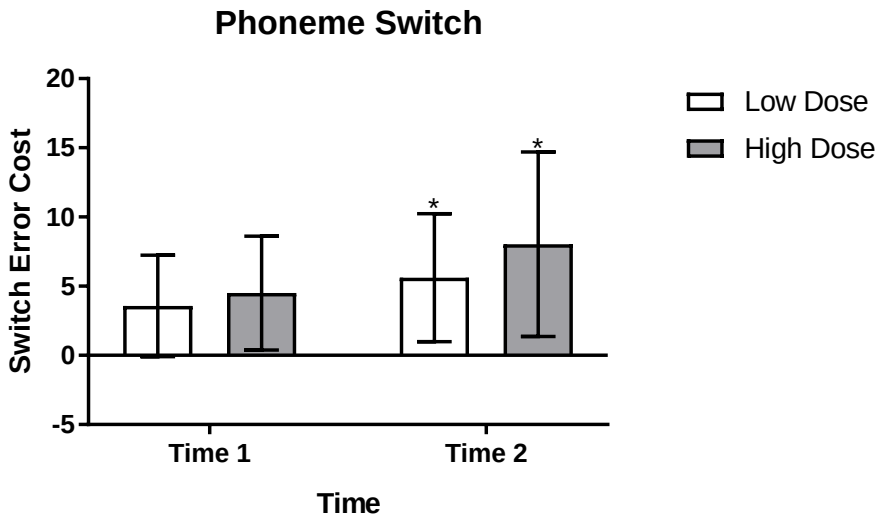


*Figure 76 Near Transfer to Increased Switch Error Cost on the Phoneme Switch Task. *p<.05 **p<.005*

For switch cost in reaction time, the analysis revealed a non-significant group x time interaction ($F(1,28)=.076$, $p=.785$, $\eta_p^2=.003$), a non-significant main effect of time ($F(1,28)=2.68$, $p=.113$, $\eta_p^2=.09$) and a non-significant main effect of dose ($F(1,28)=.213$, $p=.648$, $\eta_p^2=.008$).The low-dose experienced a small-medium effect of transfer to increased switch reaction time cost from pre (M=638.62, SD=918.30) to post (M=986.39, SD=918.62), Cohen's d=-.39. The high-dose experienced a small effect of transfer to increased switch reaction time cost from pre (M=818.86, SD=718.93) to post (M=1066.36, SD=1029.86), Cohen's d=-.29. Figure 77 presents near transfer to increased switch reaction time cost on the phoneme switch task.

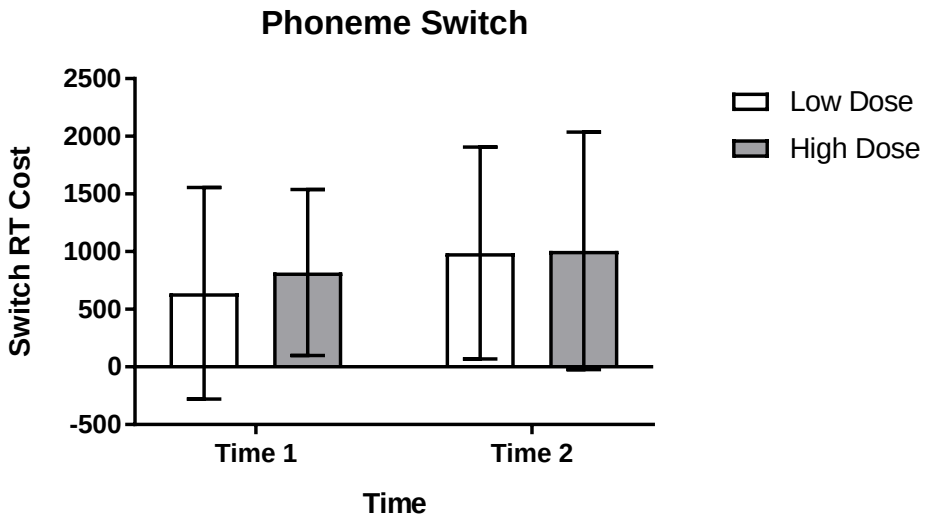


*Figure 77 Near Transfer to Increased Switch Reaction Time Cost on the Phoneme Switch Task. *p<.05 **p<.005*

Transfer to Processing Speed

Coding Task

To explore transfer of training to processing speed a mixed design ANOVA with time a within factor (pre-intervention; post-intervention) and group as a between group factor (Low-dose Active Control; High-dose Experimental) was conducted. The analysis revealed a non- significant group x time interaction ($F(1,28)=.083$, $p=.776$, $\eta_p^2=.003$), a significant main effect of time ($F(1,28)=9.16$, $p=.005$, $\eta_p^2=.247$) and a non-significant main effect of group ($F(1,28)=.000$, $p=.995$, $\eta_p^2=.000$). The significant main effect of time suggests that both high and low-dose groups experienced an improvement in processing speed as a function of training. The low-dose group experienced a medium effect for improved processing speed from pre (M=8.64, SD=2.73) to post (M=9.92, SD=2.43), Cohen's d=-.50. The high-dose group experienced a larger medium effect for improved processing speed from pre (M=8.75, SD=1.61) to post (M=9.81, SD=1.91), Cohen's d=-.60. Figure 78 presents transfer for both high and low-dose groups to improved processing speed.

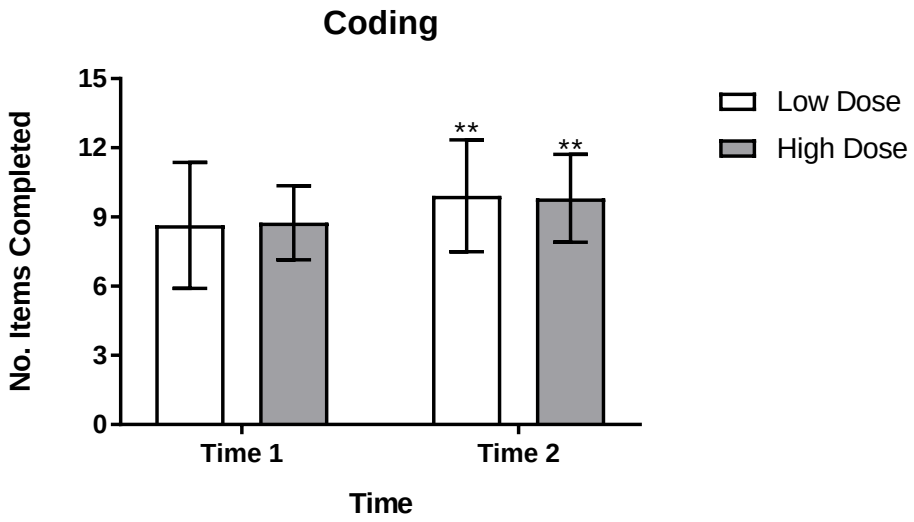


Figure 78 *Near Transfer to Improved Processing Speed on the Coding Task. *p<.05 **p<.005*

7.3.3 Far Transfer of Training to Core and Non-Core Behavioural Outcomes

Results exploring transfer of training to behavioural outcomes are summarised in Table 27 and size of transfer effects to behavioural outcomes for low and high-doses are graphed in Figure 83.

Transfer to Improved Reading Ability

To explore transfer of training to reading ability, a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (Low, High) was conducted. The analysis revealed a non- significant group x time interaction ($F(1,28)=1.09$, $p=.305$, $\eta_p^2=.038$), a significant main effect of time ($F(1,28)=25.90$, $p=.000$, $\eta_p^2=.481$) and a non-significant main effect of group ($F(1,28)=.001$, $p=.982$, $\eta_p^2=.000$). The significant main effect of time suggests that both high and low-dose groups experienced a significant improvement in reading ability as a function of training. The low-dose active control group experienced a large effect for increased reading ability from pre (M=38.29, SD=5.77) to post (M=43.21, SD=7.58), Cohen's d=-.74. The high-dose experimental group experienced a small-medium effect for increased reading ability from pre (M=39.19, SD=9.15) to post

(M=42.44, SD=8.10), Cohen's d=-.38. Figure 79 presents transfer for both high and low-dose groups to improved reading ability.

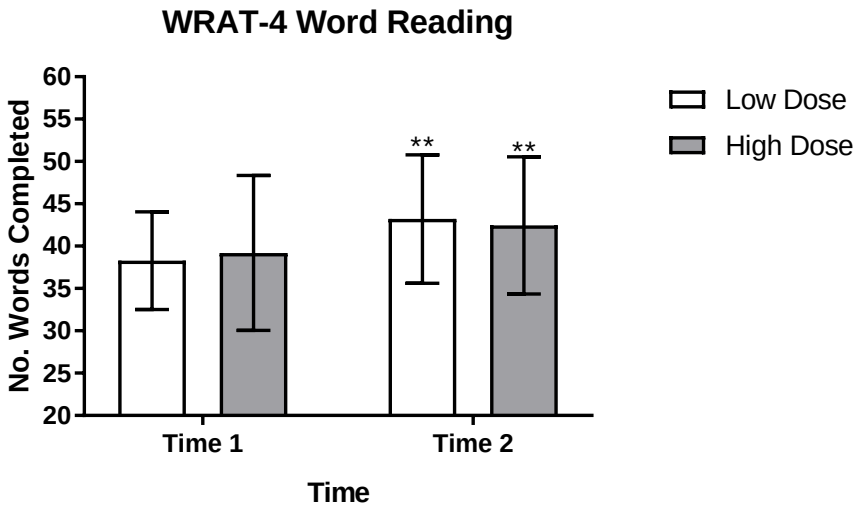


Figure 79 Far Transfer to Improved Reading Ability. *p<.05 **p<.005

Reading ability was assessed with a standardised and age normed tool, therefore it provided an opportunity to explore whether any participants experienced a clinically relevant change in their reading scores as a function of training. On an individual level, 5 participants experienced clinically relevant improvement in reading ability. In the low-dose group, 28.57% of participants (4 out of 14) experienced a clinically relevant shift in reading ability. Three participants in the low-dose group transitioned from below average to average reading ability and one participant transitioned from average to above average reading ability. In the high-dose group, 6.25% of participants (1 out of 16) experienced a clinically relevant shift in reading ability, this participant transitioned from below average to average reading ability.

Transfer to Improved Self-Regulation

To explore transfer of training to self-regulation, a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (Low, High) was conducted. The analysis revealed a non- significant group x time interaction ($F(1,28)=.963$, $p=.335$, $\eta_p^2=.033$), a trend for a significant main effect of time ($F(1,28)=7.01$, $p=.013$, $\eta_p^2=.200$) and

a non-significant main effect of group (F(1,28)=.057, p=.200 η_p^2=.813). The trend for a significant main effect of time suggests that both high and low-dose groups experienced a significant improvement in self-regulation as a function of training. The low-dose active control group experienced a medium-large effect for greater regulation from pre (M=2.98, SD=.48) to post (M=3.33, SD=.67), Cohen's d=-.61. The high-dose experimental group experienced a small effect for greater regulation from pre (M=3.12, SD=.65) to post (M=3.28, SD=.54), Cohen's d=-.27. Figure 80 presents far transfer for both high and low-dose groups to improved reading ability.

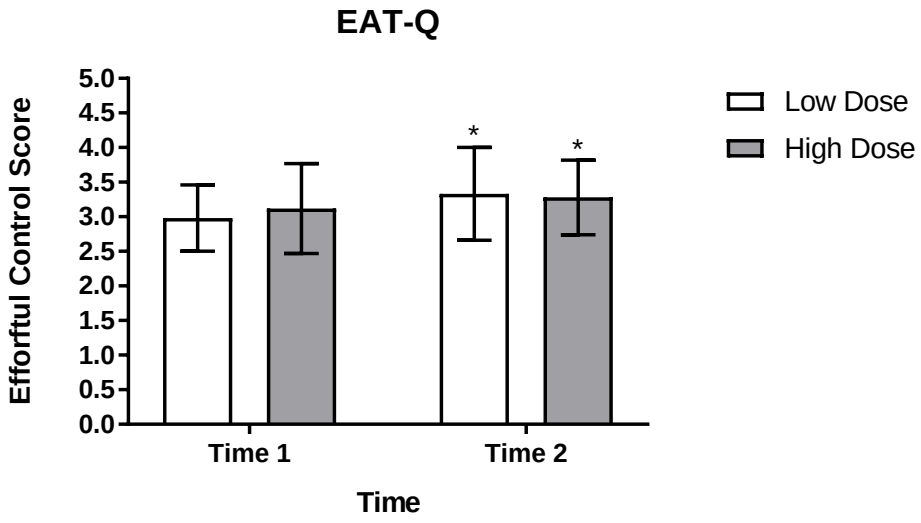


*Figure 80 Far Transfer to Improved Self-Regulation. *p<.05 **p<.005*

Transfer to Reduced Socio-Emotional Problems

To explore transfer of training to socio-emotional problems, a mixed design ANOVA with time as a within factor (pre, post) and dose as a between group factor (Low; High) was conducted. For socio-emotional problems, the analysis revealed a non-significant group x time interaction (F(1,28)=.093, p=.763, η_p^2=.003), a significant main effect of time (F(1,28)=9.16, p=.005, η_p^2=.246) and a non-significant main effect of group (F(1,28)=1.25, p=.274 η_p^2=.043). The significant main effect of time suggests that both low and high-dose conditions experienced a significant reduction in socio-emotional problems as a function of training. The low-dose active control group experienced a medium effect for reduced

socio-emotional problems from pre (M=22.64, SD=11.29) to post (M=16.14, SD=11.73), Cohen's d=.56. The high-dose experimental group also experienced a medium effect for reduced socio-emotional problems from pre (M=26.44, SD=13.86) to post (M=21.33, SD=10.75), Cohen's d=.42. Figure 81 presents transfer for both high and low-dose groups to reduced socio-emotional problems.

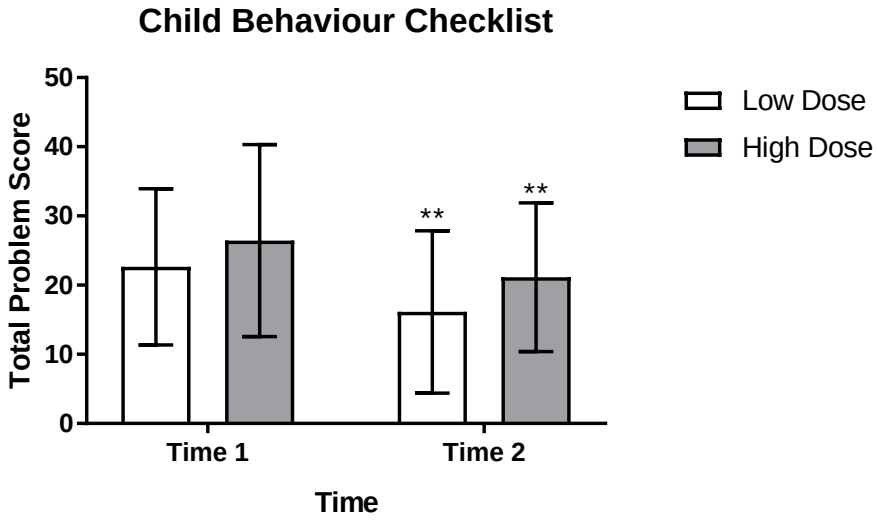


Figure 81 Far Transfer to Reduced Socio-Emotional Problems. *p<.05 **p<.005

Socio-emotional problems were also assessed with a standardised and age normed tool. Therefore, it provided an opportunity to explore whether any participants experienced clinically relevant change in socio-emotional problems as a function of training. On an individual level, at baseline only 5 participants experienced clinical level socio-emotional problems and the remaining 25 participants were in the normal range for socio-emotional problems. All of these participants experienced a clinical shift in expression of socio-emotional problems as a function of training scoring in the normal range at post-test. By chance these participants all happened to be in the high-dose training condition.

