# A

# **Transdiagnostic Profile of Executive Function in Children**

# with Neurodevelopmental Conditions



A thesis submitted in fulfilment of the requirements for the degree of

Doctor of Philosophy

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2024

#### Acknowledgements

#### Bismillah al-rahman al-rahim

All my successes and accomplishments are inspired by my faith in my religion. I am forever grateful for the immense kindness and opportunities I am bestowed. Alhamdulillah.

I am incredibly grateful and proud of the work poured into this area of research. Working with children is a great joy of mine and to be able to contribute to, and further an important area of research that furthers our understanding of neurodevelopmental conditions in children is a

#### great honour.

There are so many people I want to acknowledge for their support and kindness as I progressed through one of the most challenging milestones in my life. Firstly, I would like to thank my primary supervisor, Adam Guastella for his support as I traversed this PhD during COVID and beyond. I truly appreciate all the support, guidance and encouragement shown throughout this journey, it would not have been possible without this support. I would also like to extend my thanks to Dr Eleni Demetriou and Dr Kelsie Boulton, my secondary supervisors for proof reading, providing statistical support and cheering me on as I navigated complex PhD landmarks. To Carter, I appreciate all your coding support, you have always been patient and am grateful for everything I have learnt from you. Eleni and Carter, I really appreciate all the meetings we had and the support you provided as we entered and exited many COVID restrictions. I also want to extend my thanks to Zahava Ambarchi for making sure I stayed grounded and encouraging me to make it to the finish line.

To the funding body, the Cerebral Palsy Alliance. I am honoured to have conducted research with the support of this wonderful organisation. As a sibling to a brother with cerebral palsy, this organisation is a familiar face and am grateful to the grant committee for their

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unwavering support. Prof Nadia Badawi, thank you for being available to chat via email and assisting me in getting this PhD through the final stages.

To the team at CAN, Clinic for Autism and Neurodevelopmental Research, thank you for supporting me, cheering me on and providing ad hoc support as I needed. It was a pleasure to

work with a kind and supportive group of enthusiastic researchers.

To the hardworking team at the Child Developmental Unit at Westmead Children's Hospital, your hard work in assessing the most vulnerable members of our community has paved the way for so many children to get the help they need and further the impact of research. Thank you to you all, with special mention of Dr Antoinette Hodge, your assistance in data collection was pivotal and you assisted me greatly in organising the collection process. To Dr Natalie Silove and Dr Natalie Ong, thank you for allowing me to slot myself into clinics for data collection and providing feedback and support.

My gratitude extends to my family. You have all fostered a thirst for knowledge, ambition and nurtured my perseverance, which allows me to get up every day and complete the most challenging yet rewarding chapter of my life. To my parents, for your kindness and prayers, thank you for your love and unconditional support. You entered this country with nothing to your name, you worked hard for your children to educate themselves in this country for a better life, amidst some very challenging situations. Thank you for being proud and standing up for our values and fostering hard work within myself. I am thankful for your struggle and honoured to dedicate this to you. To my siblings, Zaineb, Ismail, Khadija and Abu Bakar, a special thanks for servicing my car, lending me your TV/movie streaming passwords so I can engage in self-care, checking in and listening to me rant on about research topics that probably bored you. This thesis is dedicated to the struggle we had to make our place in this country. The hard work poured into

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this thesis is dedicated to our struggle and it is an honour to have our family name contribute to academia.

To my amazing friends, Rhonda, Sarah, Mariana and Sophia. I think I manifested an army of brave, warm women, because you have been the exact the kind of love and connection I have needed as I completed this PhD. Rhonda, you have been the rock I needed as I went about writing this thesis, the regular catchups we had to get me over the line has been immensely useful, you have always been my cheerleader. I am grateful for you and can't wait to share so much more with you. Sarah, you made sure I engaged in self-care and made sure my heart was always full and lighter with our check-ins. Mariana, you are my soul-sister from Brazil. I appreciate the random phone calls, listening to me cry, laugh and vent about all thing's life. I appreciate you and want to share so many adventures with you. Sophia, you cheered me on and paid for endless dinner dates and have been there for me during some tough house moves. Thank

#### you, my beautiful friend.

I extend my gratitude to many other friends and family, who supported me throughout this journey. Also, a shoutout to Samrah who helped me use her office space to make final edits to the thesis.

Last but not least, my pet parrot, Bubbles, even though you understand none of what mum does, I adore you and thank you for being very quiet as mum was on zoom meetings. I love you little one.

### **Declaration of Originality**

This thesis is submitted to the University of Sydney in fulfilment of the requirement for the Higher Degree of Doctor of Philosophy.

The work presented in this thesis is to my best knowledge and belief, original except as acknowledged in the text. I hereby declare that I have not submitted this material, either in full or in part for a degree at this or any other institution.

Ayesha Khan Sadozai PhD Candidate 29 February 2024

## **Research Funding obtained during Candidature:**

## **Cerebral Palsy Alliance**

Postgraduate Research Scholarship Grant Number PHD00320

#### **COVID-19 Impact Statement**

The extended closure of physical access to the University campus, and subsequently University research partners, namely, Westmead Children's Hospital, over a period of several months due to COVID-19 restrictions meant that we could not access the clinical population until a much later point of this PhD project. This resulted in some challenges in data collection and target sample sizes as originally intended. Nevertheless, due to the considerable efforts by the research team and the University to ameliorate these restrictions through off-site research-based tasks initially, and subsequent PhD extensions, sufficient sample sizes were obtained to ensure adequate power for chapters three and four of this thesis.

#### A Note on Neuroaffirming Terminology

This doctoral thesis seeks to delve into the multifaceted nature of autism and other neurodevelopmental conditions, exploring the diverse presentations and challenges of children within this spectrum as well as children with other neurodevelopmental conditions, with a key focus on executive functioning. Autism Spectrum Disorder (ASD), as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), encompasses a range of behaviours characterised by persistent deficits in social communication and social interaction across multiple contexts, along with restricted, repetitive patterns of behaviour, interests, or activities. The exploration of ASD in this thesis will be grounded in the diagnostic framework provided by the DSM-5, ensuring a consistent and clinically relevant foundation. Where relevant, the thesis refers to the term, ASD the acronym used to describe the condition 'Autism Spectrum Disorder' which is specifically referring to the diagnostic criteria from the DSM-5. This work acknowledges that the vast majority of the autistic community has a preference for identity-first language, as it emphasises the integral role that autism plays in their identity and challenges the notion of autism as merely a diagnostic label. DSM-IV-TR terminology is also used as well as identity first language were appropriate in acknowledgment of the diverse use of terminology in both diagnostic and as well as in neuroaffirming contexts. In addition to autism, this thesis will investigate other neurodevelopmental conditions, recognising the often-comorbid nature of these disorders and the need for a comprehensive understanding of their interconnectedness, with a focus on executive function. Conditions such as Attention Deficit Hyperactivity Disorder (ADHD) and Specific Learning Disorders such as Dyslexia, among others, will be examined for their overlapping characteristics and distinct features. The goal is to provide a nuanced perspective that

acknowledges the complexity of neurodevelopmental conditions and their executive function profiles.

This research is underpinned by a commitment to person-centred and respectful language, following the guidelines and preferences articulated by the autistic community and other advocacy groups. This research examines challenges children with neurodevelopmental conditions face and extends beyond a deficit-focused lens to highlight the unique strengths and capabilities of autistic individuals and those with other neurodevelopmental conditions. By examining aspects such as executive functioning (EF), this thesis will emphasise and explore where traits are advantageous, thus contributing to and challenging the prevailing deficit narrative in autism research (Chapter 4). This approach incorporates diverse insights from autistic researchers which encourages reflection among non-autistic researchers, promoting a balanced perspective that values the lived experiences of neurodiverse individuals and respects diversity of opinion.

#### **Authorship Attribution Statement**

Chapter 2 of this thesis is currently under second round review with Nature Human Behaviour as a systematic review and meta-analysis of executive function in children with neurodevelopmental conditions. Prof Adam Guastella, Dr Eleni Demetriou and I collaborated on the protocol design and development of this study and subsequent manuscript. I was involved in data collection and extraction, guided closely by Prof Guastella and Dr Demetriou. I analysed the data and wrote the draft manuscript. A/Prof Amit Lampit and PhD student Carter Sun provided considerable support in coding, data analysis and interpretation and the production of statistical figures. Prof Guastella, Dr Demetriou, and other co-authors reviewed and provided substantial input in finalising the manuscript for submission.