Table 26 Near Transfer of training to non-trained updating abilities

	Low-dose			High-dose							ANOVA Time Effect		ANOVA Group Effect		ANOVA Interaction Effect	
Transfer Task	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*F (Time)*	*F (Group)*	*F (Inter-action)*	*df*1, *df*2	*p*-value	η_p^2	*p*-value	η_p^2	*p*-value	η_p^2
Updating																
Let 2-back Err.	21.15 (13.60)	↓18.09 (11.47)	.24	36.72 (25.60)	↓25.65 (17.18)	.85	7.47	3.328	2.49	1,27	**.010***	.223	.079	.110	.126	.084
Let 2-back RT	894.05 (156.86)	↓819.59 (106.97)	.56	960.35 (143.52)	↓859.35 (170.18)	.64	6.14	1.58	.140	1,27	**.020***	.185	.220	.055	.711	.005
Pic 2-back Err.	11.50 (7.93)	↓9.64 (7.24)	.25	16.25 (11.69)	↓15.12 (13.48)	.09	.889	2.09	.054	1,28	.351	.031	.160	.069	.818	.002
Pic 2-back RT	865.14 (130.06)	↓696.22 (72.15)	1.67	915.46 (109.56)	↓783.38 (148.09)	1.03	29.32	4.17	.439	1,28	**.000****	.511	.051	.130	.513	.015
Phon 2-back Err.	47.79 (9.61)	↓30.00 (10.91)	1.73	41.50 (11.52)	↓36.19 (12.76)	.43	34.74	.000	10.13	1,28	**.000****	.554	.989	.000	.004	.266
Phon 2-back RT	1157.95 (257.87)	↓1020.09 (192.92)	.61	1118.99 (158.93)	↓1029.47 (231.07)	.46	8.85	.049	.395	1,28	**.006***	.240	.826	.002	.535	.014
Updating Err. Com	.063 (.55)	↓-.611 (.69)	1.08	.344 (1.13)	↓-.077 (1.08)	.38	21.49	1.68	1.14	1,28	**.000****	.434	.205	.057	.294	.039

Note. Pic=Picture, Phon=Phoneme, Let=Letter, Err=Error, RT= Reaction Time, Com=Composite. *p<.05 (trend), **p<.005 (significant with Bonferroni correction)

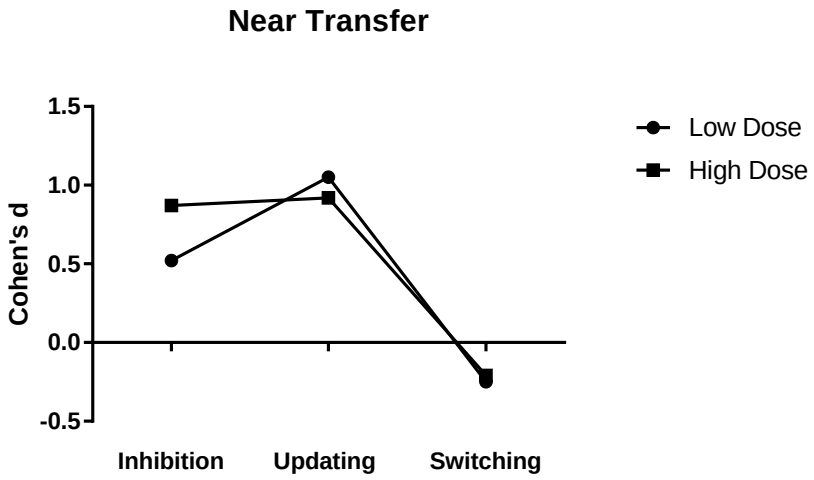
Table 27Near/Far Transfer of training to non-trained updating, switching and speed abilities and to core and non-core behavioural outcomes

	Low-dose			**High-dose**							**ANOVA Time Effect**		**ANOVA Group Effect**		**ANOVA Interaction Effect**	
Transfer Task	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*Pre M* (*SD*)	*Post M* (*SD*)	*d*	*F (Time)*	*F (Group)*	*F (Interaction)*	*df*1, *df*2	*p*-value	η_p^2	*p*-value	η_p^2	*p*-value	η_p^2
Updating RT Com.	.141 (.99)	↓.748 (.72)	1.05	.627 (.80)	↓.289 (1.20)	.92	17.48	2.99	.004	1,28	**.000****	.384	.095	.096	.951	.000
Switching																
Num-Let Err. Cost	5.79 (3.52)	↓5.69 (3.86)	.02	4.59 (3.60)	↓4.50 (3.92)	.02	.003	1.31	.036	1,28	.953	.000	.263	.045	.851	.001
Num-Let RT Cost	994.08 (597.7)	↓883.74 (620.99)	.18	1006.34 (287.69)	↑1015.92 (405.32)	-.03	.465	.197	.659	1,28	.501	.016	.661	.007	.424	.023
Ph-Sw Err. Cost	3.57 (3.67)	↑5.61 (4.62)	-.49	4.50 (4.12)	↑8.03 (6.67)	-.64	4.75	1.69	.343	1,28	**.038***	.145	.204	.057	.563	.012
Ph-Sw RT. Cost	638.62 (918.3)	↑986.39 (918.62)	-.39	818.86 (718.92)	↑1066.36 (1029.86)	-.29	2.68	.213	.076	1,28	.113	.090	.648	.008	.785	.003
Switch Err. Com.	-.163 (.76)	↑.064 (.70)	-.31	-.225 (.83)	↑.117 (.71)	-.44	2.97	.000	.121	1,28	.096	.096	.984	.000	.730	.004
Switch RT Com.	-.157 (.92)	↑-.074 (1.03)	-.25	-.036 (.532)	↑.11 (.82)	-.21	.786	.301	.059	1,28	.383	.027	.587	.011	.810	.002
Processing Speed																

Coding	8.64 (2.73)	↑ 9.92 (2.43)	-.50	8.75 (1.61)	↑ 9.81 (1.91)	-.60	9.16	.000	.083	1,28	**.005****	.247	.995	.000	.776	.003
Behavioural Outcomes																
WRAT	38.29 (5.77)	↑ 43.21 (7.58)	-.74	39.19 (9.15)	↑ 42.44 (8.10)	-.38	25.90	.001	1.09	1,28	**.000****	.481	.982	.000	.305	.038
Effortful Cont.	2.98 (.48)	↑ 3.33 (.67)	-.61	3.12 (.65)	↑ 3.28 (.54)	-.27	7.01	.057	.963	1,28	.013*	.200	.813	.002	.335	.033
Total Prob.	22.64 (11.29)	↓ 16.14 (11.73)	.56	26.44 (13.86)	↓ 21.13 (10.75)	.42	9.16	1.25	.093	1,28	**.005****	.246	.274	.043	.763	.003

Note. RT= Reaction Time, Com=Composite, WRAT= Wide Range Achievement Test, Cont=Control, INT=Internalizing, EXT=Externalizing, Prob=Problems. *p<.05 (trend), **p<.005 (significant with Bonferroni correction)

A



B

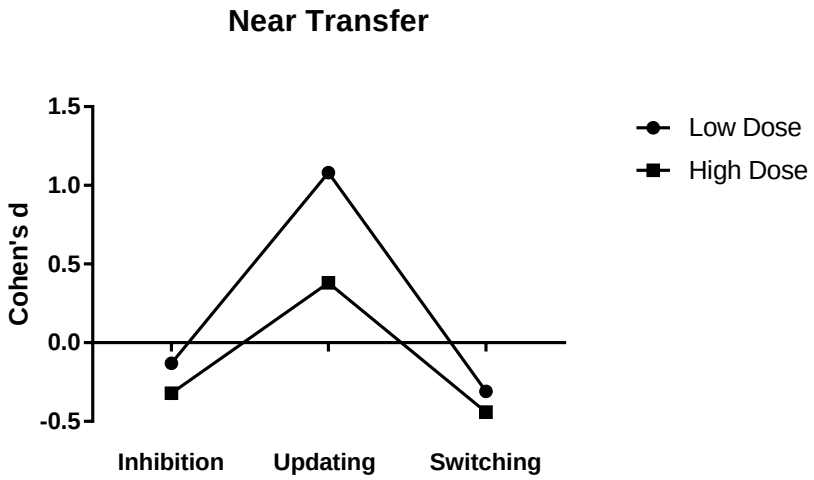


Figure 82 Panel A represents near transfer to other EFs at the RT composite level and Panel B represents near transfer to other EFs at the Error composite level. ***Note:*** *Positive Cohen's d scores represent gains in EF abilities (i.e. fewer errors and less time required post testing compared to pre) and negative Cohen's d scores represent losses in EF abilities (i.e. more errors and more time required post testing compared to pre).*

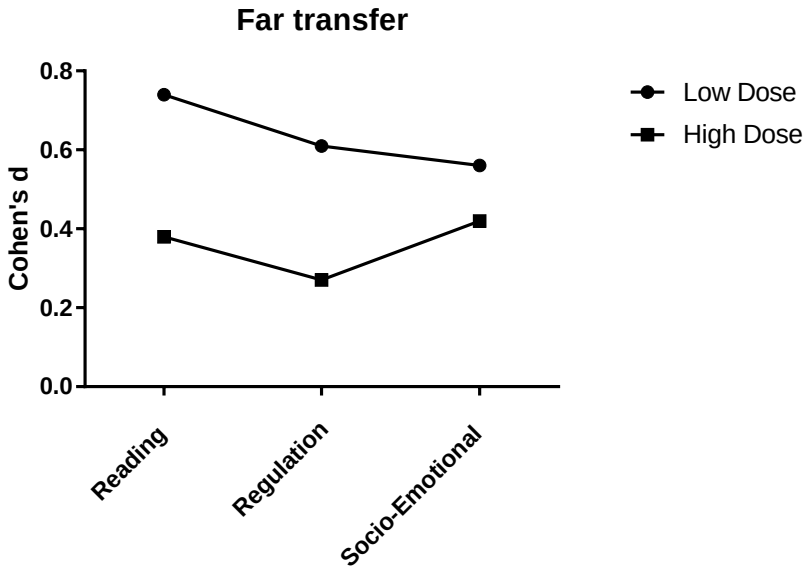


Figure 83. Far transfer to improved reading, self-regulation and reduced socio-emotional problems. Note: Directionality of Cohen's d was reversed for reading ability and self-regulation as these are competence scores (such that a positive Cohen's d reflects higher reading/regulation score post compared to pre). Initial directionality of Cohen's d for socio-emotional problems was maintained (such that a positive score reflects less socio-emotional problems post compared to pre).

7.3.4 Summary of Results

Results suggest that both high-dose (adaptive) and low-dose (non-adaptive) response inhibition training interventions experience pre-post changes to near (EF) and far (reduced symptom severity) outcomes in children with dyslexia.

A pre-post effect was observed for improved working memory updating at the RT and error levels in children with dyslexia. There was also a trend for a pre-post effect for reduced switching efficiency at the task-level in dyslexia after response inhibition training. A pre-post effects was also observed for improved processing speed in children with dyslexia. This suggests that response inhibition training is promising for changing EFs and other cognitive processes in children with dyslexia.

Results also demonstrated that response inhibition training results in pre-post effects for improved reading ability and reduced socio-emotional problems with both high and low training doses in children with dyslexia. There was also a trend for a pre-post effect for improved capacity for self-regulation as a function of training in both high and low-doses of training. Effect sizes for improved outcomes were typically larger for the low-dose compared to the high-dose condition, suggesting that low-dose training may be more effective.

However, there were no significant interaction effects observed between high and low dose training groups for response inhibition at the near (other EFs) or far (reduced symptoms) level of outcomes. The lack of a time x dose interaction effect means that transfer effects were not dose specific. In addition, the lack of suitable active and passive placebo groups means we cannot conclude that response inhibition training transfers at the near and far level as findings may reflect non-specific placebo effects.

7.4 Discussion

From previous research it is not clear whether response inhibition training transfers to untrained cognitive abilities or behavioural outcomes, with evidence both for (Liu et al., 2015; Spierer et al., 2013; Zhao et al., 2016) and against transfer effects (Enge et al., 2014; Thorell et al., 2009). Transfer effects in the EF literature in general are met with criticisms due to a difficulty in replicating effects (Enge et al., 2014; Harrison et al., 2013; Redick et al., 2013; Shipstead et al., 2012a; Shipstead et al., 2012b), and, explorations of transfer not being theoretically informed (Kirk et al., 2015, Shipstead et al., 2012a). From a theoretical perspective, we predicted that response inhibition training would transfer to changes in other EF abilities due to shared variance (updating and switching) (Friedman & Miyake, 2016; Miyake & Friedman, 2012), or antagonistic interactions with response inhibition (switching) (Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015). Response inhibition training was also predicted to transfer to reading ability, socio-emotional problems and self-regulatory behaviour in dyslexia. Response inhibition is predictive of reading impairment (Chapter 4 and 5; Wang & Yang, 2014) and socio-

emotional problems in dyslexia (Wang & Yang, 2014), and is necessary for effective self-regulation and socio-emotional wellbeing (Bridgett et al., 2013; Carlson & Wang, 2007; Diamond, 2013; Eisenberg et al., 2009; Friedman et al., 2008; Rueda et al., 2005; Snyder et al., 2015).

Using a theoretically-informed approach to exploring transfer (Diamond, 2013; Miyake & Friedman, 2012), this study (study 2) for the first time showed that both high (adaptive) and low (non-adaptive) doses of response inhibition training transferred to near (EF) and far (reduced symptom severity) outcomes in children with dyslexia. At the cognitive level (near transfer), response inhibition training transferred to improved working memory updating and processing speed abilities, and demonstrated a trend for reducing switching ability. At the behavioural level (far transfer), response inhibition training transferred to improved reading ability, reduced socio-emotional problems and demonstrated a trend for increased self-regulatory capacity. Individual level analysis suggests that some participants experienced a clinically-relevant shift (from clinical to average) on standardised reading measures and socio-emotional measures, suggesting that response inhibition may be capable of inducing clinical change for some children with dyslexia (Keshavan et al., 2014). These findings are consistent with studies showing transfer of response inhibition training in pre-school and middle age children (Liu et al., 2015; Zhao et al., 2016) and inconsistent with those showing that response inhibition training does not transfer in pre-school children and young adults (Enge et al., 2014; Thorell et al., 2009).These findings are also consistent with those showing that cognitive training in the working memory domain can transfer to improvements in reading in adults (Shiran & Breznitz, 2011) and children with dyslexia (Dahlin, 2011; Luo et al., 2013). However, this study is the first to explore response inhibition training in dyslexia and to demonstrate that training transfers to a broad range of cognitive and behavioural outcomes which are related to but also extend far beyond response inhibition. Our findings also suggest that response inhibition may be a useful intervention for targeting core reading impairments as well as non-core socio-emotional and self-regulatory problems associated with dyslexia.

The finding that response inhibition training transfers to changes in other EF abilities is consistent with Miyake and Friedman's (2012) 3-factor model of EF. Within this model EF is comprised of separable but related abilities: separable or specific aspects of EF (updating and switching) share variance with the common EF (response inhibition) (Miyake & Friedman, 2012). Therefore, within Miyake and Friedman's (2012) model of EF, improvements in response inhibition abilities should logically be mirrored by improvements in updating and switching abilities due to shared variance. More recently, the same authors have suggested that the way in which response inhibition overlaps with specific aspects of EF is differential (Friedman & Miyake, 2016; Snyder et al., 2015), suggesting that training induced changes in updating and switching may not be in the same direction. This study (Study 2) showed that response inhibition training improved updating abilities, but reduced switching abilities. Improved response inhibition may facilitate improvements in updating as the demands of these EFs are compatible: inhibition can protect the contents of working memory from distractor interference and increase attentional focus - thereby enhancing the ability to correctly update information in working memory (Friedman & Miyake, 2017; Miyake & Friedman, 2012). In contrast, improved response inhibition may prevent or disrupt switching abilities as these EFs are incompatible: response inhibition facilitates increased focus by filtering irrelevant information in a top down manner, while switching may require a degree of irrelevant information processing to consider alternative option and flexibly adapt to changing task demands (Blackwell et al., 2014; Goschke, 2000; Gruber & Goschke, 2004). Therefore, improved response inhibition may negatively impact switching abilities.

This pattern emerged in the present study, suggesting that EF may operate in a strengths and impairments manner in children with dyslexia. These findings have implications for tasks measuring pre-post training effects, as complex tasks tapping multiple EF domains may combine training effects, resulting in overall null effects of training (Snyder et al., 2015). Additionally, these findings suggest that training may result in potentially negative cognitive transfer effects -depending on the trained domain - which may also negatively impact upon related behavioural outcomes. In the previous profiling chapter 3 (Study 1),

children with dyslexia demonstrated impaired response inhibition but unimpaired switching abilities relative to neurotypical control children (converse shown in Study 2). It may be the case that the right balance between EFs is necessary to produce healthy function in children; therefore, reducing switching abilities in children with dyslexia may not result in impaired performance as it may essentially be restoring the balance of EFs to optimal function.

Interestingly, response inhibition training transferred to improved general processing speed abilities in both high and low conditions. Both high and low-dose conditions evidenced gains in processing speed, which suggests that the gains in reaction time on response inhibition measures from training may have generalised to improved speed of processing with all types of information. Functionally, the high-dose training game requires more speeded processing (see Figure 49, Chapter 6), so therefore speed gains would logically be larger in the high-dose compared to the low-dose condition. Indeed, this was the case as the high-dose experienced a larger effect for improved processing speed (Cohen's d=-.60) compared to the low-dose (Cohen's d=-.50), although speed did significantly improve for both groups. This finding is of interest as previous research suggests that processing speed may be a shared risk factor for dyslexia and ADHD (Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2005). The findings from this PhD suggest that response inhibition training can generalise to improved processing speed abilities in children with dyslexia.

Response inhibition training also significantly transferred to improved reading ability in both high and low-dose conditions, which has clinical implications for the role of response inhibition in predicting and improving reading ability in dyslexia. Current findings of response inhibition training far transfer to improved reading ability was expected given that we showed that reaction time on the response inhibition composite score predicted reading ability (Chapter 5). This finding is consistent too with previous research showing that response inhibition is important for reading ability in neurotypical control children (Arrington et al., 2014; Blair & Razza, 2007; Welsh et al., 2010) and is predictive of reading severity in children with dyslexia (Booth et al., 2014; Wang & Yang, 2014). The findings

from this PhD validate the role of response inhibition in reading ability in children with dyslexia, and further suggest that response inhibition may be causally implicated in core reading impairments in dyslexia, as directly improving response inhibition abilities transferred to improvements in reading ability. These findings are also consistent with those showing that working memory training significantly improves reading ability in children (Dahlin, 2011; Luo et al., 2013) and adults with dyslexia (Shiran & Breznitz, 2011). However, ours is the first study to show that directly modifying response inhibition can improve reading ability in children with dyslexia.

Transfer of response inhibition training was not isolated to core reading impairments in children with dyslexia as this type of training also transferred to non-core socio-emotional and self-regulatory issues in children with dyslexia. Both high and low-dose training resulted in transfer to non-core outcomes. Previous Chapters (4 and 5) did not report a predictive relationship between response inhibition and socio-emotional problems in dyslexia, and were in fact inconsistent with previous research showing that response inhibition is predictive of socio-emotional problems in children with dyslexia (Wang and Yang, 2014). Study 2 training transfer effects to socio-emotional outcomes are however, consistent with a wealth of previous research suggesting that response inhibition is necessary for the development of effortful control - a good indicator of self-regulatory and socio-emotional outcomes (Bridgett et al., 2013; Carlson & Wang, 2007; Eisenberg et al., 2009; Friedman et al., 2008; Rueda et al., 2005; Snyder et al., 2015); and that response inhibition impairments at the cognitive (Young et al., 2009) and neural levels are observed in those with socio-emotional problems (Albrecht et al., 2005; Nash et al., 2013). Findings from this study (Study 2) dovetail with studies finding that dual training of working memory and response inhibition transfer to reduced socio-emotional problems in children with ADHD (Johnstone et al., 2012, 2010). However, it is difficult to demonstrate which cognitive domain drives transfer in dual studies – a potential confound accounted for in the current set of studies. The findings from Study 2 suggest that response inhibition alone can drive transfer to socio-emotional and self-regulatory outcomes in children with dyslexia, and may be causally implicated. These findings also lend credence to suggestions

that response inhibition is a cognitive hub for a wide range of behaviours (Diamond, 2013).