The study described in Chapter 3 was supported by several people. Prof Adam Guastella, Dr Boulton and I designed the study. Participant data was collected by staff from patients of the Child Development Unit (CDU) at The Children's Hospital at Westmead. Dr Antoinette Hodge provided considerable support within the CDU to facilitate data collection. This provided substantial data for this manuscript. In addition to CDU, a substantial portion of data pertaining to the Autism sample was collected by researchers in the Clinic for Autism and Neurodevelopmental Research (CAN) team, which is led by Prof Guastella. These researchers include Dr Rinku Thapa, Dr Eleni Demetriou and Emma Guastella. Specifically, Dr Rinku Thapa, Emma Guastella and Dr Eleni Demetriou were involved in administering the ADOS-2 assessments, for these children. I extracted and analysed the data and drafted the chapter. Prof Guastella and Dr Boulton provided substantial data analysis and manuscript feedback on the chapter. Chapter 4 of this thesis was designed by Prof Adam Guastella, Dr Kelsie Boulton and I. As a large portion of the data in this study was used from the same dataset within RedCap, the CDU team, who assisted in data entry within this software, contributed in this regard to this project. Lorna Hankin and Martha Munro provided substantial data support through their research on the Parent/carer questionnaire (PCQ). I analysed the data set as a whole, with close guidance from Prof Guastella and Dr Boulton. I drafted the chapter. Prof Guastella and Dr Boulton provided feedback on the chapter.

Professor Adam Guastella provided considerable supervisory support and input on the conceptual design, data interpretation, manuscript synthesis and critical review for intellectual content of each of the empirical chapters and for the Introduction and Discussion chapters of this thesis.

As supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

Prof Adam Guastella

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29 February 2024

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Ayesha Sadozai

29 February 2024

#### **Publications and Research Papers Associated with this Doctoral Thesis.**

- I. Ayesha K. Sadozai, M (Clin Psych), Eleni A. Demetriou, PhD, Carter Sun, Hons (Engineering), Amit Lampit, PhD, Kelsie A. Boulton, PhD, and Adam J. Guastella, PhD. Executive function in children with neurodevelopmental conditions: A systematic review and meta-analysis. 2024 (*undergoing revisions following feedback, Nature Human Behaviour*).
- II. Ayesha K. Sadozai, M (Clin Psych), Antoinette Hodge, Kelsie A. Boulton, PhD, Natalie Silove, Natalie Ong, Eleni A. Demetriou, Natalie Silove, and Adam J. Guastella, PhD. Executive Function Profiles Across Neurodevelopmental Conditions: A Focus on Comorbidities in Autism, ADHD and Specific Learning Disorders in Children Presenting to a Tertiary Assessment Service. 2024 (*to be submitted for review, Autism Research*).
- III. Ayesha K. Sadozai, M (Clin Psych), Antoinette Hodge, Natalie Silove, Natalie Ong, Eleni
  A. Demetriou, Adam J. Guastella, PhD, and Kelsie A. Boulton, PhD. How Caregiver
  Reported Strengths and Challenges Relate to Delays in Executive Function Performance.
  2024. (to be submitted for review, Autism Research).

#### Additional Research Papers Co-Authored during Candidature

Carter Sun, Alistair McEwan, Eleni Andrea Demetriou, Ayesha Sadozai, Amit Lampit, Adam J. Guastella. Identifying Autism Spectrum Disorder Using Artificial Intelligence Algorithms with A Focus on Social Interaction and Facial Information. A Systematic Review and Meta-Analysis. 2024. (to be submitted for review, Nature Biomedical Engineering)

#### **Conference Abstracts and Presentations during Candidature**

Poster presentation: 'A Transdiagnostic Profile of Executive Function in Children with Neurodevelopmental Conditions: A Systematic Review and Multilevel Analysis', at the below conferences.

- I. Brain and Mind Centre, University of Sydney, Annual Symposium, November 2022,
   Sydney Australia (Presentation).
- II. ASfAR (Australasian Society for Autism Research) poster presentation at conference in Geelong, Victoria in 2022.
- III. INSAR (International Society for Autism Research) poster presentation conference in Sweden 2023.

#### Awards and Fundings

Postgraduate Research Support Scheme (PRSS) in 2022

Postgraduate Research Support Scheme (PRSS) in 2023

BMC Symposium Thesis Poster Award 2022

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Abbreviation	Definition	
ADI	Autism Diagnostic Interview	
ADOS	Autism Diagnostic Observation Schedule	
ADHD	Attention Deficit Hyperactivity Disorder	
ANOVA	Analysis of Variance	
ANT	Attention Network Test	
ACC	Anterior Cingulate Cortex	
ASD	Autism Spectrum Disorder	
BRI	Behavioural Regulation Index	
BRIEF-2	Behavioural Rating Inventory of Executive Function – 2 <sup>nd</sup> Edition	
BRIEF-P	Behavioural Rating Inventory of Executive Function – Preschool Version	
CAN	Clinic for Autism and Neurodevelopmental Research	
CANTAB	Cambridge Neuropsychological Test Automated Battery	
CDU	Child Development Unit (Westmead, Sydney)	
CHEXI	Childhood Executive Functioning Inventory	
COWAT	Controlled Oral Word Association Test	
CPT	Continuous Performance Tests	
CRI	Cognitive Regulation Index	
DCCS	Dimensional Change Card Sort Test	
D-KEFS	Delis-Kaplan Executive Function System	
DLPFC	Dorsolateral Prefrontal Cortex	
DSM	Diagnostic and Statistical Manual of Mental Disorders	

### List of Common Abbreviations

DSM-5-TR	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision		
DV	Dependent Variable		
EC	Effortful Control		
EF	Executive Function		
ERI	Emotional Regulation Index		
ERICA	Emotion Regulation Index for Children and Adolescents		
FASD	Foetal Alcohol Spectrum Disorder		
FEF	Frontal Eye Fields		
FPC	Fronto-Parietal Cortex		
GEC	Global Executive Composite		
HFASD	High-Functioning Autism Spectrum Disorder		
ICD	International Classification for Diseases		
ID	Intellectual Disability		
IED	Intra/Extra Dimensional		
IQ	Intelligence Quotient		
LD	Learning Disorders		
LFPN	Lateral Fronto-Parietal Network		
LIFG	Left Inferior Frontal Gyrus		
LPFC	Lateral Prefrontal Cortex		
MANOVA	Multivariate Analysis of Variance		
MCIN	Midcingulo-Insular Network		
MI	Metacognitive Index		

MRI	Medical Resonance Imagine	
NDC	Neurodevelopmental Condition	
OCD	Obsessive Compulsive Disorder	
PC	Parietal Cortex	
PCQ	Parent Carer Questionnaire	
PFC	Prefrontal Cortex	
R	R is a programming language for statistical computing and graphics supported by the R Core Team and the R Foundation for Statistical Computing	
REDCap	REDCap is a secure web platform for building and managing online databases and surveys.	
RD	Reading Disorder	
RRBs	Restricted Interests and Repetitive Behaviours	
SLD	Specific Learning Disorder	
SPSS	SPSS Statistical Package for the Social Sciences	
SWM	Spatial Working Memory	
TEA-Ch	Test of Everyday Attention for Children	
TPJ	Temporal Parietal Junction	
TS	Tourette Syndrome	
VLPFC	Ventrolateral Prefrontal Cortex	
WCST	Wisconsin Card Sorting Test	
WM	Working Memory	
WMS	Wechsler Memory Scale	

#### **Thesis Abstract**

Executive functioning (EF) is an umbrella term used to conceptualise a diverse range of higher order cognitive processes that are broadly conceived of selecting and successfully monitoring behaviours that facilitate goal-oriented action. This broad definition includes, but is not limited to, planning, working memory, attention, inhibition, self-monitoring, and initiation. EF processes serve important regulatory function across the lifespan and, unsurprisingly, impairments contribute to difficulties in daily life. EF impairments are common to many neurodevelopmental conditions (NDCs), despite the distinct aetiologies of the disorders. These challenges contribute to social, behavioural and mental health impairments. Findings highlight specific EF impairments that are believed to be specific to conditions such as Autism (ASD), Attention-deficit/hyperactivity disorder (ADHD) and specific learning disorder (SLD), with working memory, response inhibition and cognitive flexibility all being implicated.

The overall aim of this thesis is to advance the transdiagnostic science of EF development in NDCs. This project aims to understand and compare profiles of executive delay in children across different NDCs, such as ASD, ADHD, SLD and Tourette's syndrome. The first empirical study comprises of a systematic review and meta-analysis of EF across NDCs, with a focus comparison between ASD, ADHD and other NDCs, and then compares the degree of EF delay in different NDCs and when compared to neurotypical children. Empirical paper two aimed to evaluate informant reported EF across neurodevelopmental comorbidities in children with ASD, ADHD and SLD attending a tertiary developmental service. The study explores how EF profiles change as the number and combination of comorbidities increases. The third empirical paper aimed to explore the strengths and weaknesses of parental evaluations of children's general developmental

functioning in relation to EF outcomes and subsequently, how these evaluations are associated with reported EF delays.