For significant near and far transfer effects, larger gains were observed in the low-dose compared to the high-dose condition, which is consistent with larger direct gains in the low-dose compared to the high-dose condition (Chapter 6). Given that the low-dose experienced greater improvement in response inhibition (as indexed by larger Cohen's D in Chapter 6), it would logically flow that this group may also experience larger and further transfer to other cognitive and behavioural outcomes. Although both groups demonstrated significant transfer, the low-dose group showed greater gain (as indexed by larger Cohen's D) in updating abilities (error: 1.08, reaction time: 1.05) than the high-dose group (error:.38, reaction time: .92). The low-dose also evidenced greater transfer to improved reading ability (.74), socio-emotional outcomes (.56) and self-regulation (.61) compared to the high-dose group (reading: .38; socio-emotional: .42; self-regulation: .27). Although both groups experienced significant gain in cognitive and behavioural outcomes, the size of transfer effect for each group suggests that *low-dose training may be more effective for promoting broad transfer in children with dyslexia*.

This pattern of larger transfer in the low-dose group also emerged at the direct level of gain (as outlined in Chapter 6). Potential reasons for greater transfer in the low-dose training include more opportunities to exercise the target cognitive ability in the low-dose condition (Thorell et al., 2009), low-dose training being sufficient to induce transfer in clinically impaired groups (Jaeggi et al., 2008; Karbach & Kray, 2009; Karbach et al., 2015; Luo et al., 2013) and greater difficulty in the high-dose condition resulting in disengagement and less transfer (Jaeggi et al., 2011).

Although some studies show that children and those with clinical impairments experience more transfer from cognitive training due to room for improvement (Jaeggi et al., 2008; Karbach & Kray, 2009; Karbach et al., 2015; Luo et al., 2013), this is unlikely to be the case in the present study. If a low-dose of training is sufficient to induce transfer in children with dyslexia, then transfer effects should be larger in the high-dose training due to longer durations of training and adaptivity of the game. However, this does not play out in the

results. Instead, children in the low-dose training condition typically experienced greater transfer than those in the high-dose condition.

Mechanisms of Transfer

High-Dose Training Outside of Zone of Proximal Development

This suggests that some mechanism of the low-dose condition may promote greater transfer or some mechanisms in the high-dose condition may diminish transfer. One possibility is that the effect of transfer in the high-dose training is diminished due to steps in adaptivity being too large for children with dyslexia who may have pre-existing response inhibition difficulties. As outlined in Chapter 6, for the high-dose group, the response inhibition training adjusted difficulty based on reduced No-Go frequency and increased distracting lures, while previous research adjusted difficulty based on increased speed demands only (Benikos et al., 2013; Berkman et al., 2014b; Zhao et al., 2016). Therefore, the multidimensional increments in the difficulty of the game may have been too large for participants in the high-dose condition to completely benefit from and the low-dose training condition may have been more within dyslexic children's zone of proximal development (Vygotsky, 1978). Jaeggi et al. (2011) found that those children who found the training challenging but not too difficult demonstrated transfer (within their zone of proximal development (Vygotsky, 1978)), while those who found the game too difficult and frustrating did not demonstrate transfer (outside of their zone of proximal development (Vygotsky, 1978)). This suggests that differential difficulty level across the training conditions may influence the degree of transfer observed.

This has implications for the present study, as the high-dose of training may have been too difficult to benefit children with dyslexia who may already demonstrate response inhibition impairments. In this manner, the low-dose condition could have provided the optimal challenge for children with dyslexia by being more appropriately suited to their zone of proximal development (Vygotsky, 1978), thus promoting more transfer, while the high-dose condition may have limited transfer due to difficulty being outside of their zone

of proximal development (Vygotsky, 1978). Benikos et al. (2013) found a similar pattern suggesting that medium or low-doses of training may be more beneficial; however, they did not explore far transfer of training to other cognitive abilities or behavioural outcomes. The high-dose training did show transfer, so it is not that transfer was blocked but possibly the effect may have been reduced as the game progressed in difficulty. It may be the case that gain occurred at lower difficulty levels at the start of high-dose training and this gain may have become diluted as the game progressed in difficulty. This eventuality cannot be established within the current PhD dataset. However, a further analysis of learning curves from the training game and a method whereby training groups are tested at different intervals throughout the intervention may help determine whether gains are experienced initially but become more diluted with increased difficulty in the high-dose group. Indeed, more research is needed to understand optimal training conditions for improving response inhibition, as previous research suggests that not much is known about how to manipulate difficulty to ensure optimal transfer in response inhibition training studies (Kirk et al., 2015).

Response Inhibition Opportunity

Increased opportunity to exercise response inhibition may be one mechanism promoting transfer effects in the low-dose condition. The low-dose condition was exposed to more frequent No-Go trials, whereas exposure to No-Go trials in the high-dose condition became progressively rarer. At the outset, both conditions were exposed to a similarly high No-Go frequency rate (approx. 45%), however, this reduced to a No-Go probability of 5% towards the end of training in the high-dose condition. This initial exposure to higher No-Go frequency across both conditions may explain why both groups are experiencing significant far transfer, however it may be that the size of this transfer is greater in the low-dose training group because they were exposed to a consistently higher No-Go frequency throughout training. Therefore, this difference in opportunity to exercise the cognitive ability may be a reason for greater transfer in the low-dose compared to the high-dose condition (Thorell et al., 2009). Further research is needed to explore whether

different levels of exposure to response inhibition trials in training can result in more or less transfer. This will help further the understanding of optimal training conditions to promote transfer of response inhibition training to behavioural level improvements.

Processing Speed/ Working Memory

Given that response inhibition training transferred to improvements in working memory updating and processing speed, it may be argued that the working memory or speed demands of the response inhibition game are responsible for transfer, as some studies find working memory and processing speed, but not inhibition, to be predictive of reading ability (Christopher et al., 2012). If processing speed is the mechanism of transfer, then higher training effects should be observed for the high-dose condition where the speed demands (1,000ms) were greater than the low-dose condition (1,800ms). Although larger effect sizes were found for processing speed in the high-dose condition (-.60) compared to the low-dose condition (-.50), the low-dose condition actually demonstrated larger training transfer effects to reading, socio-emotional and self-regulatory outcomes than the high-dose - suggesting that processing speed is not the primary mechanism of transfer in the current study.

If working memory were the mechanism of transfer, then larger training effects should be observed for the high-dose condition due to increased working memory demands compared to the low-dose condition. The high-dose condition was adaptive in such a way that as a player progressed there was increased overlap between No-Go and Go targets based on the number of overlapping features between Go and No-Go targets (which served as distracting lures). For instance, a Go target could overlap with a No-Go target (e.g. a yellow trapezoid with dots) on zero features (0-F) (e.g. a green square with stripes), one feature (1-F) (e.g. a green square with dots) or two features (2-F) (a green trapezoid with dots). In the low-dose training condition, there was no overlap between Go and No-Go targets. Therefore, Go and No-Go targets were distinguishable and less information about the No-Go target had to be retained in working memory. As the high-dose training

condition adapted, the degree of overlap between Go and No-Go targets increased. This made Go and No-Go targets more difficult to distinguish and more information about the No-Go targets had to be retained in working memory to successfully respond. The high-dose training condition was more taxing on working memory abilities, yet the low-dose condition was associated with more transfer to updating, reading, self-regulation and socio-emotional outcomes suggesting that working memory is not the primary mechanism of transfer. The only other fundamental difference between high and low-dose training that could explain the transfer pattern, is that more frequent exposure to No-Go trials gave the low-dose group more learning opportunities to improve response inhibition. This pattern emerged at neural, cognitive and behavioural levels suggesting that response inhibition is the mechanism of transfer, and that low-dose training with more frequent exposure to response inhibition trials may be more effective than high-dose training at improving response inhibition abilities and promoting broad transfer.

Expectation or Motivation

Some authors suggest that even when transfer is found, it may be driven by expectation effects (Boot, Blakely, & Simons, 2011) or may be due to the motivational features of the game (Shipstead et al., 2012a). Expectation effects in the current study are unlikely as this would suggest that transfer should be similar across conditions, which is not the case for all transfer effects. In addition, expectation effects require that prior to testing, participants' can infer the hypothesis being tested, how this should manifest in the data and how they should perform relative to others (Green et al., 2014). Green et al. (2014) argue that it is unlikely that a participant would have such specific knowledge about the research design or be able to adapt abilities accordingly, especially if an impairment is present. To account for motivation effects, studies are recommended to include adaptive and non-adaptive training conditions (Shipstead et al., 2012a) and this was employed in the current study. This study accounted for the confound of motivation by including both adaptive and non-adaptive conditions, however transfer effects were still larger in the low-dose compared to the high-dose training condition. Although both conditions were matched in the type of motivation participants received, it may be the case that

participants in the low-dose group were exposed to more positive feedback (e.g. larger progress bar, more bonus points) because the game was more appropriately suited to their zone of proximal development (Vygotsky, 1978). The potentially reduced error rate and more positive feedback received by the low-dose group may have facilitated a greater sense of competence and more engagement which promoted more learning. There is no way of establishing whether the low-dose condition felt more motivated during the training intervention in the current study. One way to establish whether the low-dose training condition facilitated more motivation and feelings of competence in future studies, could be to assess participant motivation and competence at regular intervals throughout the intervention or at the end of the intervention.

Although possible mechanisms driving training transfer across conditions are discussed due to larger effect sizes in the low-dose condition, this should be interpreted with caution given that no significant time x dose interaction effects were observed at the near or far levels of transfer. As discussed in Chapter 6, without a significant interaction effect we cannot conclusively say that the low-dose group experiences more transfer than the high-dose group. In addition, given the absence of a suitably matched placebo training group (non-inhibition training), the current study cannot rule out non-specific placebo mechanisms as a possible explanation for pre-post improvements in response inhibition. Whilst the above discussion considers possible reasons for a larger effect size in the low-dose training condition and points to future research avenues which may elucidate whether response inhibition is modifiable. To draw conclusions on the effectiveness of response inhibition training in the absence of a significant dose x time interaction is limited. As outlined in Chapter 6, the response inhibition training study is underpowered to detect a significant interaction due to a small sample size. To conclude on whether response inhibition training is effective in dyslexia and results in training transfer, future research with larger sample sizes and suitable active and passive placebo groups is needed.

The present study is not without limitations. Some authors suggest that studies exploring EF training should employ an active control training intervention that does not require the

target trained cognitive process (Green et al., 2014), while others suggest that studies exploring EF training should employ a non-adaptive active control training intervention that does require the trained cognitive process (Shipstead et al., 2012a). The low-dose active control training intervention in this study also targeted response inhibition, therefore a possible limitation is that this study did not include an active control intervention which did not target the trained cognitive process (Green et al., 2014). Future studies should employ passive control, active control which does not tap the target construct, and different dose levels with altered frequency of No-Go trials in order to address whether response inhibition is modifiable and what the optimal conditions for promoting transfer from response inhibition training are.

Another limitation of this study is the possible increased likelihood of type 1 error rate due to multiple statistical testing and a small sample of participants. Although a larger sample is more ideal, this is often difficult to achieve with clinical populations such as dyslexia and a restricted age range to account for the confound of developmental improvements in EF. Therefore, to account for this limitation, the present study employed a Bonferroni correction ($p<.005$) based on *a priori* research questions while also considering trends within the data ($p<.05$). Reducing the required alpha level while also considering trends within the data allows for a relative balance between the likelihood of both type 1 and type 2 errors. Small sample sizes are also more likely to dilute transfer effects so it may be the case that training effects are more exaggerated than this research suggests (Karbach & Kray, 2009). Future studies should explore response inhibition training in dyslexia with larger sample sizes if possible. The negative impact of response inhibition training on switching abilities also suggests that not all effects from training are positive so future studies should further explore trade-offs between EFs in training and what the knock on behavioural consequences of reduced switching capacity are in dyslexia.

Overall, this study shows for the first time that response inhibition training transfers to near (updating, switching, speed) and far (reading, socio-emotional, self-regulation) outcomes in children with dyslexia. Transfer was observed in both low and high-dose

conditions; however, transfer effects were larger in the former suggesting that low-dose training is more effective for children with neurodevelopmental disorders underpinned by EF problems. This demonstrates that response inhibition is a useful intervention for ameliorating the cognitive impairments and symptoms associated with dyslexia.

Chapter 8: General Discussion

This chapter provides a general overview and discussion of the PhD. Study findings will be summarised and critically interpreted, and limitations of the research will be outlined. The theoretical and practical implications of findings will be discussed and future directions will be proposed.

8.1 PhD Rationale and Objectives

A good causal explanation of dyslexia should predict core diagnostic features (reading impairments), higher than chance comorbidity of dyslexia with ADHD and presence of non-core socio-emotional problems. Despite numerous low-level theories attempting to explain dyslexia, no clear causal pathway has been established (Pennington, 2006). Although low-level impairments are sometimes associated with dyslexia, low-level accounts of dyslexia fail to predict core diagnostic features of dyslexia (reading problems) (American Psychiatric Association, 2013), explain high comorbidity of dyslexia with ADHD (a disorder characterised by EF impairments) (Barkley, 1997), and explain the presence of non-core socio-emotional problems in dyslexia. In addition, low-level explanations are confounded by higher-level cognitive processes (such as EF, working memory and attention) which are necessary for efficient performance on tasks measuring lower-level processing capacities. EF appears to be a promising high-level causal factor which can predict core diagnostic features of dyslexia (reading problems) (Booth et al., 2014; Wang and Yang 2014), may explain comorbidity between dyslexia and ADHD (Kegel & Bus, 2013; Rommelse et al., 2009), and the presence of non-core socio-emotional problems (Wang and Yang 2014). EF can also offer promising avenues for targeted intervention in children with dyslexia, as it appears to be modifiable with training interventions (Karbach & Kray, 2009; Karbach & Schubert, 2013) which may generalise to improvements in reading ability and behavioural problems (Loosli, et al., 2012; Mezzacappa & Buckner, 2010).

Although there is compelling evidence for the promise of EF as a causal factor to be targeted in an intervention, there is variability in EF impairments associated with dyslexia, with some studies reporting EF impairments (Beneventi et al., 2010a; Brosnan et al., 2002; Helland & Asbjørnsen, 2000; Menghini et al., 2010; Moura et al., 2016) and others reporting no EF impairments (Bental & Tirosh, 2007; Bexkens et al., 2014; Peng et al., 2013). There is also debate regarding which specific aspects of EF (if any) are important for predicting core diagnostic features (reading problems). Some studies report that response inhibition and updating combined predict reading problems (Booth et al., 2014; Wang & Yang, 2014), others report that response inhibition and switching combined predict reading problems (Altemeier et al., 2008), while others fail to support the role of EF in reading problems (McGrath et al., 2011; Peterson et al., 2016). Despite the fact that EF impairments are associated with both dyslexia and ADHD (Willcutt et al., 2010), and that EF predicts dyslexia diagnosis (Booth et al., 2014; Moura et al., 2015); most studies exploring the neuro-cognitive underpinnings of comorbidity suggest that processing speed, and not EF, accounts for the overlap between dyslexia and ADHD (McGrath et al., 2011; Pennington, 2006; Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2010).

A critical review of previous literature identified inconsistent findings stemming from methodological issues such as differences in (a) screening ADHD from dyslexia alone samples, (b) lack of control for processing speed impairments, (c) theoretically informed approaches to measurement and (d) addressing disorder specific information processing. ADHD screening ranges from standardised assessment, no history of a diagnosis, to no screening, which can result in inconsistent findings as ADHD is characterised by EF impairments (Barkley, 1997) and co-occurs with dyslexia at a greater than chance rate (Willcutt & Pennington, 2000). Previous studies do not systematically control for processing speed, and this is problematic because processing speed is thought to account for comorbidity of dyslexia and ADHD (McGrath et al., 2011; Peterson et al., 2016; Willcutt et al., 2005) and can confound EF measures scored based on speed and accuracy. Additionally, the majority of studies profile EF as unitary or multiple separate abilities with complex measurement tools which require a range of EF (response inhibition, updating

and switching) and non-EF processes (Snyder et al., 2015). These approaches limit the understanding of how common (response inhibition) and unique (updating and switching) aspects of EF are compromised in dyslexia or are implicated in core and non-core symptoms (Friedman & Miyake, 2016; Miyake & Friedman, 2012; Snyder et al., 2015). Inconsistent findings may also result from the type of task content (e.g. visual versus phonemic) used across studies. Previous research suggests that dyslexia may be associated with EF impairments specific to phonemic content (Beneventi et al., 2010a; Ramus & Szenkovits, 2008), yet studies have not explored how common and unique aspects of EF manifest differently in dyslexia with general versus phonemic content.

These methodological difficulties have made it increasingly difficult to profile EFs associated with dyslexia, determine if EF can explain high comorbidity of dyslexia with ADHD and the severity of core reading and non-core socio-emotional problems in dyslexia, and which EFs to target in an intervention aimed at reducing symptom severity and ameliorating cognitive impairments associated with dyslexia. This PhD aimed to address the shortcomings of previous literature and elucidate the EF profile of dyslexia and the role of EF in core diagnostic features of dyslexia (reading problems), by employing a novel design which systematically screened for elevated ADHD, controlled for variances in processing speed, employed sensitive measures of common and unique aspects of EF, and allowed for a systematic exploration of disorder specific (phonemic) EF profile associated with dyslexia. By employing this novel approach, this PhD aimed to isolate a key aspect of EF implicated in core diagnostic features of dyslexia (reading problems) which could be further explored in a novel training intervention aimed at improving neural, EF, and symptom outcomes for children with dyslexia.