The meta-analysis results showed that EF across NDCs was significantly delayed, with a moderately delayed performance compared to neurotypical children. While EF delay may be largely conceptualised as a transdiagnostic delay observed across prominent NDCs, there was also some evidence of greater severity of delay for specific conditions on specific EF domains such as ADHD whereby working memory, response inhibition and attention is impaired. The findings for empirical paper two showed how EF delay further increased as the number of comorbidities increased, while the presence of ASD in an NDC comorbid group contributed to increased EF delay. Empirical paper three showed that the severity of EF delay was also associated with several common concerns such as behaviour and play/social domains which were reported by caregivers, but it was not associated with reports of childhood strengths from caregivers. This research contributes to a transdiagnostic science of EF delay in NDCs by demonstrating that EF delay is a largely transdiagnostic feature of NDCs, with increasing severity in children with NDC comorbidities. Importantly, EF may have potential to inform the support needs of children with NDCs in the areas of general functioning, behaviour, and developmental concerns. Future directions and theoretical implications of the findings are discussed.

### **Chapter 1: Introduction**

### A Literature Review of Transdiagnostic Profiles of Executive Function in Children with

### **Neurodevelopmental Conditions**

#### 1. General Introduction to Executive Function

Executive function (EF) is an umbrella term used to conceptualise a diverse range of cognitive processes generally described to guide purposeful behaviour and goal attainment.<sup>1</sup> These include, but are not limited to, EF domains of planning, working memory, attention, inhibition, self-monitoring, self-regulation, and initiation.<sup>2</sup> These cognitive processes encompass a wide network that guide behaviour<sup>3</sup> and are believed to be underpinned by prefrontal cortex activation.<sup>4</sup> This network undergoes many developmental and neurological changes during the first few years life, often reaching maturation well into adolescence and adulthood.<sup>5</sup> The developmental trajectory and the process of maturation has garnered much interest in developmental and cognitive psychology. Some of the earliest researchers proposed various models describing how the prefrontal cortex was the important brain region responsible for processing information and coordinating behaviour.<sup>6,7</sup> These early models of EF were often based on case studies with individuals that had sustained injury to certain parts of their frontal brain lobes. Recent advances in technology such as functional Magnetic Resonance Imaging (fMRI) has enabled researchers to explore the various neurological networks in the cerebral cortex and subcortical regions thought to house EF and conceptualise developmental influences on EF.<sup>2,8,9</sup>

The literature on EF models can be subgrouped into different types of models posited over the years. These model groupings include, EF models based on attentional systems, models based on cognitive psychology and developmental stages (e.g. Jean Piaget and Alexander Luria)<sup>10,11</sup> as well as models based on multifactorial theories. To illustrate, Michael Posner, a psychologist in 1975 coined the term 'cognitive control' and proposed a separate executive branch of the attentional system responsible for adapting to the environment depending on the goals of the individual.<sup>2,12</sup> Further, in 1977, Schiffrin and Schneider added to the theory of 'controlled process', suggesting that there is a temporary and automatic activation of skills through the attention of the individual, where repeated activation results in a well-developed cognitive skill.<sup>13</sup> Shallice in 1996 also proposed the 'Supervisory Attentional System', which refers to the mediatory role of inhibition thought to guide an individual's ability to make a decision. It proposed that cognitive attention had subtypes (i.e., orienting, alerting) which were responsible for the regulation of cognitive functions and as such a deficit in EF will lead to characteristics such as disinhibition in affected individuals.<sup>14-16</sup>. Alan Baddeley proposed the concept of the 'Central Executive' which allows for information to be manipulated in short-term memory, leading to the management of information within working memory, specifically overseeing the operational processes of both the phonological loop and the visuospatial sketchpad components.<sup>2,17</sup> This model predicted the regulation of complex behaviours, where dysfunction within these mechanisms is posited to result in widespread behavioural dysregulation.<sup>17,18</sup> More specifically, Baddeley described the central executive as managing key functions such as time-sharing, selective attention, temporary activation of long-term memory and task-switching.<sup>17</sup> These theories focus on attentional systems within EF and are positioned to be largely compartmentalised within the prefrontal cortex.

One of the pioneers of cognitive psychology, Piaget (1954), developed a theory of how EF could develop in a hierarchical and stepped framework where he proposed that children had a unique method of thinking and reasoning according to specific periods of their development.<sup>19</sup> He outlined hierarchical developmental stages of cognition and proposed how these stages shaped behaviour. The first stage, the Foundational stage was referred to as the sensorimotor stage (birth to 2 years), during which cognitive abilities such as object permanence and attention develop.<sup>10</sup>

Next, the Preoperational stage (2 to 7 years) oversees the rapid growth in inhibition and cognitive flexibility, which are key for developing symbolic thought and more complex cognitive operations. As children enter the Concrete Operational stage (7 to 11 years),<sup>10</sup> their thinking is reported to become more logical and organised, marked by improvements in inhibition, shifting, and updating abilities, supporting their ability to understand and apply logic. During the final Formal Operational stage (11 to 16 years), adolescents develop abstract and hypothetical thinking, with significant maturation in planning, problem-solving, and advanced working memory.<sup>5,10</sup> Across all stages, the development of EF is intricately linked with the brain's maturation within the prefrontal cortex, reflecting a complex interplay between cognitive growth, EF development, and anatomical and physiological changes in the brain.

Luria (1966) provided an extension of our understanding of EF development in children and postulated a model for EF based on specific developmental stages, broadening our understanding of how key areas of EF are developed.<sup>20</sup> Based on Vygotsky's complex theory of language and thought development in children, Luria proposed that EF development corresponded to neurological maturation and environmental influences (for example, culture, social engagement). Luria proposed five stages of development<sup>2</sup> whereby executive processes become more complex and multifaceted, corresponding to Piaget's stages of child cognitive development. The first stage (during the first year of life) sets the foundational neurological underpinnings for the child and involves the maturation of brain stem structures, including the reticular activating system, setting the foundational neural groundwork for subsequent cognitive development. The second stage (during the second year of life) is thought to activate primary sensory areas (vision, hearing, tactile perception) and primary motor areas for gross motor movement, enabling basic sensory processing and physical coordination. The third stage (during preschool years) of development focuses on the secondary association areas of the brain, enhancing the child's ability to recognise, reproduce, and manipulate symbolic materials and perform various physical movements, fostering initial complex cognitive skills. The fourth stage (during early School years) involve tertiary areas of the parietal lobes, integrating sensory inputs from multiple channels. This stage is crucial for the development of complex mental abilities, allowing the child to process and make sense of multifaceted sensory information.<sup>20</sup> The final fifth stage (from 8 years through adolescence) typically engages the frontal regions of the brain, particularly areas anterior to the central sulcus. This stage is vital for the development of advanced mental abilities necessary for abstract thinking, intentional memory, and complex learning and execution. This framework postulated that attention, intellectual functioning, language, sensory abilities, perception motor abilities and memory are complex but interrelated capacities.<sup>2,11,21</sup>

More recent models of EF proposed multiple components of EF functioning together as a whole rather than one central 'black box'. An example of a multifactorial model is that of Barkley (1997).<sup>22</sup> Barkley based his model on Attention-deficit/hyperactivity disorder (ADHD) presentations and stated that a deficit in 'behavioural inhibition' results from challenges in four key areas of EF; working memory, internalised speech, self-regulation of affect and reconstitution (i.e., behavioural analysis and synthesis). This earlier model has received some criticism particularly around its applicability to other developmental conditions and has since been further developed, suggesting that, working memory no longer has a mediatory role but a primary position within his model.<sup>23</sup> Another multifactorial model, proposed by Friedman and Miyake (2000)<sup>24</sup> suggests some EF constructs may be interrelated and some may be distinct. This model adds that

core EFs like updating, shifting, inhibition reveal a common underlying ability (unity), but also maintain a degree of separability (diversity). This duality suggests both a shared basis and distinct aspects within these cognitive processes.<sup>25</sup> More recently, Miyake and Friedman (2012) highlighted the substantial genetic contribution to EFs overall and specifically to the commonality in EFs but also in the distinctive aspects of EFs such as updating and shifting abilities.<sup>26</sup> In concordance with Barkley's model, these EF components were shown to have a strong predictive power for various behaviours linked to behavioural disinhibition, which are associated with ADHD, conduct disorder or substance use disorder. Further, he argued that these components demonstrate developmental EF stability, implicating that executive delay within specific EF domains in certain conditions remain impacted over time.<sup>27,28</sup>

Anderson (2002)<sup>6</sup> also proposed a developmental model of EF in children to improve the multifactorial model, encompassing four interrelated domains: attentional control, cognitive flexibility, goal setting, and information processing. These domains were proposed to collaboratively facilitate executive control, integral to goal-oriented behaviour and goal attainment. Attentional control was posited to develop initially, rapidly maturing in early childhood, while the remaining domains experience significant maturation between ages seven and nine, achieving relative maturity by twelve years. As adolescence approaches, a transitional phase led to the amalgamation of executive control. The prefrontal cortex, with its extensive neural network, is central to EF,<sup>1</sup> and influences various aspects of cognitive functioning, emotional regulation, and influences behaviour (i.e., decision-making). The intricate interplay between these domains and their neurological underpinnings highlights the importance of nuanced assessment

and intervention in children exhibiting executive impairment, which has implicated deficits in impulse control, planning, and adaptability.

Another multifactorial model proposed by Diamond<sup>19</sup> emphasises the role of EFs in topdown mental processing as essential for modulating conduct, thoughts, and emotions, especially when instinctive or habitual responses are inadequate or maladaptive. Central to this framework were three core EFs: inhibition, working memory, and cognitive flexibility. Inhibition encompasses control over attention and behaviour to resist internal or external temptations, working memory involves holding and manipulating information for complex cognitive tasks, such as reasoning and planning, and cognitive flexibility pertains to the ability to adapt thinking and behaviour in response to changing demands or perspectives.<sup>19</sup> In summary, the development of these faculties is closely linked to the maturation of the prefrontal cortex and its extensive neural networks, pivotal for managing and executing these functions. To date, research has recognised that EF is best understood as an umbrella term which conceptualises various neurocognitive processes that include specific constructs (e.g., working memory, planning), the execution of actions and goal-directed behaviours.<sup>1</sup> These processes undergo maturation and are often involved in a nuanced interplay of successive stages of development subject to the child's environment, genes and neurological groundwork. Table 1.1 summarises the main developmental models of EF.

Author/s	EF Model	EF Mechanism and/or Neurological Underpinnings
Piaget (1953) <sup>10</sup>	Hierarchical model of	Piaget proposed a hierarchical model of cognitive development in children,
	cognitive development in	highlighting distinctive cognitive skills and executive functions that unfold in
	children	stages. Initially focusing on basic cognition and attention in early childhood,
		children progress through increasingly complex stages, culminating in abstract
		reasoning and sophisticated problem-solving abilities during adolescence. This
		developmental trajectory corresponds to the ongoing maturation of the prefrontal
		cortex and the interdependent evolution of cognitive and executive capacities.
Luria (1966, 1973) <sup>11</sup>	Theory of brain functioning	Luria's theory focused on higher cortical functioning and divided the brain into
	from a psychophysiological	three components with reference to EF mechanisms. These components include the
	perspective and developed	lower brain stem structures, the cerebral cortex posterior to the central sulcus
	five stages of development.	(fissure of Rolando), and the cerebral cortex anterior to the central sulcus or the
		fissure of Rolando.
Posner (1990, 2012) <sup>29</sup>	Attentional Models of EF	Posner's attentional models of EF implicate three core networks: the alerting,
	implicating three core	orienting, and executive networks.
	networks: the alerting,	• Alerting network: tied to the brain stem and right hemisphere systems, this
	orienting, and executive	network regulates sustained vigilance and readiness. It is influenced by
	networks.	noradrenaline, with activity in the locus coeruleus facilitating phasic
		alertness, modulated by various pharmacological agents.
		• Orienting network: associated with the parietal cortex (PC) and other areas
		like the frontal eye fields (FEF), this network is crucial for prioritising
		sensory input. It is modulated by cholinergic systems and shows

## Table 1.1. Summary of Prominent Developmental Models of Executive Function

		considerable involvement in directing attention spatially and modally,
		significantly influenced by cues and context.
		Executive network: involving the midline frontal and anterior cingulate cortex, this
		network is central to managing and directing attention, particularly in the face of
		conflicting information or tasks.
Barkley (1997) <sup>22</sup>	Barkley's model of EF for	Barkley's model distinguishes EF as a series of self-directed, regulatory behaviours
	adapting and responding to	critical for adapting and responding to social environments. Barkley argues that EF
	social environments (with a	components collectively enable individuals to modify their behaviour strategically,
	series of self-directed,	optimising long-term social and personal outcomes. The model highlights the
	regulatory behaviours	intricate interplay between cognitive growth, executive function advancement, and
	critical).	the maturation of neurological structures, notably within the prefrontal cortex
		implicated in EF development.
Anderson (2002) <sup>30</sup>	Anderson's model of EF for	Anderson proposes a model of EF incorporating four discrete yet interrelated
	comprehensive executive	domains: attentional control, cognitive flexibility, goal setting, and information
	control.	processing. These domains integrate and enable comprehensive executive control,
		essential for goal-directed behaviour. The development of implicated EF domains
		essential for goal-directed behaviour. The development of implicated EF domains varies, with attentional control emerging early in infancy and rapidly developing in
		essential for goal-directed behaviour. The development of implicated EF domains varies, with attentional control emerging early in infancy and rapidly developing in early childhood, while cognitive flexibility, goal setting, and information
		essential for goal-directed behaviour. The development of implicated EF domains varies, with attentional control emerging early in infancy and rapidly developing in early childhood, while cognitive flexibility, goal setting, and information processing undergo critical development between 7 and 9 years of age, maturing
		essential for goal-directed behaviour. The development of implicated EF domains varies, with attentional control emerging early in infancy and rapidly developing in early childhood, while cognitive flexibility, goal setting, and information processing undergo critical development between 7 and 9 years of age, maturing substantially by age 12. A transitional period is observed at the onset of
		essential for goal-directed behaviour. The development of implicated EF domains varies, with attentional control emerging early in infancy and rapidly developing in early childhood, while cognitive flexibility, goal setting, and information processing undergo critical development between 7 and 9 years of age, maturing substantially by age 12. A transitional period is observed at the onset of adolescence, leading to the emergence of full executive control. The anterior
		essential for goal-directed behaviour. The development of implicated EF domains varies, with attentional control emerging early in infancy and rapidly developing in early childhood, while cognitive flexibility, goal setting, and information processing undergo critical development between 7 and 9 years of age, maturing substantially by age 12. A transitional period is observed at the onset of adolescence, leading to the emergence of full executive control. The anterior regions of the brain, particularly the prefrontal cortex, are implicated in mediating

		including the occipital, temporal, and parietal lobes, as well as limbic and
		subcortical regions.
Miyake (2000, 2012) <sup>26,31</sup>	Miyake's model of EF with a	Miyake's model focuses on three primary EF domain: updating, shifting and
	focus on three primary EF	inhibition. Miyake positions that these distinct EFs exhibit both correlation,
	domains (updating, shifting	suggesting a shared underlying capability (unity), and individuality (diversity). The
	and inhibition).	model positions the neural network within the framework of the Prefrontal Cortex
		Basal-Ganglia Working-Memory (PBWM) model, as developed by O'Reilly and
		colleagues, <sup>32</sup> to investigate the complex interplay and distinct features of EFs. This
		methodological approach facilitates a deeper understanding of the nuanced
		relationships and specific characteristics of EFs.
Diamond (2002) <sup>33</sup>	Diamond's collection of top-	Diamond identifies EF as a collection of top-down mental processes crucial for
	down mental processes	modulating behaviour, thoughts, and emotions, particularly when habitual
	crucial for modulating	responses, instincts, or intuitions would be insufficient. Core EFs identified by
	behaviour, thoughts, and	Diamond include inhibition, working memory, and cognitive flexibility. The
	emotions.	implicated domains of inhibitory control, working memory, and cognitive
		flexibility are linked to the maturation of various brain regions, particularly the
		prefrontal cortex. This area of the brain, along with its extensive network
		connections to other cortical and subcortical regions, is crucial for the modulation
		and execution of these functions.