The specific objectives of this PhD were to:

1. Establish the EF profile (strengths and impairments in common: response inhibition, and unique: updating and switching abilities) associated with dyslexia and examine whether this manifests more severely in comorbid dyslexia-ADHD at the EF z-mean composite level using Miyake and Friedman's (2012) framework while controlling for individual differences in processing speed.

2. Determine whether EF profile manifests differently in dyslexia and comorbid dyslexia-ADHD with disorder specific information (phonemic content).
3. Develop and validate EF z-mean predictive models for core and non-core symptoms associated with dyslexia alone while systemically screening for potentially undiagnosed ADHD, and, controlling for individual differences in processing speed.
4. Assess whether training key EFs implicated in core and non-core symptoms of dyslexia are modifiable with cognitive and neural effects and ultimately capable of inducing change at the level of symptom expression.

8.2 Summary of Key Findings

Type and Severity of EF Impairments are Variable in Dyslexia

Overall, the findings from this PhD suggest that the EF profile (strengths and impairments in response inhibition, updating and switching) associated with dyslexia is variable. Study 1 of this PhD showed that children with dyslexia demonstrated response inhibition ($p=.004$, significant) and updating ($p=.021$, trend) impairments, and switching strengths (unimpaired) relative to an age matched neurotypical control group. However, in a separate validation study (Study 2), these response inhibition and updating impairments were not confirmed. Instead, findings from study 2 showed that children with dyslexia demonstrated a switching impairment ($p=.032$, trend), and, response inhibition and updating strengths (unimpaired) relative to an age matched neurotypical control group. The EF profile associated with dyslexia alone did not manifest more severely with disorder specific (phonemic) content, suggesting that EF is domain general in dyslexia. Although it is possible that differences in the type of EF impairments (response inhibition, updating or switching) associated with dyslexia across studies is due to changes in the number of tasks comprising the response inhibition composite score or changes in timing across all EF measures, it is also possible that the type and severity of EF impairments associated with dyslexia are variable across samples.

Previous research had suggested that dyslexia is associated with a disorder specific EF impairment (phoneme content) (Beneventi et al., 2010a; Ramus & Szenkovits, 2008), yet no study had systematically explored whether EF abilities manifest differentially with general versus disorder specific content by adapting pre-existing validated measures grounded in EF theory to include disorder specific content in dyslexia (Goschke, 2014). This PhD systematically explored general versus phonemic content across all three key EFs and found that *EF abilities manifest in a general, not a disorder specific way in dyslexia*.

From previous research, it was unclear which key aspects of EF (if any) are compromised in dyslexia, with inconsistent findings emerging for response inhibition (Bental & Tirosh, 2007; Booth et al., 2014; Brosnan et al., 2002; Marzocchi et al., 2008; Wang & Yang, 2014), updating (Beneventi et al., 2010b; Bental & Tirosh, 2007; Peng et al., 2013) and switching (Bental & Tirosh, 2007; De Lima et al., 2012; Poljac et al., 2010). This PhD isolated plausible reasons for inconsistent findings across previous literature and systematically addressed these shortcomings by excluding elevated ADHD from dyslexia alone samples, controlling for processing speed, employing sensitive composite measurements of EF constructs and exploring disorder specific EF processing. Despite our attempts to elucidate the exact EF impairments associated with dyslexia, we found inconsistencies between the EF impairments associated with dyslexia in study 1 and study 2. Although EF impairments were associated with dyslexia across both studies, the type of EF impairments (response inhibition, updating and switching) associated with dyslexia were variable across study 1 (response inhibition, updating) and study 2 (switching). In addition to variability in the type of EF impairment, there was also variability in the severity of EF impairment across study 1 (response inhibition: p=.004; updating: p=.021), and study 2 (switching: p=.021). This suggests that there may be a subtype of dyslexia associated with more severe EF impairments, or, subtypes of dyslexia characterised by different types of EF impairment.

The variability in type of EF impairment associated with dyslexia across studies may relate to trade-offs between response inhibition and switching abilities (Blackwell et al., 2014; Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015). For instance, in study 1 response inhibition and updating impairments, and, switching strengths were associated

with dyslexia. Whereas, in study 2 switching impairment, and, response inhibition and updating strengths were associated with dyslexia. This trade-off pattern emerged in our studies while using sensitive measures (z-mean composites) of each EF construct which filter out non-EF noise (Snyder et al., 2015). The majority of EF profiling studies thus far have been ill-equipped to detect such patterns as most use non-sensitive and complex EF tasks which require all three EFs and implicate non-EF processes (Snyder et al., 2015). Our findings with the EF z-mean composite approach suggest that there may be trade-off mechanisms at play in the variability of impairments associated with dyslexia. The latent variable approach remains the most suitable and sensitive approach for profiling common (response inhibition) and unique (updating, switching) aspects of EF (Friedman & Miyake, 2016; Miyake & Friedman, 2012; Snyder et al., 2015). This approach could not be employed here due to sample size constraints, but exploring the EF profile associated with dyslexia with the latent variable technique in a much larger sample size will shed light on trade-off mechanisms, variability of profile and whether there is an EF subtype of dyslexia.

Despite the noted variability across studies 1 and 2 in relation to type and severity of EF impairment(s), an important finding from this PhD is that *EF impairments are associated with dyslexia alone when systematically controlling for processing speed*. Peng et al. (2013) found that processing speed accounted for response inhibition and updating impairments in dyslexia, and, a number of other researchers suggest that processing speed is a shared impairment in dyslexia and ADHD accounting for overlap (McGrath et al., 2011; Peterson et al., 2016; Willcutt et al., 2005). While systematically controlling for potential processing speed confounds, both studies 1 and 2 found EF impairments associated with dyslexia – suggesting that EF impairments are independent of processing speed in dyslexia.

Overlap in EF Impairments Account for Comorbidity

The findings from this PhD suggest that EF is a candidate cognitive process explaining dyslexia and high comorbidity of dyslexia and ADHD. Study 1 of this PhD showed that children with dyslexia and comorbid dyslexia-ADHD demonstrate similar EF impairments. Both groups demonstrated response inhibition (dyslexia: p=.004; comorbid: p=.002) and

updating impairments (dyslexia: p=.021, comorbid: p=.006), and, switching strengths (unimpaired). In fact, both clinical groups significantly differed from an age matched neurotypical control group. However, they did not significantly differ from each other on any of the EF z-mean composites. Although, there was almost a trend for a more severe response inhibition impairment in children with comorbid dyslexia-ADHD compared to dyslexia alone, suggesting that there may be some compound effect in the Common EF (response inhibition) with dual diagnosis of dyslexia and ADHD. In addition, effect size analyses suggested that comorbid dyslexia-ADHD was associated with more severe response inhibition, updating, working memory and processing speed impairments than dyslexia alone. Both dyslexia and comorbid dyslexia were associated with a trend for processing speed impairments, however, response inhibition and updating impairments were more severe than processing speed impairments and remained so while controlling for processing speed abilities. These findings suggest that *both dyslexia and comorbid dyslexia-ADHD are characterised by the same underlying EF (response inhibition and updating) impairments.* There was almost a trend towards more severe response inhibition impairments in comorbid dyslexia-ADHD suggesting that this aspect of EF could account for overlap between dyslexia and ADHD. These findings are consistent with studies suggesting that EF is a candidate endophenotype explaining overlap between dyslexia and comorbid dyslexia-ADHD (Kegel & Bus, 2013; Rommelse, 2009).

The findings from this study support the multiple deficit hypothesis of comorbidity (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010), which suggests that each condition is associated with multiple impairments. However, multiple deficit studies thus far have typically argued that dyslexia is characterised by phonological and processing speed impairments, ADHD is characterised by response inhibition and processing speed impairments, and, therefore processing speed is a shared impairment accounting for comorbidity (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010). In contrast, the findings from study 1 suggest that common EF: response inhibition, and not processing speed, is the most severe overlapping impairment in dyslexia and comorbid dyslexia-ADHD. This study (study 1) is the first to systematically control for processing

speed abilities while exploring dyslexia and comorbid dyslexia-ADHD differences on sensitive measures of common (response inhibition) and unique (updating and switching) aspects of EF and is the first to report that response inhibition, and not processing speed explains the overlap. The profile overlapping appeared to manifest more severely in comorbid dyslexia-ADHD across each cognitive domain (with effect size analyses) and there was a trend for an additional low-level phonemic processing impairment in comorbid dyslexia-ADHD. This suggests that the comorbid group may be characterised by more severe and additional impairments like the cognitive subtype hypothesis suggests (Rucklidge & Tannock, 2002). Although it is not clear within study 1 whether additional impairments in comorbid dyslexia-ADHD are due to ADHD diagnosis as this study did not include an isolated ADHD sample.

Despite a trend for a low-level phonemic impairment in comorbid dyslexia-ADHD, study 1 also showed for the first time that response inhibition impairments manifest in a general way (no difference in severity with visual versus phonemic content) across conditions. The disorder specificity (phonemic) of updating impairments could not be assessed due to floor effects in the phonemic updating task in study 1. So, study 2 adapted the updating tasks to account for floor effects and further confirmed that updating abilities also manifest in a general way in dyslexia alone. It did not include a comorbid group to further tease out the issue of disorder specificity of updating as study 2 focused on further validating EF profile and predictive models and exploring the modifiability of EF in dyslexia alone. Although response inhibition accounts for overlap between dyslexia and ADHD in study 1, it is difficult to say whether this pattern would be found in study 2 as we didn't include comorbid dyslexia-ADHD.

The Common EF (Response Inhibition) is Clinically Relevant for Dyslexia

Despite the variability in the type of EF impairments (response inhibition, updating or switching) associated with dyslexia from study 1 to study 2, *response inhibition was shown to be consistently implicated in reading* – the core diagnostic feature of dyslexia. Study 1 of this PhD showed that response inhibition significantly predicts (p=.000) and updating demonstrates a trend (p=.021) for predicting variance in reading ability while controlling

for processing speed abilities. Consistent with the central role of response inhibition in core reading problems, study 2 of this PhD showed that response inhibition alone significantly (p=.001) predicted variance in reading ability while control for processing speed abilities. In the core reading model developed in study 1, processing speed initially explained 11.4% of the variance in reading ability. When EF processes were entered into the predictive model, processing speed was no longer a significant predictor and response inhibition was the only significant predictor of reading ability and updating demonstrated a trend for predicting reading ability. The overall model explained 45.9% of the variance in reading ability and the relationship was such that those who had a higher error rate on response inhibition and updating z-mean composites had poorer reading ability, while those who had lower error rates on response inhibition and updating demonstrated better reading ability.

In the core reading model developed in a secondary sample in study 2, processing speed initially explained 18.4% of the variance in reading ability. When EF processes were entered into the model, processing speed was no longer significant and response inhibition again was the only significant predictor of reading ability. The overall model explained 36.8% of the variance in reading ability, and the relationship was such that those with higher reaction time on the response inhibition z-mean composite (reflective of reduced efficiency) had poorer reading ability, while those with lower reaction time on the response inhibition z-mean composite (reflective of increased efficiency) had better reading ability. These confirmatory findings indicate that response inhibition is an important underlying cognitive process explaining variability in reading across the developmental trajectory from typical to atypical. Although updating demonstrated a trend for predicting reading in study 1, the role of updating in reading ability is variable in different samples of children as it played no predictive role in study 2.

The findings from this PhD are partially consistent with previous studies that report response inhibition and updating predict reading ability in neurotypical (Arrington et al., 2014; Welsh et al., 2010), and dyslexia samples (Booth et al., 2014; Wang and Yang 2014). However, by employing purer z-mean composite measures of each EF construct which

filter out non-EF noise (Snyder et al., 2015) and systematically controlling for processing speed in all predictive models, this PhD showed for the first time that *response inhibition alone is the most consistent and only significant EF predictor of reading ability*. The predictive strength of response inhibition for reading ability was stable in study 1 where it was shown to be an impairment in dyslexia and in study 2 where it was not shown to be an impairment in dyslexia, which suggests that regardless of whether response inhibition is impaired in dyslexia it underlies efficient (and inefficient) reading which is the core diagnostic feature of dyslexia.

This finding is in stark contrast with studies reporting that switching is predictive of reading ability (Cartwright, 2012) or the multiple deficit literature which suggests that although there are EF impairments in dyslexia, these are of no clinical significance as they do not predict variability in core reading features (McGrath et al., 2011; Pennington, 2006; Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2010). These studies typically find that processing speed is a key predictor of reading ability that also explains overlap of ADHD with dyslexia, yet when we systematically controlled for this in our studies, response inhibition and not processing speed emerged as the only significant predictor of reading ability. Therefore, the Common-EF (response inhibition) explains more variance in reading ability than processing speed and should be regarded as an important cognitive process implicated in the core diagnostic features of dyslexia. This finding also suggests that response inhibition is the most viable EF process to train in an intervention aimed at improving the core diagnostic features of dyslexia. Although response inhibition impairments are not consistently associated with dyslexia, response inhibition is a key predictor of variability in reading across the developmental trajectory from typical to atypical, suggesting that it plays a facilitative role in reading skills. As such, efforts to increase response inhibition may improve reading ability.

Surprisingly *EF was not found to be clinically relevant for predicting non-core socio-emotional problems* across the trajectory from typical to atypical. Non-core socio-emotional problems were consistently associated with dyslexia in study 1 and study 2, yet neither processing speed nor EF predicted variability in socio-emotional problems. This

finding is inconsistent with a wealth of literature suggesting that response inhibition is involved in socio-emotional problems (Brunnekreef et al., 2007; Albrecht et al., 2005; Kooijmans et al., 2000; Young et al., 2009). Although this suggests that EF is not implicated in socio-emotional problems associated with dyslexia, an alternative is that the relationship between EF and socio-emotional outcomes is not linear and therefore is difficult to disentangle. Eisenberg's (2005) concept of over-control suggests that those high in effortful control express internalizing problems while those with lower effortful control are under-controlled and tend to express externalizing problems. In support of this view, some studies have found that moderate levels of EF are more conducive to adaptive socio-emotional outcomes, as both reduced and enhanced EF is associated with socio-emotional problems (Carlson & Wang, 2007). In addition, others report that children with enhanced inhibitory control are more likely to have internalizing and those with impaired inhibitory control are more likely to have externalizing problems (Kooijmans et al., 2000). Our approach explored predictive relationship between EF composites and a combined measure of socio-emotional problems, given that EFs may differentially relate to internalizing and externalizing problems, an approach which explores how EF relates to internalizing and externalizing problems in dyslexia with non-linear modelling may help disentangle how EF is related to socio-emotional problems.

In addition to being the most consistent and only significant predictor of the variance in core reading features characteristic of dyslexia, response inhibition also appeared to be the only consistent aspect of EF with potential for predicting disorder likelihood. In study 1, response inhibition ($p=.008$) and updating ($p=.023$) demonstrated a trend for predicting dyslexia likelihood while controlling for processing speed. Although this predictive relationship was not confirmed in study 2, the error z- mean composite model suggested that switching almost demonstrated a trend ($p=.05$) for predicting dyslexia, and, the reaction time z-mean composite model suggest that response inhibition almost demonstrated a trend ($p=.06$) for predicting dyslexia. The response inhibition and updating predictive model developed in study 1 demonstrated good ability to classify dyslexia (sensitivity: 81.5%) and non-dyslexia participants (specificity: 75%). Although

neither model was statistically significant in study 2, both almost demonstrated a trend for predicting dyslexia after controlling for processing speed and differed with regard to successful detection of dyslexia and non-dyslexia cases. The response inhibition reaction time model was more sensitive to detect dyslexia cases (80.6%) than the switching error model (59%), while the switching error model was more specific to detect non-dyslexia cases (74.2%) than the response inhibition reaction time model (50%). Response inhibition was the only EF construct which featured in dyslexia diagnostic models across study 1 and study 2, and, appeared more sensitive to predict dyslexia cases. The reduced sensitivity of response inhibition as a predictor of dyslexia diagnosis across studies may reflect the variability of EF profile associated with dyslexia across samples.

The findings partially support previous research that shows response inhibition and updating predict dyslexia (Booth et al., 2014), and research that shows switching predicts dyslexia (Moura et al., 2015). Our study explored for the first time the strength all 3 aspects of EF for predicting dyslexia diagnosis with purer z-mean composite measures of each construct (Snyder et al., 2015) while systematically controlling for processing speed. Although a significant predictive model was developed in study 1, it wasn't confirmed in study 2, which may relate to variability in EF impairments across samples. Although, response inhibition and switching almost demonstrated a trend for predicting dyslexia in study 2, switching was not found be of clinical importance for explaining variance in reading ability and therefore would not be viable to target in an intervention aimed at improving core reading features of dyslexia. Indeed, response inhibition was the only EF construct showing a predictive pattern across both studies, suggesting that it is the most promising aspect of EF for targeting in an intervention aimed at improving reading ability in children with dyslexia.

The Common EF is Modifiable and Transfers to Improved Core and Non-Core Outcomes in Dyslexia

The findings from this PhD suggest that response inhibition is modifiable at the cognitive and neural levels in dyslexia with computerised training, and can transfer to reductions in core reading and non-core socio-emotional outcomes. Study 2 found that both high

(adaptive) and low (non-adaptive) doses of computerised response inhibition training over a 6-week period can significantly reduce reaction time on response inhibition measures (p=.000) and markedly increase the amplitude of response-inhibition related ERPs ($p < .05$). Both training groups took significantly less time on the response inhibition measures after training compared to before training, and experienced larger N2 mean amplitude for both Go and No-Go trials (p=.033) and larger P3 amplitude for both Go and No-Go trials (p=.018) post training. Both high and low-doses of training transferred to improvements in updating (p=.000), processing speed (p=.005), reading ability (p=.000), socio-emotional problems (p=.005) and self-regulatory capacity (p=.013).