#### 1.1. Neural Mechanisms of Executive Functioning

Findings from neuroimaging studies have shaped many of the organising principles of these EF models. Studies have found that the dorsolateral prefrontal cortex (DLPFC) is associated with action planning and the ventrolateral prefrontal cortex (VLPFC) is associated with language and objects processing.<sup>34</sup> More recent research has distinguished EF according to their emotional and motivational attributes and to those that rely on cognitive processes alone. These are referred to as 'hot' EFs located in the medial regions of the (prefrontal cortex) PFC and 'cold' EFs located in the lateral regions of the PFC.<sup>35</sup> Hot EFs allude to the processing of information linked with goal-driven, emotional or affective decision-making and motivational attributes, and are assessed by tasks such as Iowa Gambling task<sup>36</sup> whereas cold EFs relate to logical and cognitive processing attributes and utilises measures such as the Stroop<sup>37</sup> or Tower of London task.<sup>38</sup> EF literature has tended to focus on more "cold" cognitive measures of EF measured by abstract and isolated problem-solving neglecting more "hot" cognitive thinking processes influenced by social and emotional variables.<sup>39</sup> This thesis will now focus on cold EF faculties and touch upon relevant hot EFs which are a focus of the experimental measures therein. Figure 1.1 and 1.3 depict the EF structure for examples of cold and hot components of EF.

#### 1.1.2. Cold Executive Functions

Cold EFs encompass a range of specific faculties that are known to orchestrate distinct roles in EF development and subsequently guide behaviour. Given the interrelatedness of EF domains, it is not uncommon for EF faculties to tap into other domains when activated. For example, the activation of inhibition and working memory is necessary for the use of higher order domains such as cognitive flexibility.<sup>19</sup> This interdependence highlights the complex, intertwined nature of EFs and their collective impact on behaviour. In addition to the core EFs discussed within this thesis, attention, often considered a higher order EF, will be listed among
the range of cold EFs. Attention is positioned to be both a mechanism involved in EF and is a subcomponent of EF. It is noted that this mechanism is highly interrelated and plays a key role within 'hot EFs', however executive attention is often best measured through performance measures of EF which are largely categorised within cold EFs within the literature and are treated as such within this project.<sup>40-43</sup> The following constructs have been found to be key in extensively shaping and informing EF and will be explored as part of this thesis and the experimental research therein. Based on the review of literature, Figure 1.2 depicts a concise neurobiological map of cold EFs.

#### 1.1.3. Working Memory

Working memory (WM) refers to the ability to cognitively hold and apply information for a specified task or purpose.<sup>44</sup> Other subcomponents of WM include auditory and visual spatial WM, these subcomponents are auditory and visual mechanisms for the temporary storage of information and the storage of information.<sup>45</sup> It is closely associated with the dorsolateral prefrontal cortex (DLPFC) and typically begins to develop in toddlers<sup>25,46</sup> Additionally, brain imaging studies suggest involvement of the fronto-parietal (FPC) regions in working memory.<sup>47</sup> An example of common measures of WM include tasks such as the Letter Sequencing task, the Digits Backwards task from the Wechsler Memory Scale (WMS) and the Spatial Working Memory (SWM) from the CANTAB battery (see supplementary table 4 in appendix A for a full list of these tests).<sup>48</sup> Tasks such as Digit Backwards are designed to place load on the child's memory, by asking the child to recite back numbers and seeks to place load on the child's WM by asking the child to recite and organise said digits backwards. Such tasks are designed to tap into the central executive component of Baddeley's model.<sup>17</sup>. WM assessment can be conducted in children as young as 6 months<sup>4</sup> and is believed to reach full maturity by late adolescence.<sup>49</sup>

#### **1.1.4.** Cognitive Flexibility

Cognitive flexibility encompasses two primary components: set shifting and set switching, although the literature often refers to these terms interchangeably.<sup>50</sup> It refers to the ability to adapt and transition between tasks and mental states, as well as adjust behaviour to execute a goal oriented action.<sup>6,46</sup> Tasks assessing cognitive flexibility often aim to measure perseveration, which is the inability to adjust one's response in light of new, relevant information, resulting in the execution of an earlier response. These tasks typically establish a response pattern in children, and then introduce rule changes to challenge the pre-established pattern. The complexity of these rule changes directly influences the difficulty level for children to assimilate the new information and accordingly adapt their action.

An example of a commonly used task measuring cognitive flexibility is The Wisconsin Card Sorting Test (WCST)<sup>51</sup> Children are asked to sort response cards based on categories such as colour, shape or number. A sorting rule is taught which subsequently changes and outcomes such as the number of categories successfully completed, the total number of errors, and, particularly relevant to compulsivity, the number of perseverative errors (mistakes made after the rule has changed) are recorded. This particular executive function, crucial for flexible thinking and adaptive behaviour, tends to develop progressively throughout middle childhood and adolescence.<sup>52</sup> Brain imaging studies implicate large brain networks encompassing the lateral frontoparietal network (LFPN) and the midcingulo-insular network (MCIN) across the lifespan.<sup>53</sup>

# 1.1.4.1 Set-Shifting and Mental Flexibility/Set Switching

Set-shifting refers to the ability to transition efficiently between cognitive tasks,<sup>24</sup> with neuroimaging studies reporting activation in the parietal cortex (PC).<sup>54</sup> Measures of setshifting include the Wisconsin Card Sorting Test<sup>55</sup> (WCST), the Intra/Extra Dimensional (IED) shift test from the Cambridge Neuropsychological Test Automated Battery<sup>48</sup> (CANTAB), and the Dimensional Change Card Sort Test<sup>56</sup> (DCCS). Children as young as 12 months display basic set shifting skills, which become refined as cognitive flexibility develops.<sup>57</sup> Cognitive or mental flexibility, also referred to as set switching involves adapting to cognitive demands and shifting between mental operations.<sup>58</sup> Studies have demonstrated the involvement of the prefrontal cortex (PFC) and frontoparietal areas of the brain during a set-switching task.<sup>59,60</sup> Common measures include the Trails Making Test which assess the ability to switch between two mental operations; letters and numbers.<sup>61,62</sup>

#### 1.1.5 Fluency

Fluency refers to the ability to accurately recall verbal and non-verbal patterns in the environment.<sup>58</sup> Neuroimaging studies have shown increased activation in the Left Inferior Frontal Gyrus (LIFG) and increased blood flow to the dorsal regions associated with phonological verbal fluency.<sup>63</sup> Common measures used to assess this construct include the Controlled Oral Word Association Test<sup>64</sup> (COWAT) and the Design Fluency test from the D-KEFS battery.<sup>65</sup> In verbal fluency tasks (VFT), children are required to generate words, either spoken or written, that correspond to a specific phonemic category (such as a letter of the alphabet) or a semantic category (like animals or fruits). Typically, each trial has a time limit.<sup>66</sup>

# 1.1.6. Planning

Planning is defined as the cognitive ability to formulate a decision and execute thought processes around the decision. It also includes making evaluations of the environment, individuals and oneself and is largely deemed a higher-order and complex EF faculty.<sup>67</sup> Neuroimaging results show there is increased activation in the DLPFC and frontostriatal networks during executive planning tasks.<sup>68,69</sup> Measures of planning include the Tower of London<sup>70</sup>, 2004), the Tower of Hanoi<sup>71</sup> and the CANTAB One Touch Stockings of Cambridge.<sup>48</sup> Tasks such as the Tower of Hanoi involve motor planning which consists of pegs

and disks of various sizes, the task involves reaching a goal state in which the disks are stacked for instance, in descending order on a particular peg. There are often movement constraints such as, being able to move one peg at a time. Outcomes include the number of movements involved to reach the goal position.<sup>72</sup> Motor planning is often developed by infancy and more complex planning skills are matured and refined with the development of inhibitory control and working memory.<sup>4,73</sup>

#### 1.1.7. Response Inhibition

Response inhibition is described as the executive ability to refrain from acting on an automatic inclination<sup>24</sup> with many studies finding the DLPFC, VLPFC, and PC is activated during response inhibition tasks.<sup>74</sup> Common measures include Stroop test and the Colour-Word Interference test from the D-KEFS battery, the Go/no-Go task and the Hayling test.<sup>65,75-78</sup> Tasks such as the go/no-go task, children are presented with a series of stimuli and must ascertain whether to perform 'go' action or refrain from acting ("no-go") based on specific rules. For instance, they might be instructed to press a button when a certain stimulus appears (go signal) and to withhold pressing the button when a different stimulus appears (no-go signal).<sup>79</sup> Such measures assess the child's ability to inhibit a response with the task parameters. Response inhibition is refined from early childhood (3 to 5 years) to early adulthood.<sup>4,80</sup>

### 1.1.8. Attention

Attention is largely described in the literature as a set of cognitive processes (overall alertness) that allow for engagement with the environment which serves to be adaptive and efficient.<sup>81</sup> Attention is considered to be a comprehensive EF faculty and based on the works of Posner and colleagues,<sup>29,82</sup> was originally characterised as comprising of three distinct networks: orienting or selective attention, alerting or sustained attention, and executive control or executive attention.<sup>29</sup> The orienting network is key in spatial or distribution of attention to

stimuli, reaching maturity by approximately six months of age.<sup>83</sup> The alerting network, governs the maintenance of a vigilant and ready state, facilitating continuous information processing and responding to unexpected stimuli.<sup>84</sup> Lastly, the executive network is associated with selfregulated attentional action and is intricately linked to a broader range of EFs.<sup>19,83</sup> Research to date has identified subcomponents of attention which include, divided, selective and sustained attention.<sup>85</sup> Divided attention is the cognitive ability to share and process more than one task simultaneously, whereas selective attention is the cognitive attentional resource that hones in on one task or object while ignoring irrelevant stimuli.<sup>85,86</sup> Sustained attention is the capacity to maintain attentional faculties over a prolonged period of time.<sup>86</sup> Measures such as the Continuous Performance Tests (CPTs), Test of Everyday Attention for Children (TEA-Ch), Attention Network Test (ANT) have been used to tap into domains of attentional networks.<sup>87</sup> Tasks such as the TEA-Ch evaluates various aspects of attentional control in children, including selective attention, sustained attention, and attentional switching. One example of a task in the TEA-Ch is "Map Mission," where children are asked to find and circle specific target symbols on a map filled with distracting symbols, measuring their ability to focus on relevant information while ignoring distractions.<sup>88</sup> Neurobiological research often implicates multiple brain regions such as the Anterior Cingulate Cortex (ACC), parietal lobes (particularly the superior parietal lobe and intraparietal sulcus), Temporal Parietal Junction (TPJ) and DLPC, which undergo coordinated action to execute the process of attention.<sup>89,90</sup>



Figure.1.1 EF Structure for Examples of Cold Components of EF.



Figure 1.2 Neurobiological Map of Cold EFs

#### **1.2.1. Hot Executive Functions**

The following hot EF constructs, although not exhaustive, have been found to be of key significance in shaping our understanding of hot EFs and will be undertaken as part of this thesis and the experimental research explored as part of this thesis. Figure 1.4 depicts a concise neurobiological map of hot EFs, based on a review of the literature.

#### **1.2.2.** Attentional or Effortful Control

Attentional or effortful control (EC) is a multifaceted construct that relates to temperament or biologically based characteristics or processes that modulate regulatory behaviours.<sup>91</sup> EC encompasses mechanisms that govern motivation and the intentionality of thoughts, emotions and behaviours.<sup>92</sup> EC plays a key role in emotional regulation, and is often correlated with emotional regulation.93 Research in EC implicates inhibitory mechanisms of behaviours (i.e., inhibitory control<sup>94</sup> or executive attention<sup>91</sup>), however, EC, a hot EF faculty differs from cold faculties of EF by measuring behavioural inhibitory mechanisms that relate to strong emotions (e.g. motivation/desire/arousal or frustration) measured in social dynamics or settings.<sup>93</sup> EC is linked to activation in the anterior cingulate gyrus and lateral prefrontal cortex (LPFC)<sup>95</sup> and is often measured using assessment tools such as the Attention Network Task (ANT),87 Kochanska's multitask battery,96,97 and Puzzle box task (a measure of behavioural persistence/effortful control).98,99 The ANT evaluates the efficiency of three attentional networks: alerting, orienting, and executive control. For instance, children are shown a series of fish on a screen and must determine the direction of the central fish while ignoring flanking fish. This setup includes cues to test alertness and attention shifts, and varying congruence of surrounding fish to test conflict resolution.<sup>100</sup> EC is often implicated in externalising and internalising behaviours<sup>98</sup> and educational functioning.<sup>101</sup>

#### **1.2.3. Emotional Regulation**

Emotion regulation is a mechanism (explicit or implicit) by which individuals modify their emotional experience.<sup>102,103</sup> This ability to self-regulate one's emotions or behaviours encompasses one's ability to modulate their reactivity in response to external or internal agitation.<sup>104</sup> Emotional regulatory processes by extension, are a complex skillset that uses mechanisms outlined in EC. This function is implicated in brain regions associated with emotion and executive functioning. These include the amygdala, the ventral striatum (associated with transmission of arousal), the VLPFC, anterior insula, and as well as to the angular gyrus.<sup>105,106</sup> The DLPFC is believed to process the information received from the VLPFC and initiates the emotion regulation mechanism which is then executed through the angular gyrus, amygdala and ventral striatum.<sup>107,108</sup> Emotional regulation is often measured through informant based measures such as the Emotion Regulation Index within the Behavioural Rating Inventory of Executive Function (BRIEF) measure<sup>109</sup> and the Children and Adolescents (ERICA).<sup>110</sup> An emotional regulation deficit is implicated in an array of mental health conditions and behavioural challenges in children.<sup>111-113</sup>



Figure 1.3. EF Structure for Examples of Hot Components of EF



Figure 1.4. Neurobiological Map of Hot EFs in children.

#### 1.3. Assessments of Executive Functioning in Children

The literature to date on EF is rich with assessment tools for tapping into the above EF constructs. Some measures cater to the developmental stage of the child, with important considerations such as language, IQ and ecological validity. Measures of EF can be divided into two categories, performance-based measures which assess discrete EF functions in the frontal cortex (e.g., working memory scales from the Wechsler Memory Scale) and behavioural measures of EF based on self and informant ratings. These includes the Behavior Rating Inventory of Executive Function - Preschool and the Childhood Executive Functioning Inventory (CHEXI) (i.e. BRIEF-P and CHEXI).<sup>114,115</sup> Within the discrete components of EF, some measures tap into more affect laden measures of EF also known as "hot" EF. They are cognitive thinking processes influenced by social and emotional variables. Other measures tap into "cold" cognitive measures of EF, assessed by abstract and isolated problem-solving.<sup>25</sup> Key components of the BRIEF tap into cold EF faculties (e.g., working memory subscale within Cognitive Regulation Index, CRI), however there are some domains which also cover 'hot' EF faculties, these include subscales within the Emotional Regulation Index (ERI) domain and scales such as self-monitor within the Behavior Regulation Index (BRI). The research encompassed within this thesis will largely focus on cold EF faculties, with some references to hot EF faculties, as captured within the BRIEF measure. Several challenges to measuring EF in children exist. EF measures often draw on multiple underlying processes and a child's performance may not reflect a cognitive deficit of a discrete EF.<sup>4</sup> Performance based measures of EF tap into quantitative responses (response time and accuracy) to assess performance<sup>116</sup> and are often known as the gold standard of discrete EF measurement. These measures may have limited ecological validity<sup>117</sup> and often inconsistent predictive validity.<sup>4</sup> Many considerations such as language use, normed samples and IQ are often important considerations within the use of performance-based measures.<sup>116</sup> As such, performance measures are heavily

influenced by factors such as cognitive ability or language skill which impact EF performance.<sup>118</sup>

Informant based measures of EF tend to provide a holistic indicator of behaviour that purports to tap into executive ability performed in everyday life.<sup>119</sup> Such measures often assess behaviour over a long period of time, as opposed to time-specific ability in performance measures.<sup>118</sup> The BRIEF questionnaire scales have been found to be reliable and valid for use as informant reports of young children in both clinical and research settings.<sup>116</sup> The BRIEF consists of questionnaires for teachers and parents, aimed at evaluating executive functioning in children and adolescents aged between the ages of 5 and 18 years.<sup>119</sup> The BRIEF evaluates eight executive function subdomains organized into two primary indices: the Behavioral Regulation Index (BRI), including the Shift, Emotional Control, and Inhibit subdomains, and the Metacognitive Index (MI) encompassing Working Memory, Initiate, Organization of Materials, Monitor, and Plan/Organize subdomains. The BRI and MI collectively contribute to the Global Executive Composite (GEC). The BRI correlates with hyperactivity/impulsivity symptoms while the MI is linked with inattention symptoms.<sup>119</sup> The BRI is purported to measure the child's ability to monitor and self-regulate their behaviour (and reported to tap into cognitive regulation) and is summarised using the Inhibit and Self-Monitor scales<sup>109,120</sup>. The GEC is the total summary score based on all clinical scale results and is evaluated to be a valid parent based measure of overall executive performance in children<sup>109</sup>.

The BRIEF measure demonstrates sound discriminant validity with studies demonstrated its ability to distinguish children with certain neurodevelopmental conditions. For example, a recent study examined the BRIEF and its ability to differentiate those with ADHD from controls,<sup>121</sup> with BRI differentiating neurotypicals from those with ADHD. The

BRIEF's Working Memory scale evaluations by parents and teachers were considerably higher (i.e., higher scores are indicative of impairment) for children with ADHD-Inattentive type and ADHD-Combined type compared to controls when testing predictive validity.<sup>122</sup> In a study reviewing the concurrent validity of the BRIEF with performance based measures<sup>123</sup> it was found that the BRIEF may correlate with same source/method of information (i.e., parent interviews) as opposed to performance-based measures.