The finding that response inhibition transfers to improvements at the cognitive and neural levels in children with dyslexia suggests that response inhibition is modifiable with training which results in underlying neurophysiological changes. This finding is consistent with previous research showing that response inhibition training can result in neurophysiological changes in ERPs in neurotypical groups (Benikos et al., 2013; Berkman et al., 2014; Manuel et al., 2010, 2013). However, Study 2 showed for the first time that *response inhibition training can alter the neurophysiology of children with dyslexia by increasing amplitude of N2 and P3 ERPs*. Response inhibition training significantly improved updating abilities in children with dyslexia, which supports previous theoretical frameworks which suggest that response inhibition overlaps with updating (Miyake & Friedman, 2012) and that response inhibition and updating facilitate each other (Diamond, 2013). Transfer of response inhibition training to improved reading ability in children with dyslexia provides further evidence for response inhibition being causally implicated in reading, as strengthening response inhibition resulted in significant improvements in reading ability. This finding is consistent with previous research showing that response inhibition is predictive of reading ability in dyslexia (Booth et al., 2014; Wang & Yang, 2014). Additionally, Study (2) showed for the first time that response inhibition training can transfer to improved reading ability in children with dyslexia. The finding that response inhibition training significantly improves processing speed suggests that response inhibition may contribute to processing speed, as directly strengthening

response inhibition abilities transferred to improved processing speed. However, the training intervention required to respond quickly and this speed demand may have resulted in improved processing speed.

Although no predictive relationship was found between response inhibition and socio-emotional problems in dyslexia in studies 1 and 2, dyslexia was associated with more severe socio-emotional problems compared to neuro-typical control participants (p=.000). Previous research has suggested that response inhibition is implicated in socio-emotional problems, although the relationship appears to be non-linear (Carlson & Wang, 2007; Eisenberg et al., 2005; Kooijmans et al., 2000). Response inhibition training significantly reduced socio-emotional problems in dyslexia, suggesting that although no predictive relationship was found pre-intervention, response inhibition underlies socio-emotional problems as strengthening of response inhibition transfers to reduced socio-emotional outcomes. However, it is important to note that reduced socio-emotional problems may also be a placebo effect as the measure was a parental administered questionnaire and no EF predictive relationship was found across studies 1 and 2. To address whether reduced socio-emotional problems are due to placebo effects, future studies should explore transfer of response inhibition training in dyslexia with the use of an active control group.

Study 2 also found a trend for response inhibition training negatively impacting switching with reduced efficiency after the training intervention at the individual task level (phoneme specific). This finding supports previous research suggesting that there are performance trade-offs between response inhibition and switching, as directly strengthening response inhibition led to reduced switching efficiency (Blackwell et al., 2014; Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015). The training trade-off pattern was only found at the individual task level and not at the composite level, this suggests that the pattern of trade off may not emerge at the level of switching as a process as task-level differences may also be confounded by the specific non-EF content (Snyder et al., 2015).

Future studies should further explore training trade-offs between response inhibition and switching at the latent variable level with a larger sample size of dyslexia participants (Friedman & Miyake, 2016; Miyake & Friedman, 2012; Snyder et al., 2015).

Overall, these findings indicate that response inhibition training is a useful cognitive intervention for improving a range of cognitive processes (response inhibition, updating and processing speed) and reducing reading, socio-emotional and self-regulatory problems in children with dyslexia. This suggests for the first time that response inhibition training is a useful intervention for improving the core diagnostic (reading) and non-core features (socio-emotional) of dyslexia.

Although there were no statistically significant differences in transfer effects between the high and low-dose training conditions, additional effect size analyses reflected a pattern of larger gain for the low-dose group across near (response inhibition) and far (updating, reading, socio-emotional, self-regulation) outcomes compared to the high-dose group. The most plausible explanations for differences in size of transfer are that the adaptive increments in the high-dose training made the game too difficult to promote optimal engagement and learning; or that the increased exposure to No-Go trials in the low-dose condition provided more opportunity to exercise response inhibition and these increased learning opportunities promoted more transfer. Previous research has shown that when training is too difficult, and therefore outside a child's zone of proximal development it can result in less transfer (Jaeggi et al., 2011) and low-medium levels of difficulty are more beneficial than high-levels of difficulty for improving response inhibition (Benikos et al., 2013). While others have suggested that limited exposure to No-Go trials in response inhibition may be a reason for a difficulty in observing far transfer of training (Thorell et al., 2009). In general, adaptivity of cognitive training is thought to be a pre-requisite for transfer of training (Diamond, 2014; Diamond & Ling, 2016), yet our findings suggest for the first time that this may not be the case for response inhibition training, where adapting the difficulty based on No-Go frequency may lead to less opportunities to exercise response inhibition and therefore reduced transfer. Although it is difficult to disentangle whether the increased exposure to No-Go trials in the low-dose condition

promoted larger gains or increased difficulty in the high-dose condition diminished gains, the main findings from this study point to future directions for exploring the optimal conditions for promoting transfer of response inhibition training.

Overall, findings from this PhD are also consistent with previous research showing that response inhibition training transfers to improved outcomes in pre-school and middle-aged children (Liu et al., 2015; Zhao et al., 2016), but inconsistent with those showing that response inhibition training does not transfer to improved outcomes in pre-school children and young adults (Enge et al., 2014; Thorell et al., 2009). Transfer of cognitive training in general has been previously debated due to the replication crisis confusing training efficacy (Enge et al., 2014; Harrison et al., 2013; Redick et al., 2013; Shipstead et al., 2012a; Shipstead et al., 2012b), and, explorations of transfer not being theoretically informed (Kirk et al., 2015, Shipstead et al., 2012a). Using a "theoretical approach" to transfer informed by Miyake and Friedman's (2012) unity (common EF: response inhibition) and diversity (updating and switching) model of EF, predictive relationships between the common EF (response inhibition) and reading (Booth et al., 2014; Wang and Yang, 2014) and the common EF and socio-emotional problems (Wang and Yang, 2014). For the first time, studies 2 and 2 found that response inhibition is modifiable in children with dyslexia and transfers to a range of improved outcomes at the neural (ERPs), cognitive (response inhibition, updating, processing speed) and behavioural levels (reading, socio-emotional, self-regulation).

8.3 Theoretical and Practical Implications

The findings from this program of research have implications for causal explanations of dyslexia. As outlined in Section 8.1, a good causal explanation of dyslexia should be able to predict core diagnostic features (reading problems), account for comorbidity of dyslexia and ADHD, and presence of non-core socio-emotional problems in dyslexia. Response inhibition is a candidate explanation as it consistently predicts core diagnostic features of dyslexia, accounts for comorbidity of dyslexia with ADHD and is modifiable with training transferring to improvements in core diagnostic and non-core features of dyslexia.

Findings from study 1 suggest that response inhibition is the only significant EF impairment associated with dyslexia (p=.004), demonstrates a trend for predicting dyslexia likelihood (p=.008) and is the only significant predictor of reading ability (p=.000). Even though response inhibition was not confirmed as an EF impairment associated with dyslexia in study 2, it almost demonstrated a trend for predicting clinical status (p=.06) and was the only confirmed significant predictor of reading ability (p=.001). An impairment in a cognitive ability does not necessarily mean that it is clinically relevant as we saw with the multiple deficit studies, and, a cognitive ability does not have to be impaired to be clinically meaningful. Some studies show that behavioural inhibition can predict socio-emotional problems in dyslexia despite being unimpaired (Wang & Yang, 2014), and others show that despite multiple cognitive impairments in dyslexia (speed, working memory, phonological, naming), only some impairments (speed, phonological) are clinically meaningful for predicting reading. Study 2 of this PhD found that despite no apparent response inhibition deficit in a secondary sample of children with dyslexia, targeting response inhibition abilities with training can improve reading and socio-emotional problems, and increase self-control in children with dyslexia. This suggests that despite variability of EF impairments in dyslexia, response inhibition is a good predictor of reading ability and response inhibition training can improve reading ability in dyslexia.

Although the EF profile associated with dyslexia and predictive models of dyslexia diagnosis were not confirmed across studies 1 and 2, this does not limit the impact of response inhibition as a predictor of core reading features. In fact, both EF profile and diagnostic predictive models are categorical approaches to understanding dyslexia. Categorical approaches are limited insofar as they cannot explain important neuro-cognitive processes underpinning variability in core symptoms, and, therefore, limit the development of new treatments targeted at addressing neuro-cognitive processes implicated in core symptoms (Insel, 2013). The research domain criteria (RDoC) approach introduced by the US National Institute of Mental Health suggests that neuro-cognitive processes predictive of core symptoms across the trajectory from typical to atypical can shed light on the underlying etiology of complex conditions such as dyslexia (Cuthbert &

Insel, 2013). This PhD found that response inhibition is consistently predictive of core reading symptoms across the trajectory from typical to atypical reading development, which suggests that response inhibition is implicated in the etiology of dyslexia. Approaching dyslexia in this way helped isolate response inhibition as an effective treatment route for remediating core and non-core symptoms, and, for strengthening response inhibition at the cognitive and neurophysiological levels in children with dyslexia.

The findings from this PhD point to pre-frontal brain areas as important for understanding dyslexia and reading problems, and intervention routes for strengthening these brain areas. Although the profile of EF impairments associated with dyslexia was not confirmed, response inhibition consistently predicted severity of reading problems and response inhibition training significantly improved reading ability in dyslexia. Firth's (1999) 3-level framework for exploring the neural underpinnings of dyslexia suggests that cognitive processes which are predictive of core reading behaviours can help refine the understanding of dysfunctional neural systems in dyslexia. In line with this view, our findings point to possible dysfunctional pre-frontal systems in dyslexia. Our colleague found that the neurophysiology of N2 and P3 response inhibition biomarkers were reduced in the same sample of children with dyslexia (Lonergan, 2017). Following this, our training study showed that response inhibition training can alter the neurophysiology of this same sample of dyslexia participants by increasing N2 and P3 response inhibition biomarkers. Response inhibition training effectively improved reading ability in these children with dyslexia, which suggests that dyslexia may also be associated with activation or structural differences in a range of prefrontal cortex (anterior cingulate circuit, dorsolateral circuit, orbitofrontal circuit) and other subcortical areas which are important for EF (Powell & Voeller, 2004). Previous research show that frontal areas associated with EF are underactive in children with dyslexia during working memory updating (Beneventi et al., 2010), and children with dyslexia demonstrate abnormal response inhibition-related ERPs relative to typically developing children (Liotti et al., 2010; van der Schoot et al., 2002). These response inhibition-related ERPs were markedly larger ($p<.05$) in children with dyslexia post response inhibition training intervention (compared to baseline) and

improvements in reading were also observed. Given that significant improvements were found on neural indices of response inhibition in children with dyslexia, future research should explore the underlying structural and functional differences in dyslexia during response inhibition tasks with fMRI and explore whether response inhibition training can significantly increase brain activity in prefrontal areas or result in structural alterations in children with dyslexia. Indeed, a recent review suggests that EF training may result in functional and structural neural changes (Karbach & Schubert, 2013). Given our promising findings, future studies should explore whether response inhibition results in altered brain activity in children with dyslexia and whether the strengthening of pre-frontal networks leads to improved outcomes as a function of training.

Although previous literature suggested disorder specific (phonemic) EF processing in dyslexia (Beneventi et al., 2010a; Ramus & Szenkovits, 2008), the findings from this PhD do not support disorder-specific EF processing in dyslexia. Previous research had shown that dyslexia was associated with significant impairments and reduced activation in frontal areas necessary for EF during a disorder specific (phonemic) updating task (Beneventi et al., 2010). In addition, a critical review of evidence supporting a phonological impairment in dyslexia suggested that impairments are only found on tasks requiring EF (such as manipulation, holding or updating phonemic information) (Ramus & Szenkovits, 2008). This led us to posit that perhaps dyslexia is associated with disorder specific EF impairments, however, EF abilities were found to manifest in a domain general way in dyslexia. Domain general response inhibition abilities were also the only consistent predictor of reading ability. These finding suggest that a general response inhibition underpins reading ability, and, may also underpin phonological processing in dyslexia given that impairments only emerge with EF task demands (Ramus & Szenkovits, 2008). Future studies should explore whether response inhibition and other EFs predict a wide range of phonological processing abilities in dyslexia at the latent construct level.

In terms of comorbidity between dyslexia and ADHD, the findings from this PhD suggest that response inhibition may be the cognitive mechanism by which dyslexia and ADHD overlap. Findings from study 1 indicate that children with dyslexia and comorbid dyslexia-

ADHD do not significantly differ on EF profile, however, a pattern did emerge whereby there was a trend for more severe response inhibition impairments in comorbid dyslexia-ADHD. Similarities in the underlying EF profile suggest that response inhibition may be an overlapping transdiagnostic risk factor for dyslexia and ADHD. This finding has implications for previous theories attempting to isolate cognitive risk factors which explain high comorbidity between dyslexia and ADHD. The results from this PhD do not support single deficit explanations of comorbidity such as the phenocopy hypothesis (Pennington et al., 1993). The phenocopy hypothesis (Pennington et al., 1993) suggests that dyslexia and comorbid dyslexia-ADHD are characterised by phonological and not EF impairments, and that overlap with ADHD occurs due to the frustrations with reading resulting in attentional problems. In conflict with this view, the findings from the first study of this PhD suggest that EF impairments are characteristic of dyslexia and comorbid dyslexia-ADHD.

These findings support multiple deficit explanations of comorbidity such as the cognitive subtype hypothesis (Rucklidge & Tannock, 2002) and the multiple deficit hypothesis (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010). The cognitive subtype hypothesis (Rucklidge & Tannock, 2002) suggests that comorbid dyslexia-ADHD is associated with more severe and additional impairments than either isolated condition, while the multiple deficit hypothesis suggests that both conditions are associated with multiple distinct and overlapping impairments which may explain comorbidity (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010). Although it is difficult to disentangle the source of impairments in the comorbid group due to no ADHD alone group in our design, the findings are in support of a multiple shared cognitive deficits in dyslexia and comorbid dyslexia-ADHD such as response inhibition, updating, processing speed, and working memory capacity, which is in support of the multiple deficit hypothesis (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010). However, there was almost a trend for more severe response inhibition impairments and a trend for additional phonemic processing impairments in comorbid dyslexia-ADHD compared to dyslexia alone which is arguably in support of a cognitive subtype explanation (Rucklidge & Tannock, 2002). It is difficult to determine whether these impairments would be present in ADHD alone or of

the same level of severity in ADHD alone, which suggests that future research should explore EF in all four groups with our methodological approach.

Although our findings support multiple deficits in dyslexia and comorbid dyslexia-ADHD (McGrath et al., 2011; Pennington, 2006; Willcutt et al., 2010), there is some conflict between multiple deficit explanations of comorbidity and the findings of this PhD. For instance, Willcutt et al. (2010) found that although there are multiple deficits associated with dyslexia, ADHD and comorbid dyslexia such as response inhibition, working memory and processing speed, only some cognitive processes are clinically relevant for predicting dyslexia (working memory, phonological processing, processing speed, verbal reasoning) and ADHD (response inhibition and processing speed). Similarly, McGrath et al. (2011) found that phonological processing is a unique predictor of reading, response inhibition is a unique predictor of attention problems and working memory and processing speed are shared and overlapping predictors of both. These studies consistently suggest that EF is not clinically relevant for dyslexia, yet the first study of this PhD suggests that EF is impaired and may play a role in comorbidity of dyslexia with ADHD, and EF (particularly response inhibition) is clinically relevant for predicting dyslexia diagnosis and core reading ability. Despite variability in the extent to which EFs were found to be impaired in dyslexia in study 2, response inhibition was consistently found to be a key predictor of variance in reading ability. This was found even while accounting for processing speed, which is thought to be the strongest candidate cognitive process explaining overlap between dyslexia and ADHD (McGrath et al., 2011; Pennington, 2006; Peterson et al., 2016; Shanahan et al., 2006; Willcutt et al., 2010). From our findings in study 1, it appears that response inhibition is a stronger candidate factor than processing speed for explaining overlap of dyslexia with ADHD and predicting reading ability. Our findings also support other reports that suggest that response inhibition is clinically relevant for reading (Booth et al., 2014; Wang & Yang, 2014).

Previous research has also linked dyslexia and ADHD at the genetic level via genes important for developing prefrontal dopamine receptors crucial for the development of EF (Kegel & Bus, 2013), suggesting that EF may be a good explanatory framework for self-

regulatory behaviours (Crosbie et al., 2008; Friedman et al., 2008; Rommelse et al., 2009), ADHD (Castellanos & Tannock, 2002; Rommelse et al., 2009) and may explain overlap between ADHD and dyslexia (Rommelse et al., 2009). However, from previous research it was unclear whether dyslexia is associated with EF impairments (Bental & Tirosh, 2007; Moura et al., 2015; Peng et al., 2013; Poljac et al., 2010), let alone whether EF was an endophenotype for dyslexia. Addressing potential reasons for inconsistent findings, this PhD indicates that although there is variability in the type and severity of EF impairments associated with dyslexia across studies 1 and 2, response inhibition is consistently predictive of core reading ability. Although the findings from study 1 strengthen the role of response inhibition as a possible transdiagnostic factor implicated in dyslexia and comorbid dyslexia-ADHD. The non-confirmed profile of EF impairment associated with dyslexia make it difficult to determine which aspects of EF are candidate endophenotypes for dyslexia and comorbidity with ADHD (Gottesman and Gould, 2003). However, our findings do suggest that response inhibition is an important aspect of EF underpinning reading, response inhibition training can improve reading and response inhibition in study 1 is the most promising aspect of EF accounting for overlap of dyslexia with ADHD. This suggests that response inhibition may be a candidate endophenotype associated with dyslexia and ADHD.

No study to date has explored EF as an endophenotype in dyslexia alone or whether it is a shared endophenotype for dyslexia and ADHD at the latent construct level. Although our findings across studies 1 and 2 did not confirm the EF profile of dyslexia alone, dyslexia participants in study 1 had more severe EF impairments than dyslexia participants in study 2, which suggests that EF may be an endophenotype for a subgroup of children with dyslexia. The findings from this PhD suggest that response inhibition is a promising causal factor for core diagnostic features of dyslexia (reading) and for overlap of dyslexia with ADHD. However, an EF endophenotype study exploring whether the same EF impairments are associated with dyslexia and unaffected siblings to a greater degree than the general population will help elucidate the role of EF as a candidate endophenotype. Employing the most sensitive latent EF variable measures in line with Miyake and Friedman's (2012)

approach may shed more light on which aspects of EF (if any) are an endophenotype for dyslexia.