Contemporary EF research indicates that informant ratings and performance-based assessments of EF might delineate distinct dimensions of EF.<sup>116</sup> Both measures are deemed uniquely valuable, offering complementary insights in the evaluation of EF. Particularly, informant measures might encapsulate the longitudinal and anticipatory elements of EF more effectively than performance-based methods.<sup>118</sup> This is attributed to the fact that rating scales consider the individual's daily life performance over time, while performance-based assessments are confined to evaluating EF at a singular moment through structured tasks. Barkley and Fischer (2011)<sup>118</sup> advocate for a hierarchical view of EF as a meta-construct, wherein each subsequent level operates with increased complexity, building upon the foundational lower levels. This structure suggests that the informant and performance-based measures might be assessing different tiers of EF. As such, these two assessment types should not be seen in competition but rather as integral parts of a multifaceted approach to understanding EF. Specifically, it's posited that while performance-based assessments may target the more fundamental aspects of EF, informant measures might provide insight into the more advanced, longer-term aspects of executive functioning. This distinction highlights the necessity of employing both methods for a comprehensive understanding of EF and its manifestations across various contexts and time frames. The current project will use the BRIEF questionnaire as a key measure of executive functioning across neurodevelopmental conditions (NDCs) in order to elucidate specific EF impairments that are either shared, contrasting, or uncommon across conditions.

#### 1.3.1. Caregiver Evaluations of Children within Neurodevelopment Assessments

Caregiver evaluations of children undergoing screening and assessment for NDCs are pivotal for holistic, systems-orientated approaches to assessment of the child.<sup>124</sup> These evaluations often provide valuable and comprehensive information on a child's executive performance. Caregiver reports frequently serve as the primary source of information during paediatric reviews, rendering caregiver perspectives invaluable for thorough assessments. A systems lens regards children as integral component of their families, acknowledging that the family system contains structural and functional characteristics that influence the child's presentation.<sup>124</sup> For example, research indicates that caregiver well-being can directly affect a child's development<sup>125</sup> and influence their adjustment within the context of their disability.<sup>126</sup> Studies have shown that parents expressing concerns about behaviour and social skills accurately predicted mental health challenges for their children, particularly for those over four years old.<sup>127</sup> While focusing on concerns has led to a better understanding of a child's challenges and guided assessment and intervention, evaluations of NDC conditions often focuses on concerns without assessing strengths. Examining both strengths and concerns reported by caregivers is imperative for enhancing the ability to recognise and provide early intervention for NDCs, potentially ameliorating functional challenges and improving long-term outcomes,<sup>127-129</sup> as well as enhancing executive performance<sup>130,131</sup> and fostering a neuroaffirming support network for children. This project aims to recognise the importance of a holistic, neuro-affirming framework when considering caregiver evaluations of children's executive abilities. Adopting a neuro-affirming lens within this emerging field acknowledges the importance of understanding and building upon the positive characteristics of children NDCs to enhance overall well-being.<sup>132</sup>

#### 1.4. Executive Functioning in Key Neurodevelopmental Conditions

The DSM-V-TR<sup>133</sup> refers to NDCs as a group of conditions typically emerging during early developmental stages of a child, characterised by an array of functional, cognitive and behavioural deficits causing impairment in the child's personal, social and learning domains.<sup>134,135</sup> EF is one key marker of cognitive adaptability in children NDCs. Impairments in EF can lead to difficulties in sustaining attention, impulsivity, and an inability to transition between, and flexibly manage, multiple tasks.<sup>2</sup> These EFs are often best captured through measures which are often linked to specific brain regions and conceptualised as differing cognitive faculties, as mentioned above.<sup>33,136-139</sup> EF impairments are often found in various neurodevelopmental conditions such as Autism Spectrum Disorder (ASD),<sup>140</sup> ADHD,<sup>141</sup> Tourette's Disorder (TD)<sup>142</sup> and Specific Learning Disorders (SLD).<sup>143</sup> Impairments in EF domains are increasingly considered a transdiagnostic feature of neurodevelopmental conditions (NDCs).<sup>144</sup> Their presence may signal divergences in brain development, and they can contribute to lifelong challenges requiring long-term support.<sup>2,4</sup> EF impairments have been documented across a range of NDCs, prompting research efforts aimed at delineating EF profiles within these conditions.<sup>145,146</sup> This section aims to synthesise the existing literature of EF in NDCs in children. Childhood represents a critical developmental stage where assessment of EF impairments plays a vital role in guiding educational intervention.

# 1.4.1 Autism Spectrum Disorder and Executive Functioning

Autism is a lifelong neurodevelopmental condition defined by the DSM-5 by criteria of social communication difficulties and restricted, repetitive behaviours or interests.<sup>134</sup> Children with ASD present with social impairments and behavioural challenges often associated with a poor quality of life.<sup>147</sup> Individuals diagnosed with ASD frequently experience significant mental health concerns, such as anxiety, conduct problems and depression.<sup>148</sup> ASD is found to impact up to 2.5% of children in Australia,<sup>149</sup> 3.13% in Europe and up to 1.85% in

North America.<sup>150</sup> Leung (2016) found that delays in EF (i.e., inhibition, shifting, and emotional control), along with social functioning, predicted the social impairments of people with ASD.<sup>140</sup>

Delays in EF are thought to contribute to many of the social difficulties core to ASD. For instance, delays in inhibition, information recall, flexibility, and the ability to monitor, update, and select socially appropriate responses are purported to contribute to social impairments of ASD.<sup>151,152</sup> Moreover, some of the restricted, repetitive behaviours observed in ASD may be partially attributable to delays in EF. For example, meta-analyses conducted by Iversen and Lewis (2021) found that elevated levels of repetitive and restrictive behaviours, characteristics of ASD, were correlated to poor flexibility (i.e. set-shifting) and inhibitory control tasks.<sup>153</sup> A lack of cognitive flexibility, for example, may explain some of the rigid and perseverative behaviours commonly observed in ASD.<sup>154,155</sup>

Children with ASD continue to present with EF impairments over time and these impairments seem to predict poorer outcomes later in life. A study by Vogan (2018)<sup>156</sup> found that children with ASD showed impaired scores of EF on the BRIEF with no significant improvement over 2 years, compared to controls. Further analysis revealed earlier difficulties in behavioural regulation (i.e., BRIEF BRI) predicted symptoms associated with heightened anxiety and depression two years later in children with ASD. Furthermore, both behavioural regulation and metacognitive problems (i.e., working memory, task initiation as measured by BRIEF) at baseline predicted externalising symptoms two years later, specifically oppositionality, conduct and aggressive/disruptive behaviours. Moreover, EF deficits are integral to the clinical trajectory of some conditions, although research indicates variability in their impact across different age ranges. Studies exploring developmental EF deficits highlight the developmental trajectory between different age groups where younger children (ages 6-8) have challenges with inhibition, while planning is more impaired in older children (ages 1214), acknowledging the impact of age-related differences.<sup>157</sup> This thesis acknowledges that autism or autistic person is preferred language by the neurodiverse community. The thesis attempts to use this term where appropriate, however at times refers to diagnostic language ASD when referring to this presentation from a purely diagnostic lens as the thesis utilising data from diagnostic services for children.