If response inhibition is an endophenotype mediating the gene symptom pathway of dyslexia, then this has implications for early detection and early intervention in those at risk. EF abilities appear to be a necessary cognitive pre-requisite for learning to read (Gooch et al., 2016; Thompson et al., 2015), demonstrate high heritability (Friedman & Miyake, 2016), are sensitive for detecting prodromal disorder phases in at risk populations and are linked to severity of functional outcome (Glahn et al., 2014, 2016; Goschke, 2014; Miller & Rockstroh, 2013; Snyder et al., 2015). High heritability rates suggest that the EF system may be an early warning sign for risk of developing dyslexia or ADHD. As such, early detection approaches could profile children at risk of inheriting EF impairments when entering school and administer appropriate interventions to boost EF abilities to aid with acquisition of reading skills. Given our evidence that response inhibition can improve reading ability in dyslexia even in the absence of an impairment, children at risk for developing dyslexia due to their parents having a diagnosis could also be given early response inhibition interventions to strengthen their abilities. Such an approach may prevent children at genetic risk ever receiving a diagnosis of dyslexia. In such a way, abnormal trajectories in reading development could be prevented with targeted EF intervention prior to symptom expression. Early detection of EF impairment may also be useful for prevention and early intervention with a range of other EF related conditions such as OCD, autism, schizophrenia, mania, personality disorder and substance abuse (Robbins et al., 2012).

The findings from this PhD also have implications for approaches to profiling EF in dyslexia and other psychological conditions, as it appears that EF operates in a strengths and impairments manner and should not be profiled with complex EF measures. Extensive research within cognitive psychology suggests that EF is comprised of related (common EF: response inhibition) yet separable (specific EFs: updating and switching) abilities (Friedman & Miyake, 2016; Miyake & Friedman, 2012), that are most sensitively measured at the latent (Friedman et al., 2007, 2008; Friedman & Miyake, 2016; Miyake et al., 2000;

Miyake & Friedman, 2012) or z-mean composite level when sample sizes do not suffice (Snyder et al., 2015). The common EF (response inhibition) appears to overlap with specific aspects of EF in different directions, for instance response inhibition and updating appear to have compatible demands and therefore have a facilitative interaction, inhibition can protect the contents of working memory from distractor interference and increase attentional focus, thereby enhancing the ability to correctly update information in working memory (Friedman & Miyake, 2017; Miyake & Friedman, 2012). Response inhibition and switching on the other hand appear to have incompatible demands and therefore have an antagonistic relationship, inhibition facilitates focus by shielding information from irrelevant distractors in a top down manner (provides stability), while switching requires interference from distractors to consider alternative options and to flexibly adapt to changing demands (mental flexibility) (Blackwell et al., 2014; Friedman & Miyake, 2016 Goschke, 2000; Gruber & Goschke, 2004; Snyder et al., 2015). This suggests that EF profiles may emerge in a strengths and impairments pattern. However, there is a lack of transfer of knowledge on how EF operates from cognitive psychology to informed explorations of EF profiles associated with psychological conditions in clinical psychology (Snyder et al., 2015).

Using a method of exploring EF abilities in dyslexia informed by advances in cognitive psychology (Friedman & Miyake, 2016; Miyake & Friedman, 2012; Snyder et al., 2015) and using the most appropriate means of assessing EF with sample size constraints by employing EF z-mean composite scores (Snyder et al., 2015), study 1 found evidence to support this strengths and impairments pattern in executive functioning. In the first profiling study both dyslexia and comorbid dyslexia-ADHD were associated with impairments in response inhibition and a trend for impairments in updating, yet both conditions were associated with unimpaired switching abilities. There was a trend for more severe response inhibition impairments in comorbid dyslexia-ADHD, and although not significant, the comorbid dyslexia-ADHD condition had reduced switch costs relative to control participants suggesting that as response inhibition abilities reduce switching abilities may benefit. This suggests that in some conditions with more severe response

inhibition impairments there may be spared or somewhat improved switching abilities. In study 2, there was a trend for impaired switching in dyslexia and now a pattern of unimpaired response inhibition and updating abilities which is consistent with facilitative/antagonistic patterns of EF. Most interestingly, directly targeting response inhibition with training in dyslexia resulted in a trend for reduced switching abilities and significantly improved updating abilities, providing further evidence for this strengths and impairments pattern of EF which emerges due to how unique aspects of EF (updating and switching) are compatible/incompatible with the demands of the common EF (response inhibition).

This has implications for measures used to explore EF impairments across a wide range of clinical conditions, a range of studies view EF as a unitary ability or multiple separate unrelated abilities measured with complex EF tasks (Snyder et al., 2015). Complex EF tasks such as the Wisconsin Card Sort Task are limited tools as they lack specificity in detecting which aspects of EF are impaired as fluid performance taxes all EF processes and a number of non-EF processes (Snyder et al., 2015). These measures also fail to address theoretical advances in EF inter-relations, suggesting that the common EF (response inhibition) may be a help (updating) or a hindrance (switching) to specific aspects of EF (Blackwell et al., 2014; Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015). Findings from this PhD partially support this view, a strengths and impairments pattern may emerge across a range of conditions, yet most methodological approaches are not equipped to capture such interactions if they are present. Future research should explore EF implication in dyslexia and other psychological conditions at the level of latent variables as they provide more specific and purer measurements than EF z-mean composites, and thus can provide more detailed information on the strengths and impairments pattern of EF abilities in dyslexia.

This strengths and impairments pattern in EF abilities may also have implications for behaviours associated with dyslexia and other psychological conditions. If a response inhibition impairment operates like a double edge sword, such that more severe response inhibition impairments may lead to switching strengths, this then may have some

explanatory power for understanding strengths and impairments at the behavioural level. At the behavioural level, dyslexia is characterised by impairments in reading (diagnostic criteria), and socio-emotional control (Dahle et al., 2011; Heiervang et al., 2001; Knivsberg & Andreassen, 2008; Mugnaini et al., 2009). Yet, dyslexia also appears to be associated with strengths in innovative thinking and creativity (Everatt, Steffert, & Smythe, 1999; Tafti, Hameedy, & Baghal, 2009; Wolff & Lundberg, 2002). Viewing these behaviours within an EF framework may enhance the understanding of how strengths and impairments at a behavioural level are underpinned by strengths and impairments at a cognitive level. This research study suggests that response inhibition is predictive of reading abilities in dyslexia, and previous research suggests that it also plays a role in socio-emotional problems in dyslexia (Wang & Yang, 2014). While enhanced switching may provide an explanation for better creative skills in dyslexia as the uninhibited brain often leads to more creative and innovative thinking (Carson, 2011; White & Shah, 2006). Therefore, viewing dyslexia within an EF framework may provide an explanation for reading and self-regulatory behaviours as well as enhanced creative skills. Future research should explore how EF strengths and impairments impact behavioural outcomes in dyslexia using latent variable methods.

The findings PhD also have implications for the modifiability of response inhibition abilities in general and for targeted treatment aimed at improving functional outcomes for children with dyslexia and a range of other clinical conditions.

Prior to this study, response inhibition training remained unexplored as a targeted intervention aimed at ameliorating cognitive deficits and improving symptoms in children with dyslexia. From previous research it was unclear whether response inhibition abilities were modifiable. Although direct improvements were observed at the cognitive and neural levels (Benikos et al., 2013; Berkman et al., 2014), it was unclear whether response inhibition training could transfer to untrained cognitive or behavioural outcomes, with evidence both for (Liu et al., 2015; Spierer et al., 2013; Zhao et al., 2016) and against transfer effects (Enge et al., 2014; Thorell et al., 2009). Exploring transfer of response inhibition training with a theoretically informed design, this PhD found that response

inhibition training directly altered neural and cognitive indices of response inhibition, transferred to improved updating abilities which may be due to shared variance and compatible demands (Friedman & Miyake, 2016; Miyake & Friedman, 2012) and reduced switching abilities which may be due to incompatible demands (Friedman & Miyake, 2016; Goschke, 2000; Snyder et al., 2015). Training effects transferred to improved reading ability, reduced socio-emotional problems and increased capacity for self-regulation, as response inhibition is predictive of reading, socio-emotional problems (Wang & Yang, 2014) and appears to be necessary for effective self-regulation and socio-emotional wellbeing (Bridgett et al., 2013; Carlson & Wang, 2007; Diamond, 2013; Eisenberg et al., 2009; Friedman et al., 2008; Rueda et al., 2005; Snyder et al., 2015). These findings suggest that response inhibition may be a useful intervention for inducing broad gains in children with dyslexia.

Both adaptive high-dose and non-adaptive low-dose interventions resulted in significant transfer to all domains, however, low-dose transfer effects were larger as indexed by Cohen's d effect sizes, suggesting that low-dose training may be more useful for children with dyslexia. These findings have implications for how response inhibition is most effectively trained. Previous research has suggested that adaptive training interventions are more effective than non-adaptive training intervention for improving working memory (Melby-Lervaag & Hulme, 2013; Peng & Miller, 2016; Schwaighofer et al., 2015), yet this may not be the case for response inhibition training.

The transfer effects may be partially diminished in the high-dose training condition due to adaptive steps being too large for children with dyslexia benefit from. Jaeggi et al. (2011) found that subjective perception of difficulty resulted in different levels of transfer, those who found the game too difficult and frustrating (outside their zone of proximal development) did not demonstrate transfer while those who found the training moderately challenging demonstrated transfer. It may be the case that the lower level of difficulty in the low-dose condition could have provided the optimal challenge for children with dyslexia to benefit from, while the high-dose training condition may have limited transfer due subjective challenge. Increased exposure to No-Go trials in the low-dose

condition may also explain larger transfer effects (Thorell et al., 2009). Further research is needed to explore the optimal conditions for promoting transfer of response inhibition training. However, it appears that regardless of what is driving transfer, low-dose training is more beneficial for children with dyslexia.

The finding of modifiability of response inhibition which transfers to a range of behavioural outcomes in children with dyslexia, also has implications for response inhibition training in neurotypical children and a range of conditions characterised by response inhibition impairments. Response inhibition training transferred to outcomes even when the sample of children with dyslexia were not clinically impaired compared to neurotypical participants. This suggests that the effects may be similar in children without dyslexia, and as such response inhibition training could be used to enhance children's cognitive, reading and self-control abilities or could be explored as an educational intervention. A previous critical review of training studies suggests that working memory training is the most explored type of training for promoting academic outcomes such as math, spelling and reading ability (Titz & Karbach, 2014). Yet, most of the studies explore the effectiveness of working memory training with learning disabilities or cognitive impairments, and, train multiple types of working memory which can make it difficult to isolate the cognitive factors promoting change (Morrison & Chein, 2011; Titz & Karbach, 2014). This PhD found that isolated response inhibition training can improve reading, reduce socio-emotional problems and increase self-control in children with dyslexia without a response inhibition impairment. Therefore, response inhibition may also be effective in children without dyslexia for improving children's reading ability, attentional focus and classroom behaviour. In addition to the educational applications, response inhibition training could be used to ameliorate the response inhibition impairments associated with a wide range of clinical conditions such as schizophrenia, autism, substance abuse, personality disorder, and mania (Robbins et al., 2012). Future studies, should further explore response inhibition training as an educational intervention aimed at improving academic outcomes in children and as a clinical intervention aimed at improving symptom expression in a range of response inhibition-related conditions.

8.4 Future Directions

Although this PhD addressed the EF profile associated with dyslexia and whether this differed from comorbid dyslexia-ADHD, it cannot address whether the EF profile is additive or more severe in relation to dyslexia and ADHD alone, as an ADHD alone group was not included. A design with dyslexia alone, ADHD alone and comorbid dyslexia-ADHD is optimal for teasing out the source of impairments in the comorbid group and for assessing shared risk factors, however, it could not be implemented in this PhD due to difficulties in recruiting ADHD alone and subsequent sample size issues. Therefore, future research should explore the profile of EF impairments associated with dyslexia alone, ADHD alone and comorbid dyslexia-ADHD using sensitive measures of each EF construct while controlling for processing speed to address whether the profile of impairments in the comorbid group is an additive combination or a more severe profile than either condition alone. Future research should also explore whether EF (particularly response inhibition) is implicated at the endophenotype level in dyslexia alone and whether it is a transdiagnostic endophenotype explaining overlap between dyslexia and ADHD.

The current PhD explored EF in dyslexia and comorbid dyslexia-ADHD with EF z-mean composite scores which are sensitive for measuring common (response inhibition) and unique (updating and switching) aspects of EF when sample sizes are limited (Snyder et al., 2015). A more sensitive approach to measuring common and unique aspects of EF is with latent variables (Miyake & Friedman, 2012; Snyder et al., 2015). Future research should explore EF impairments, and predictive relationships between symptom severity and EF processes in children with dyslexia and comorbid dyslexia-ADHD at the latent variable level and with larger sample sizes to more reliably isolate whether specific or common aspects of EF are implicated in reading ability. Research should also explore the impact of strengths and impairments of EF profile (measured by latent variables) on a range of behavioural outcomes in dyslexia such as reading, socio-emotional regulation and enhanced creativity and problem solving. As well as exploring the predictive relationship between EF composites and behavioural outcomes such as reading ability, future studies

should incorporate other cognitive process which are shown to be important into predictive models.

The current Study 2 found that both low-dose and high-dose response inhibition training transferred to a broad range of cognitive and behavioural outcomes in dyslexia, however it did not include a passive control or an active control group who did not train on response inhibition. It is also unclear what the optimal conditions underpinning larger transfer effects in the low-dose condition were. Therefore, future studies should also explore optimal conditions for promoting transfer of response inhibition training in children with dyslexia using a combination of passive control, active control not trained on the cognitive process, and different dose and adaptivity levels with altered No-Go frequency to understand the best approaches for modifying response inhibition abilities. Negative impacts of response inhibition training should also be explored in future research as well as what the behavioural consequences of trade-offs between EFs are from training interventions. Future studies should also explore whether response inhibition training can improve symptoms in a range of conditions associated with response inhibition impairments.

8.5 Conclusion

The findings of this PhD provide evidence that response inhibition abilities are implicated in the reading issues associated with developmental dyslexia. Findings also indicate that response inhibition is a candidate overlapping cognitive ability for explaining why dyslexia and ADHD so frequently co-occur. Response inhibition abilities also appear to be modifiable with training resulting in direct improvements at neural and cognitive levels which transfer to improvements in updating, processing speed, reading ability, socio-emotional problems and self-regulation abilities in children with dyslexia. This suggests that response inhibition training may be a useful intervention that could be used to target symptoms and behavioural difficulties frequently observed in dyslexia. Low-dose training interventions were found to be more effective, which suggests that those with pre-existing impairments may benefit more from low-level training.

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Appendix A: DCU Research Ethics Approval for Experiments 1-5 (Study 1 and 2)

Appendix A (i). Ethics approval for study 1

Ollscoil Chathair Bhaile Átha Cliath
Dublin City University

DCU

Ms Caoilainn Doyle
School of Nursing and Human Sciences

15th October 2014

REC Reference: **DCUREC/2014/167**

Proposal Title: **Executive Function in Dyslexia, Attention Deficit Hyperactivity Disorder (ADHD) and Comorbid ADHD-Dyslexia**

Applicants: Ms Caoilainn Doyle, Dr Lorraine Boran, Dr Geraldine Scanlon, Prof. Alan Smeaton

Dear Caoilainn,

Further to expedited review, the DCU Research Ethics Committee approves this research proposal. Materials used to recruit participants should note that ethical approval for this project has been obtained from the Dublin City University Research Ethics Committee. Ethical approval is subject to authorisation from the participating Schools. Should substantial modifications to the research protocol be required at a later stage, a further submission should be made to the REC.

Yours sincerely,

DCU
Research & Innovation

Dónal O'Mathúna

Dr. Donal O'Mathuna
Chairperson
DCU Research Ethics Committee

Taighde & Nuálaíocht Tacaíocht
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Appendix A (ii). Ethics approval for study 2

Ollscoil Chathair Bhaile Átha Cliath
Dublin City University

DCU

Ms Caoilainn Doyle
School of Nursing and Human Sciences

14th December 2015

REC Reference:	**DCUREC/2015/254**
Proposal Title:	**Executive Function Training in Developmental Dyslexia**
Applicants:	**Ms Caoilainn Doyle, Dr Lorraine Boran, Ms Aoife Lonergan, Dr Jessica Bramham, Dr Geraldine Scanlon, Prof Alan Smeaton, Dr Robert Whelan, Dr David Delaney**

Dear Caoilainn,

Further to ethical review, the DCU Research Ethics Committee approves this research proposal. Should substantial modifications to the research protocol be required at a later stage, a further amendment submission should be made to the REC.

Yours sincerely,

Dónal O'Mathúna

DCU Research & Innovation

Dr. Donal O'Mathuna
Chairperson
DCU Research Ethics Committee

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Appendix B: Child and Parent Information Sheets Study 1

(i) Child Information Sheet

Hello There

Would you like to take part in a very cool research project?! This sheet gives you information on the project. Once you have read it and talked to your mum or dad about it, you can decide if you would like to take part!

What do we want to find out?

We want to find out if playing our computer games is related to how well you do your school work and how you behave in class.

Why are we doing this?

We want to help understand children who might have some difficulty learning in school because they have attention problems (also called ADHD) or problems reading (also called dyslexia)

Why you?

We need children your age (10-12years old) to be a part of this research because we feel that it is important to help understand why children have difficulty with their school work and behaviour.

Who are we?

We are a team of researchers from Dublin City University: Caoilainn, Lorraine, Geraldine and Alan. Wow- we are a big group!

What are we asking you to do?

We are asking you to play some computer puzzle games, and do some school work like reading.

Where?

If you want to take part in our research, you will come to our computer lab in the School of Nursing and Human Sciences, at Dublin City University.

What will happen if you choose to take part?

At the session, you will be given a computer on which to complete the computer game puzzles. The visit will be about 2 hours, but we will have lots of breaks – promise! We will not be grading you; we just want you to do your best. We hope you'll have fun taking part.

Do you have to take part?

No. If you do not want to take part, that's fine. If you are not sure about taking part, take your time to decide. Talk to your parents or carers or come to our information evening with your parents on Dec 10th

Can you change your mind about taking part?

Of course! If, at any time, you don't want to take part anymore, just tell us or tell your parents or carers. Nobody will be cross with you.

What happens when the research ends?

We will use the information from this research project to write a report on how solving these computer game puzzles relates to school work and school behaviour.

Thank You!

Thank you for reading this- feel free to ask us any questions you need to.

If you have any questions, or want more information about our research project, you can talk to Caoilainn or Lorraine – your parent has the phone number and email addresses for both!

(ii) Parent Information Sheet

Dear Parent/Guardian,

We are presently undertaking a research study as part of a PhD programme being conducted by Caoilainn Doyle, examining Executive Function (EF) in children with Dyslexia, Attention Deficit Hyperactivity Disorder (ADHD), and co-occurring Dyslexia/ADHD (where a diagnosis of both has been made). The executive function system acts like the brain's CEO or conductor and serves to coordinate and regulate the activity of other brain areas. As such it underpins a range of higher order thinking abilities including our ability to order our thoughts and handle incoming new information, inhibit inappropriate thoughts and behaviours, and our capacity for mental flexibility.

The EF study will:

- help us understand the extent to which different aspects of executive function are affected in children with Dyslexia alone, ADHD alone or co-occurring Dyslexia-ADHD.
- help us discover how the executive function system relates to reading ability and behaviour in dyslexia, ADHD and co-occurring Dyslexia/ADHD

Thank you for taking the time to read about our exciting study,
With very best wishes,
Yours sincerely,
Caoilainn Doyle

Parental Information Sheet

About The Study

The Executive Function study is a new, collaborative study between researchers in the Schools of Nursing and Human Sciences, Education and Computing in DCU. The study will investigate how executive function is related to Dyslexia alone, Attention Deficit Hyperactivity Disorder (ADHD) alone, and a combination of both (also called comorbid ADHD/Dyslexia).

The executive function system acts like the brain's CEO or conductor and serves to coordinate and regulate the activity of other brain areas. As such it is responsible for complex thinking processes including our ability to order our thoughts, handle incoming information, inhibit (prevent) inappropriate thoughts and behaviours, and our capacity to rapidly adapt to changing situations (mental flexibility). The executive function system also plays a role in social behaviour (for example how much time is spent playing and socialising with friends), emotional behaviour (for example tendency to argue or cry a lot) and academic performance (for example performance on math problems, and fluent reading ability). Problems with the executive function system are associated with a range of psychological conditions such as Dyslexia, ADHD, and Autism Spectrum Disorder (ASD). Although problems with executive functioning are documented in Dyslexia and ADHD alone cases, the executive function profile (strengths and weaknesses) of each condition alone and the co-occurring condition (diagnosis of both dyslexia and ADHD) remain unknown.

How useful the executive function system is in explaining (1) behaviours such as the tendency to socialise with other children (social behaviour), (2) behaviours such as the tendency to argue and cry (emotional behaviour), and (3) fluent and effortless reading ability in Dyslexia alone, ADHD alone, or co-occurring Dyslexia/ADHD is unknown. Executive function is important for fluent reading ability; however, it is not fully understood if executive function problems are at the core of reading difficulties in Dyslexia, ADHD and co-occurring Dyslexia/ADHD. Problems with executive function can also explain the social and emotional behavioural difficulties in ADHD. There is evidence of social (lack of socialising and poor peer relationships) and emotional (tendency to experience more negative moods) behavioural difficulties in dyslexia. However, it is not well understood if executive function is at the core of these social and emotional difficulties in Dyslexia and co-occurring Dyslexia/ADHD.

This Executive Function study will:

- help us understand the extent to which executive function plays a role in Dyslexia alone, ADHD alone and co-occurring Dyslexia/ADHD;
- help us discover how executive function may explain differences in behaviour (social and emotional) and reading ability in Dyslexia alone, ADHD alone and co-occurring Dyslexia/ADHD.

Why is this study important?

Different psychological conditions are associated with different patterns of deficits in executive functioning (strengths and weaknesses). This observation is important because the severity of deficits is typically strongly linked to the severity of symptoms, or impact, of the disorder. It is unclear from previous research if executive function is related to Dyslexia, ADHD and co-occurring Dyslexia/ADHD, and if differences in executive function can explain differences in reading ability and social and emotional behaviours in Dyslexia, ADHD and co-occurring Dyslexia/ADHD.

This study will use computerised measures of executive function, which compare performance on processing language versus images.

By examining executive function in this way, we will be able to determine:

- The usefulness of this approach for understanding differences and similarities between Dyslexia, ADHD and Co-occurring Dyslexia/ADHD
- How executive function relates to social and emotional behaviour and reading ability in Dyslexia, ADHD and co-occurring Dyslexia/ADHD

How does the study work?

The EF study will take place in the School of Nursing and Human Sciences in Dublin City University.

We invite:

- Your child to complete a 2 hour psychological testing session (with breaks) in one of our psychology laboratories
- You to complete a brief child behaviour rating scale and demographics questionnaire

Below we outline this framework in more detail:

The psychological testing sessions will take place during a 2-hour session separated by a number of breaks supervised by one of our research team in DCU. You (parent) will be invited to sit in on the testing session as well. You will also be invited to fill out a child behaviour checklist that involves answering questions about your child's social and emotional behaviours. This checklist is a pen and paper questionnaire and you will not be asked to discuss your child's behaviour in detail.

Are there any risks involved?

There are no known risks associated with participation in this study, apart from fatigue or boredom. However, a member of our research team will explain the study to you and your

child, and answer questions as they arise. Also, you will have an opportunity to meet the research team on 14th or 28th of January at one of our information evenings prior to the commencement of the study (if you choose to attend).

When will the results of the study be published?

We aim to present our initial findings as a publication and conference paper in 2015.

Confidentiality

All participant information collected in this study is treated in the strictest of confidence to the extent permitted by laws and regulations such as those described under The Child Protection Act. While it is not anticipated that any concerns could arise from participation in the study, the procedures set out by DCU under their Child Protection policy will be followed under any such instance.

All participant data will be used exclusively for research purposes. Participant data will be fully anonymised (e.g. it will not be possible to identify participants) in any scientific publication.

The data collected from your child will include his/her age, gender, reaction time and responses on computerised tasks. The data collected from you (parent) will include responses made on a child behaviour scale. Participant information will be stored separately from the signed consent form. Data will be held on a password protected computer stored in a locked office at DCU, with backup of data and any written material stored in a locked filing cabinet. In accordance with standard research data management practices, data belonging to you and your child will be securely retained for 5 years in Dublin City University after the study is completed; and will then be shredded (hardcopy) and deleted (softcopy). This material will not be used in future unrelated studies without obtaining further specific permission from you.

This study will be run with the approval of DCU Research Ethics Committee.

Where can I find more information?

For more details on what the study will involve contact Caoilainn Doyle at: caoilainn.doyle96@mail.dcu.ie, 017006868, or Dr Lorraine Boran (supervisor) at: lorraine.boran@dcu.ie, 017007923.

If participants have concerns about this study and wish to contact an independent person, please contact: *The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000.*

Appendix C: Parent Consent and Child Assent Forms Study 1

(i) Child Assent Form

Child Assent Form

Project Title: Executive function in Dyslexia, ADHD and Co-occurring Dyslexia-ADHD Study

Investigators: The study will be carried out by Lorraine Boran and Caoilainn Doyle from the School of Nursing and Human Sciences, Dublin City University (contact 01-7007923 lorraine.boran@dcu.ie; 017006868 caoilainn.doyle96@mail.dcu.ie), Geraldine Scanlon from the School of Education Studies, and Alan Smeaton from the School of Computing, Dublin City University.

Please circle your response to the following statements

- I have read and understand the information on this sheet YES NO
- The researchers have answered my questions and concerns YES NO
- I have a copy of this assent form YES NO
- I understand that by signing this form I will be included in the research YES NO
- I understand that I can stop the study at any time by telling the researchers or tell my parents to tell the researchers YES NO

Students Signature: _____
Name in Block Capitals: _____
Witness Signature: _____
Name in Block Capitals: _____
Date: _____

(ii) Parent Consent Form

Parental Consent form

Project Title: Executive function in Dyslexia, ADHD and Co-occurring Dyslexia-ADHD Study

Investigators: The study will be carried out by Lorraine Boran and Caoilainn Doyle from the School of Nursing and Human Sciences, Dublin City University (contact 01-7007923 lorraine.boran@dcu.ie; 017006868 caoilainn.doyle96@mail.dcu.ie), Geraldine Scanlon from the School of Education Studies, and Alan Smeaton from the School of Computing, Dublin City University.

Please circle your response to the following statements

- I have read and understand the attached information sheet YES NO
- The researchers have addressed my questions and concerns YES NO
- I have received enough information about this study YES NO
- I understand that my child has assented to participating in this study YES NO
- I understand that my child is free to withdraw at any point YES NO
- I agree for my child to take part in this study YES NO
- I understand that I will supervise my child during the testing session YES NO
- I understand that I will be asked to complete a questionnaire YES NO

Parents Signature: _____

Name in block capitals _____

Date _____

Appendix D: Child and Parent Information Sheets Study 2

(i) Child Information Sheet Control Participants

Hello There

Would you like to take part in a very cool research project?! This sheet gives you information on the project. Once you have read it and talked to your mum or dad about it, you can decide if you would like to take part!

What do we want to find out?

We want to find out if there are differences in how the brain works while playing our computer game puzzles in people with and without reading difficulties (also called dyslexia).

Why are we doing this?

We want to help understand why people with dyslexia have difficulties with reading and behaviour.

Why you?

We need children your age (10-12years old) to be a part of this research because we feel that it is important to help children who have difficulty with reading and behaviour.

Who are we?

We are a team of researchers from Dublin City University: Caoilainn, Lorraine, Geraldine and Alan; University College Dublin: Aoife, Jessica; and Maynooth University: Richard. Wow we are a big group!

What are we asking you to do?

We are asking you to come to DCU to play some computer game puzzles while you wear a special cape that records your brain activity.

Where?

If you want to take part in our research, you will come to our computer lab in the School of Nursing and Human Sciences at Dublin City University.

Do you have to take part?

No. If you do not want to take part, that's fine. If you are not sure about taking part, take your time to decide. Talk to your parents or carers.

Can you change your mind about taking part?

Of course! If, at any time, you don't want to take part anymore, just tell us or tell your parents or carers. Nobody will be cross with you.

Thank You!

Thank you for reading this- feel free to ask us any questions you need to. If you have any questions, or want more information, you can talk to Caoilainn or Aoife- your parent has the phone number and email address for both!

What will happen if you choose to take part?

At the session, you will be given a computer on which to complete the computer game puzzles.

During two of our puzzles you will also get to wear our cap which records your brain (it's called an EEG cap). Here is a picture of the cap.

This cap has special sensors which record what your brain is doing while you play our games. The special sensors pick up electrical signals in your brain. These signals are hard to pick up sometimes, so we also use some gel which helps the sensors pick up the signals. This gel will be in your hair while you play our games. When you are finished playing our games your parent/guardian can wash the gel from your hair in our washroom.

The visit will be about 40 minutes. We will not be grading you; we just want you to do your best. We hope you'll have fun taking part.

What happens when the research ends?

We will use the information from this research project to write a report on what the brain does when people with and without dyslexia play our puzzles.

(ii) Child Information Sheet Dyslexia

Hello There

Would you like to take part in a very cool research project?! This sheet gives you information on the project. Once you have read it and talked to your mum or dad about it, you can decide if you would like to take part!

What do we want to find out?

We want to find out if playing our computer game for 6 weeks can improve how well you do your school work (e.g. reading), how well you behave and how your brain works.

Why are we doing this?

We want to see if our computer game can help improve reading and behaviour in children who have difficulty in school because of reading problems (also called dyslexia).

Why you?

We need children your age (10-12years old) to be a part of this research because we feel that it is important to help children who have difficulty with school work and behaviour.

Who are we?

We are a team of researchers from Dublin City University: Caoilainn, Lorraine, Geraldine and Alan; University College Dublin: Aoife, Jessica; and Maynooth University: Richard. Wow we are a big group!

What are we asking you to do?

We are asking you to come to DCU to play some computer game puzzles and do some school work like reading. For some of the computer game puzzles we will ask you to wear a special cap that records what your brain is doing.

After your first visit we will ask you to play our computer game for 6 weeks online at home while your parents supervise.

After the 6 weeks we will invite you back to DCU to play some computer game puzzles, do some school work and wear the cap again.

Where?

If you want to take part in our research, you will come to our computer lab in the School of Nursing and Human Sciences at Dublin City University twice (once before the 6 weeks and once after).

You will play our computer game for 6 weeks online at home while your parents supervise.

Do you have to take part?

No. If you do not want to take part, that's fine. If you are not sure about taking part, take your time to decide. Talk to your parents or carers.

Can you change your mind about taking part?

Of course! If, at any time, you don't want to take part anymore, just tell us or tell your parents or carers. Nobody will be cross with you.

What will happen if you choose to take part?

At the first session, you will be given a computer on which to complete the computer game puzzles.

During two of our puzzles you will also get to wear our cap which records your brain (it's called an EEG cap). Here is a picture of the cap.

This cap has special sensors which record what your brain is doing while you play our games. The special sensors pick up electrical signals in your brain. These signals are hard to pick up sometimes, so we also use some gel which helps the sensors pick up the signals. This gel will be in your hair while you play our games. When you are finished playing our games your parent/guardian can wash the gel from your hair in our washroom.

The visit will be about 2 hours, but we will have lots of breaks – promise! We will not be grading you; we just want you to do your best. We hope you'll have fun taking part.

Then you will complete our computer game for 6 weeks at home.

After the 6 weeks, you will come back to our computer lab and do the same games as the first session.

What happens when the research ends?

We will use the information from this research project to write a report on how playing our computer games improves your school work and behaviour.

Thank You!

Thank you for reading this- feel free to ask us any questions you need to. If you have any questions, or want more information, you can talk to Caoilainn or Aoife- your parent has the phone number and email address for both!

(iii) Parent Information Sheet Control Participants

E-Fun Study

About The Study

The Executive Function (E-Fun) study is a new, collaborative study between researchers in the Schools of Nursing and Human Sciences, Education and Computing in DCU, and researchers in the School of Psychology in UCD and NUIM. The study will investigate executive function, brain activation, reading ability and self-control in children with and without dyslexia.

The executive function brain system is like the brain's CEO or conductor as it coordinates and controls the activity of other brain areas. It is responsible for many complex mental abilities such as our ability to order information in memory (also called working memory updating), prevent/stop inappropriate thoughts or behaviours (also called inhibition or impulse control) and our ability to rapidly adapt to changing situations (also called mental flexibility).

The executive function brain system also plays a role in how we control our behaviour and emotions (also called self-control) and in academic performance (for example performance on math problems and fluent reading ability). Problems with executive function are often associated with dyslexia and appear to be related to reading and self-control difficulties.

However, the exact profile of executive function (strengths and weaknesses in working memory updating, inhibition and mental flexibility) associated with dyslexia and how it is related to reading and self-control difficulties is not clear from previous research. Also, differences in brain activation between children with and without dyslexia while performing executive function tasks is unknown. Exploring brain activation differences may enhance our understanding of how executive function is related to reading and self-control difficulties in dyslexia.

This study will:

- Help us understand if different aspects of executive function are affected in children with dyslexia compared to children without dyslexia
- Help us understand how executive function relates to reading ability and self-control behaviour in children with and without dyslexia
- Help us understand the brain bases of executive function in children with dyslexia compared to children without dyslexia
- Help us understand how the brain bases of executive function relates to reading ability and self-control behaviour in children with and without dyslexia

Why is this study important?

Different psychological conditions are associated with different patterns of deficits in executive functioning (strengths and weaknesses). This observation is important

because the severity of deficits is typically linked to the severity of symptoms. Executive function appears to play a role in the symptom severity of dyslexia. However, it is unclear from previous research which aspects of executive function (updating, inhibition, mental flexibility) are affected in dyslexia (at a brain and behaviour level) and how this relates to differences in reading and self-control behaviour in children with and without dyslexia.

This study will examine performance of children with and without dyslexia on a range of measures of executive function, reading ability and self-control. During two measures of executive function brain activation will be recorded to further explore the link between executive function, reading and self-control abilities in children with and without dyslexia. This will allow us to determine if brain level measures of executive function can enhance our understanding of reading and self-control difficulties in children with and without dyslexia.

How does the study work?

The study will take place in the School of Nursing and Human Sciences at Dublin City University.

This study will involve:

- Your child completing a 2 hour assessment session (with breaks) in the School of Nursing and Human Sciences at DCU.
- You completing a number of questionnaires about your child's self-control behaviour in the School of Nursing and Human Sciences at DCU.

Below we outline this framework in more detail:

The assessment will take place during a 2 hour session separated by a number of breaks at the School of Nursing and Human Sciences at DCU. During this 2 hour session your child will complete a number of computerised measures of executive function (inhibition, working memory updating and mental flexibility) and a measure of reading ability. Your child's brain activation will be recorded while completing some of the executive function measures using EEG technology.

EEG technology records electrical activity in the brain in response to a task being completed. The technology is non-invasive, pain free and there are no risks associated. EEG recording involves fitting a cap with electrodes (which pick up electrical activity) to your child's head. We will also apply some gel to your child's head once the cap is on, the gel helps the electrode to record electrical activity in the brain. At the end of the EEG brain activation recording your child will have some water soluble gel in their hair and there are hair washing facilities provided on site at DCU if you would like to wash your child's hair at the end of the session.

During the 2 hour session you (parent/guardian) will be asked to complete a number of questionnaires on your child's behaviour. These questionnaires are pen and paper measures and you will not be asked to discuss your child's behaviour in detail. You will be asked to indicate the extent to which statements apply to your child on a likert scale (numbers indicating level of agreement), examples of statements are: "Can't concentrate, can't pay attention for too long"; "Likes taking care of other people";

"Runs or climbs when he/she is not supposed to." For copyright reasons we do not enclose questionnaires in this letter. You (parent/guardian) will be requested to sit in on the testing session for child safety and protection reasons.

Are there any risks involved?

There are no known risks associated with participation in this study, apart from fatigue, boredom or discomfort during EEG recording due to gel being in hair. If your child experiences discomfort you can notify a member of the research team and you and your child are free to withdraw from the study at any point. A member of the research team will explain the study to you and your child and answer questions as they arise.

When will the results of the study be published?

We aim to present our study findings as a publication and conference paper in late 2016/early 2017.

Confidentiality

All the information collected in this study is treated in the strictest of confidence. It will be used exclusively for research purposes. Participant data will be fully anonymised in any scientific publication. We ensure proper safeguards so that participation is confidential and data are securely stored and protected. This study will be run with the approval of DCU Research Ethics Committee (DCUREC/2015/254).

In accordance with standard research data management practices data belonging to you and your child will be securely retained for 5 years in Dublin City University after the study is completed. This material will not be used in future unrelated studies without obtaining further specific permission from you.

Where can I find more information?

For more details on what the study will involve contact Caoilainn Doyle at (Phone: 017006868, Email: caoilainn.doyle96@mail.dcu.ie) or Aoife Lonergan (Phone: 0873669288, Email: aoife.lonergan@ucdconnect.ie)

If participants have concerns about this study and wish to contact an independent person, please contact:

The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000.

(iv) Parent Information Sheet Dyslexia

E-Fun Study

About The Study

The Executive Function Training study is a new, collaborative study between researchers in the Schools of Nursing and Human Sciences, Education and Computing in DCU, and researchers in the School of Psychology in UCD. The study will investigate if executive function training can improve reading ability, self-control and brain activation in children with developmental dyslexia.

The executive function brain system is like the brain's CEO or conductor as it coordinates and controls the activity of other brain areas. It is responsible for many complex mental abilities such as our ability to order information in memory (also called working memory updating), prevent/stop inappropriate thoughts or behaviours (also called inhibition or impulse control) and our ability to rapidly adapt to changing situations (also called mental flexibility).

The executive function brain system also plays a role in how we control our behaviour and emotions (also called self-control) and in academic performance (for example performance on math problems and fluent reading ability). Problems with executive function are often associated with dyslexia and appear to be related to reading and self-control difficulties.

The executive function system is modifiable, with training interventions resulting in improvements in executive function, behaviour and academic outcomes in children. However, the usefulness of such interventions is mixed with uncertainty whether training induced improvements translate into improvements in behaviour (such as reading and self-control).

How useful executive function training is in: (1) improving executive function, (2) improving symptom expression, and (3) increasing brain activation is in dyslexia is unknown.

This Executive Function Training study will:

- help us understand if executive function can be improved in dyslexia with training
- help us understand if executive function training can improve symptom expression in dyslexia

Why is this study important?

Different psychological conditions are associated with different patterns of deficits in executive functioning (strengths and weaknesses). This observation is important because the severity of executive deficits is typically strongly linked to the severity of

symptoms. Executive function appears to pay a role in the symptom expression of dyslexia. Executive function may be improved with training interventions and may result in improved symptom expression. However, the usefulness of executive function training at improving symptom expression in dyslexia remains unknown.

This study will examine the usefulness of a 6 week computerised executive function (inhibition) training intervention in improving executive function, brain activation and symptom expression in dyslexia.

By examining executive function training, we will be able to determine:

- The usefulness of this intervention in improving executive function and brain activation in dyslexia
- The usefulness of this intervention in improving symptom expression in dyslexia

How does the study work?

<u>The E-FUN training study will take place in the School of Nursing and Human Sciences at Dublin City University and online training will be completed at home by your child.</u>

This study will involve:

- Your child completing a 2 hour assessment session (with breaks) in the School of Nursing and Human Sciences at DCU before the training intervention commences.

- You completing a number of questionnaires about your child's behaviour in the School of Nursing and Human Sciences at DCU before the training intervention commences.

- Your child playing the E-FUN training game online for 6 weeks (30 minutes 3 times per week) at home under parental supervision.

- Your child completing a 2 hour assessment session (with breaks) in the School of Nursing and Human Sciences at DCU at the end of the training intervention.

- You completing a number of questionnaires about your child's behaviour in the School of Nursing and Human Sciences at DCU at the end of the training intervention.

Below we outline this framework in more detail:

The pre and post intervention assessment will take place during a 2 hour session separated by a number of breaks at the School of Nursing and Human Sciences at DCU. During this 2 hour session your child will complete a number of computerised measures of executive function (inhibition, working memory updating and mental

flexibility) and a measure of reading ability. Your child's brain activation will be recorded while completing some of the executive measures using EEG technology.

EEG technology records electrical activity in the brain in response to a task being completed. The technology is non-invasive, pain free and there are no risks associated. EEG recording involves fitting a cap with electrodes (which pick up electrical activity) to your child's head. We will also apply some gel to your child's head once the cap is on, the gel helps the electrode to record electrical activity in the brain. At the end of the EEG brain activation recording your child will have some water soluble gel in their hair and there are hair washing facilities provided on site at DCU if you would like to wash your child's hair at the end of the session.

During the 2 hour session you (parent/guardian) will be asked to complete a number of questionnaires on your child's behaviour. These questionnaires are pen and paper measures and you will not be asked to discuss your child's behaviour in detail. You will be asked to indicate the extent to which statements apply to your child on a likert scale (numbers indicating level of agreement), examples of statements are: "Can't concentrate, can't pay attention for too long"; "Likes taking care of other people"; "Runs or climbs when he/she is not supposed to." For copyright reasons we do not enclose questionnaires in this letter. You (parent/guardian) will be requested to remain on site at DCU for the duration of the testing session for child safety and protection reasons.

After the initial assessment session, your child will be required to complete a 6 week (30 minutes 3 times per week) executive function (inhibition) training intervention online in your home under parental supervision. A username and log in details will be provided to you at the end of the initial assessment and the intervention will be outlined in detail. Due to the nature of this study, participants can be randomly allocated to a high or low dose training group. Both doses involve a Go No-Go inhibition training game, in the high dose the game will be more difficult than in the low dose.

Upon completion of the 6 week intervention you and your child will be invited back to the School of Nursing and Human Sciences at DCU to complete the same 2 hour assessment session as before the training commenced.

Are there any risks involved?

There are no known risks associated with participation in this study, apart from fatigue, boredom or discomfort during EEG recording. If your child experiences discomfort you can notify a member of the research team and you and your child are free to withdraw from the study at any point. A member of the research team will explain the study to you and your child and answer questions as they arise.

When will the results of the study be published?

We aim to present our study findings as a publication and conference paper in early-late 2017.

Confidentiality

All the information collected in this study is treated in the strictest of confidence. It will be used exclusively for research purposes. Participant data will be fully anonymised in any scientific publication. We ensure proper safeguards so that participation is confidential and data are securely stored and protected. This study will be run with the approval of DCU Research Ethics Committee (DCUREC/2015/254).

In accordance with standard research data management practices data belonging to you and your child will be securely retained for 5 years in Dublin City University after the study is completed. This material will not be used in future unrelated studies without obtaining further specific permission from you.

Where can I find more information?

For more details on what the study will involve contact Caoilainn Doyle at (Phone: 017006868, Email: caoilainn.doyle96@mail.dcu.ie) or Aoife Lonergan (Phone: 0873669288, Email: aoife.lonergan@ucdconnect.ie)

If participants have concerns about this study and wish to contact an independent person, please contact:

The Secretary, Dublin City University Research Ethics Committee, c/o Research and Innovation Support, Dublin City University, Dublin 9. Tel 01-7008000.

Appendix E: Parent consent and child assent forms study 2

(i) Child Assent Form Control

Child Assent Form

Project Title: Executive function Study

Investigators: This study will be carried out by Caoilainn Doyle from the School of Nursing and Human Sciences, Dublin City University (contact: 017006868 caoilainn.doyle96@mail.dcu.ie) and Aoife Lonergan (contact: 0873669288 aoife.lonergan@ucdconnect.ie) from the School of Psychology, University College Dublin.

Please circle yes if you agree with the following statements and sign your name below if you want to take part in this research project.

- I have read and understand the information on this sheet YES NO
- The researchers have answered my questions and concerns YES NO
- I have a copy of this assent form YES NO
- I understand that by signing this form I will be included in the research YES NO
- I understand that I can stop the study at any time by telling the researchers or tell my parents to tell the researchers YES NO

Students Signature: _____
Name in Block Capitals: _____
Witness Signature: _____
Name in Block Capitals: _____
Date: _____

(ii) Child Assent Form Dyslexia

Child Assent Form

Project Title: Executive function (E-FUN) Training Study

Investigators: This study will be carried out by Caoilainn Doyle (contact: 017006868 caoilainn.doyle96@mail.dcu.ie) from the School of Nursing and Human Sciences, Dublin City University and Aoife Lonergan (contact: 0873669288 aoife.lonergan@ucdconnect.ie) from the School of Psychology, University College Dublin.

Please circle yes if you agree with the following statements and sign your name below if you want to take part in this research project.

- I have read and understand the information on this sheet YES NO
- The researchers have answered my questions and concerns YES NO
- I have a copy of this assent form YES NO
- I understand that by signing this form I will be included in the research YES NO
- I understand that I can stop the study at any time by telling the researchers or tell my parents to tell the researchers YES NO
- I understand that my parent or guardian will supervise me while I play the brain training game YES NO

Students Signature: _____
Name in Block Capitals: _____
Witness Signature: _____
Name in Block Capitals: _____
Date: _____

(iii) Parental Consent Form Control

Parent Consent Form

Project Title: Executive function Study

Investigators: This study will be carried out by Caoilainn Doyle from the School of Nursing and Human Sciences, Dublin City University (contact: 017006868 caoilainn.doyle96@mail.dcu.ie) and Aoife Lonergan (contact: 0873669288 aoife.lonergan@ucdconnect.ie) from the School of Psychology, University College Dublin.

Please circle your response to the following statements

- I have read and understand the attached information sheet YES NO
- The researchers have addressed my questions and concerns YES NO
- I have received enough information about this study YES NO
- I understand that my child has assented to participating in this study YES NO
- I understand that my child is free to withdraw at any point YES NO
- I agree for my child to take part in this study YES NO
- I understand that I will supervise my child during the testing session YES NO

Parents Signature: _____
Name in block capitals _____
Date _____

(iv) Parental Consent Form Dyslexia

Parent Consent Form

Project Title: Executive Function (E-FUN) Training Study

Investigators: This study will be carried out by Caoilainn Doyle (contact: 017006868 caoilainn.doyle96@mail.dcu.ie) from the School of Nursing and Human Sciences, Dublin City University and Aoife Lonergan (contact: 0873669288 aoife.lonergan@ucdconnect.ie) from the School of Psychology, University College Dublin.

Please circle your response to the following statements

- I have read and understand the attached information sheet YES NO
- The researchers have addressed my questions and concerns YES NO
- I have received enough information about this study YES NO
- I understand that my child has assented to participating in this study YES NO
- I understand that my child is free to withdraw at any point YES NO
- I agree for my child to take part in this study YES NO
- I understand that I will supervise my child during the testing session YES NO
- I understand that I will be asked to complete a questionnaire YES NO
- I understand that I will supervise my child during their training intervention online at home YES NO

Parents Signature: _____
Name in block capitals _____
Date _____

Appendix F: Group Differences at Task Level Study 1

	Dyslexia V Comorbid			Comorbid V Control			Comorbid V Dyslexia		
Measure	**F/U**	***Df***	**P**	**F**	***Df***	**P**	**F/U**	***Df***	**P**
Stroop RT effect	.061	1,53	.807	3.79	1,41	.058	4.02	1,39	.052
Stroop err. effect	U=282	Z=-1.8	.071	U=138	Z=-1.98	.048*	U=179.5	Z=-.61	.545
Pic. GNG % Comm.	8.50	1,52	.005**	7.60	1,40	.009*	.652	1,39	.424
Pic. GNG RT	2.47	1,53	.122	.17	1,40	.682	3.19	1,39	.082
Phon. GNG % Comm.	2.59	1,53	.114	4.26	1,41	.045*	1.89	1.39	.177
Phon. GNG RT	2.63	1,53	.111	.624	1,41	.434	.136	1,39	.715
SART % Comm.	5.91	1,53	.019*	10.94	1,41	.002*	3.68	1,39	.062
SART RT	.35	1,53	.554	3.86	1,41	.056	3.08	1,39	.087
Inhibition Comp	9.29	1,52	.004**	11.55	1,40	.002**	3.54	1,39	.067
Let. 2-back % error	15.41	1,53	.000**	13.00	1,41	.001**	.041	1,39	.840
Let. 2-back RT	1.37	1,53	.247	6.85	1,41	.012*	1.35	1,39	.252
Pic. 2-back % error	3.88	1,53	.054	25.75	1,41	.000**	5.21	1,39	.028*
Pic. 2-back RT	U=353	Z=-.63	.268	U=162	Z=-1.37	.160	U=141	Z=-1.61	.106
Phon. 2-back % error	.003	1,53	.957	.155	1,41	.696	.154	1,39	.697
Phon. 2-back RT	1.71	1,53	.197	20.05	1,41	.000**	9.88	1,39	.003**
Updating Comp	5.68	1,53	.021*	8.49	1,41	.006*	.61	1,39	.440

	Dyslexia V Comorbid			Comorbid V Control			Comorbid V Dyslexia		
Measure	**F/U**	***Df***	**P**	**F**	***Df***	**P**	**F/U**	***Df***	**P**
Num-Let SW err. Cost	1.13	1,53	.293	.000	1,41	.998	1.17	1,39	.295
Num-Let SW RT cost	1.16	1,53	.286	.814	1,41	.372	.000	1,39	.994
Phon. SW err. cost	.266	1,53	.608	.026	1,41	.872	.135	1,39	.715
Phon. SW RT cost	2.07	1,53	.156	8.08	1,41	.007*	2.85	1,39	.099
Switch Comp.	.131	1,53	.719	.011	1,41	.918	.20	1,39	.657

Appendix G: Core Reading Predictive Model Control and Dyslexia Alone Study 1

Linear Regression Model Predicting Reading Ability Dyslexia Alone

	Reading Ability Across Groups				
	B	SEB	β	F/T-Value	P
Step 1				.201	.658
Constant	32.01	6.53			
Processing speed	.357	.795	.089	.448	.658
Step 2				2.71	.07
Constant	34.11	6.32			
Processing speed	.249	.759	.062	.329	.745
Response inhibition	-7.56	2.99	-.461	-2.52	.019*
Updating	-.846	2.08	-.081	-.407	.688
Switching	-2.036	1.89	-.233	-1.22	.235

Note Step 1: R^2=.008, ; Step 2: R^2 =.275. *p<.05, **p<.004.

Linear Regression Model Predicting Reading Ability Control Alone

	Reading Ability Across Groups				
	B	SEB	β	F/T-Value	P
Step 1				2.85	.103
Constant	41.51	5.48			
Processing speed	.954	.565	.314	1.67	.103
Step 2				2.31	.088
Constant	45.52	5.54			
Processing speed	.091	.650	.030	.140	.890
Response inhibition	-5.60	2.88	-.403	-1.94	.064
Updating	-4.16	2.17	-.373	-1.91	.069
Switching	-.195	2.29	.016	-.085	.933

Note Step 1: R^2=.099 ; Step 2: R^2 =.287. *p<.05, **p<.004.

Appendix H: Group Differences Task Level Study 2

	Dyslexia V Control		
Measure	**F**	***Df***	**P**
Pic. GNG % Comm.	.488	1,51	.488
Pic. GNG RT	3.50	1,51	.067
Phon. GNG % Comm.	1.72	1,51	.196
Phon. GNG RT	.545	1,51	.464
Let. 2-back % error	.423	1,51	.158
Let. 2-back RT	1.23	1,51	.272
Pic. 2-back % error	.518	1,52	.475
Pic. 2-back RT	.134	1,52	.715
Phon. 2-back % error	.101	1,52	.752
Phon. 2-back RT	.161	1,52	.690
Num-Let Switch cost error	3.60	1,51	.06
Num-Let Switch cost RT	.068	1,51	.796
Phon Switch cost error	5.13	1,51	.028*
Phone Switch RT	1.12	1,51	.293

Appendix I: Core Reading Predictive Model Control and Dyslexia Alone Study 2

Linear Regression Model Predicting Reading Ability Dyslexia Alone

	Reading Ability Across Groups				
	B	SEB	β	F/T-Value	P
Step 1				4.14	.051
Constant	26.6	5.81			
Processing speed	1.35	.663	.354	2.035	.051
Step 2				1.88	.143
Constant	30.89	6.70			
Processing speed	.960	.730	.251	1.315	.200
Response inhibition	-2.54	2.01	-.276	-1.27	.216
Updating	-.242	2.32	-.023	-.104	.918
Switching	2.59	1.86	.265	1.39	.177

Note Step 1: R^2=.125, ; Step 2: R^2 =.225. *p<.05, **p<.005.

Linear Regression Model Predicting Reading Ability Control

	Reading Ability Across Groups				
	B	SEB	β	F/T-Value	P
Step 1				5.878	.025*
Constant	39.94	5.72			
Processing speed	1.38	.568	.477	2.43	.025*
Step 2				5.58	.005**
Constant	41.07	5.66			
Processing speed	1.19	.576	.413	2.07	.054
Response inhibition	-3.29	.989	-.569	-3.327	.004**
Updating	.188	1.464	.023	.129	.899
Switching	-1.77	1.56	.-212	-1.14	.270

Note Step 1: R^2=.227, ; Step 2: R^2 =.568. *p<.05, **p<.005.