#### 1.4.2. Attention Deficit Hyperactivity Disorder and Executive Functioning

Attention-deficit/hyperactivity disorder (ADHD) is characterised by heightened levels of inattention and/or impulsivity and hyperactivity, with affected children experiencing difficulties on many day-to-day tasks.<sup>133</sup> The prevalence of this neurodevelopmental condition has been substantial, affecting 7.2% of children worldwide<sup>158</sup> and with Australian prevalence rates being comparable, approximately at 7.8%.<sup>159</sup> Children diagnosed with ADHD often encounter learning challenges, significant behavioural and socio-emotional impairments.<sup>160-163</sup> Executive functioning impairments in children with ADHD has been linked to poor inhibition, attentional processes and memory (including short term and working memory) when performance based measures where utilised.<sup>164-166</sup> These deficits may hinder a child's ability to engage in pro-social behaviour and peer relationships, particularly as they enter the educational setting.<sup>167</sup>

#### 1.4.3. Specific Learning Disorders and Executive Functioning

Specific Learning Disorders (SLD) are a category of neurodevelopmental conditions characterised by learning impairments in one or more three key areas: reading, writing, and mathematics.<sup>133,168</sup> Typically identified in school-aged children, it affects approximately 5 to 15% of children.<sup>169-171</sup> The three affected areas are assigned specific diagnostic labels, namely dyslexia, dysgraphia and dyscalculia, respectively. Dyslexia refers to impairments in decoding

and accurate, fluent word recognition in the context of sound intellectual and sensory abilities.<sup>172</sup> Dysgraphia, often termed the 'disorder of written expression', involves impairment in translating thoughts and words onto paper, with individuals experiencing challenges in spelling, grammar, punctuation, and handwriting.<sup>173</sup> Dyscalculia refers to the impairment in making numerical calculations or learning mathematical functions, manifesting in struggles with math reasoning, problem solving and overall arithmetic skills.<sup>174</sup> Studies have associated specific learning disorders with key executive processes. For instance, research by Schuchardt (2008) used performance-based measures and found working memory deficits in children with specific learning disorders, highlighting that children with dyscalculia have more impairments in visual-spatial memory, while those with dyslexia show more impairments in phonological and central executive functioning areas.<sup>175</sup> Additionally, further research has implicated other key cognitive processes such as attention, alongside phonological deficit, in dyslexia.<sup>176</sup>

#### 1.4.4. Other NDCs and Executive Functioning

Emerging research on EF has also shed light on a range of other NDCs such as Foetal Alcohol Spectrum Disorder (FASD) and Tourette's disorder (TD), with global EF impairments and identified areas of cognitive weaknesses. FASD arises from prenatal alcohol exposure and encompasses a broad spectrum of cognitive impairment.<sup>177</sup> Executive functioning deficits are prevalent in FASD, with affected children demonstrating problems with working memory,<sup>178</sup> inhibition<sup>179</sup> and set-shifting.<sup>179,180</sup> These deficits are often associated with compromised emotional and behavioural functioning in young children.<sup>181</sup> TD, on the other hand, is characterised by repetitive and involuntary muscle movements and vocalisations (tics), <sup>133,168</sup> accompanied by cognitive and behavioural challenges. Executive functioning impairments are commonly observed in TD, manifesting as difficulties in sustained attention<sup>182</sup> and working memory.<sup>183</sup> Further, executive functioning difficulties such as inhibitory deficits, likely

contribute to the social inappropriateness observed in some children with TD, negatively affecting their everyday functioning.<sup>184</sup>

# 1.5. Neurodevelopmental Conditions and Executive Function: Profiles Across Conditions

Impairments in executive functioning are evident across a range of conditions and can significantly affect day-to-day functioning. These impairments can include difficulties in sustaining attention, impulsivity, and challenges in transitioning between and managing multiple tasks.<sup>1,2</sup> Research has documented EF deficits in various neurodevelopmental conditions (NDCs), with efforts made to delineate these impairments across different conditions and within comorbid presentations.<sup>146</sup> Recently, Frances and colleagues (2022) conducted a systematic review on DSM-5 based NDCs and their prevalence, revealing incidence rates fluctuate, ranging from 4.7% to 88.5% globally.<sup>185</sup>

#### 1.5.1. ASD and ADHD

Prior to 2013, DSM iterations did not acknowledge the potential co-occurrence of ASD and ADHD. However, current iterations recognise this pattern of comorbidity, allowing more recent research to capture their diagnostic commonalities. Studies investigating executive functioning impairments across key neurodevelopmental conditions have revealed both similarities and differences in the degree of impairments. Some of these similarities may be attributed to the high rates of comorbidity between certain conditions, such as ADHD and ASD, which often co-occur at rates ranging from 38.5% to40.2%.<sup>146,186,187</sup>

Some studies comparing EF impairments across different conditions have found that certain areas of executive functioning may be more impaired in one condition compared to another. However, the literature on EF deficits across conditions presents with some variability. For example, a study by Corbett et. al., 2009<sup>166</sup> assessed EF deficits in children with ADHD, ASD and controls aged 7-12 years and found children with ASD to have significant impairments in response cognitive flexibility/switching, and working memory compared to both groups. Similarly, a comparative review by Craig (2016)<sup>188</sup> found that children with ASD were more impaired in working memory and flexibility when compared to children with ADHD with no difference in planning and attention amongst both clinical groups. Further, when reviewing comorbid presentations, some studies indicated that ASD and ADHD comorbid group and the ADHD alone group had more impairments in working memory, flexibility, and planning than children with a single disorder ASD alone.<sup>189</sup>

Results of EF profile varied depending on the type of measure utilised (e.g., informant versus performance-based measures). For example, performance measures showed impact on working memory, planning and organisation in children with comorbid ASD and ADHD, while informant-based measures revealed significant impairments in attention alone<sup>190</sup>. In a recent study by Townes and colleagues<sup>191</sup> (2023), a systematic review and meta-analysis explored ASD and ADHD, aiming to summarise the existing research on how these NDCs perform across EF domains. The findings indicated that children diagnosed with ASD and ADHD both exhibited worse performance in EF domains, including attention, flexibility, visuospatial abilities, working memory, processing speed, and response inhibition compared to typically developing children. These findings suggest a shared underlying mechanism<sup>192</sup> in ASD and ADHD, despite them being distinct clinical disorders. Condition specific executive information tends to be nuanced, and a holistic transdiagnostic EF evaluation of NDCs can aid in addressing the daily challenges associated with EF.

#### 1.5.2. ADHD and SLD

ADHD and SLD are highly comorbid with a prevalence rate of 31% to 45% globally.<sup>193</sup> Functional challenges within these comorbid conditions often play out in reciprocal manner. For example, deficits within ADHD such as attention, working memory, planning and organisation can subsequently impact a child's ability to plan and execute a written task.<sup>194</sup> Cross condition studies reveal isolated impairments in EF. A study by Faedda and colleagues (2019) compared ADHD and SLD together and found that the SLD group performed better than the ADHD group in inhibition, cognitive flexibility, and some working memory domains.<sup>165</sup> Similarly, another study found that flexibility and response inhibition were more impaired in children with ADHD than SLD.<sup>195</sup> More recent reviews on ADHD identify cognitive control and vigilance as key cognitive markers.<sup>196</sup> Comorbidity studies reveal that when prevalent in conjunction with one another, EF deficits within these NDCs are often nuanced. Some studies reveal an additive impact of EF deficits, i.e., isolated condition deficits being pooled together or an interactive effect, where a distinct EF profile emerges. For example, a study by de Jong and colleagues found that inhibition and lexical decision was impaired in the comorbid group for children with both ADHD and reading disorder (RD).<sup>197</sup> Another study found evidence of interactive effects with the comorbid group presenting with rapid naming deficits as well as increased working memory deficits.<sup>198</sup> Further, a recent study by Crisci and colleagues (2021), found a specific EF profile where children with both ADHD and SLD had more impaired abilities in visuospatial updating tasks compared to single condition groups.<sup>199</sup> These results highlight the complexity of EF performance across this NDC group particularly when they co-occur. Studies evaluating cognitive training allude to the additive effect, suggesting increased support is required for children with comorbid ADHD and RD.<sup>200</sup> That is, various types of SLD (i.e., dyscalculia, dyslexia and dysgraphia) may contribute to uniquely to EF deficits within this cooccurring group.<sup>176,201</sup> Largely, cognitive control (e.g. response inhibition) and regulatory mechanisms are impaired in ADHD,<sup>196</sup> and working memory and phonological regions appear to be impaired in SLD.<sup>176,196,201,202</sup> Recent studies indicate both additive and interactive effects on the co-presentation of ADHD with SLD with areas such as working memory and visuospatial updating appear to impact this comorbidity group.<sup>199,203</sup> These findings highlight the complexity of understanding the cognitive markers of single NDCs versus comorbid NDCs, illustrating the need to better understand how EF cognitive profiles manifest transdiagnostically in children.

#### 1.5.3. Comorbidities in Other NDCs

The neurodevelopmental research arena is rich with studies evaluating the mechanisms of EF within certain conditions such as ASD, SLD and ADHD, with little focus on little-known NDCs such as foetal alcohol spectrum disorder (FASD), TS and other rare genetic conditions. There is, nonetheless, emerging literature that is attempting to capture how EF impacts lesser known NDCs, with some interesting findings. Conditions such as TS and FASD are often highly comorbid with ADHD and ASD,<sup>204,205</sup> with emerging research on their EF profiles. Some research illuminates the presence of global EF deficits with minimal cross-condition differences and other's highlight nuanced EF differences across NDCs. In comparative study by Verte and Geurts (2005)<sup>206</sup> children with TS alone and children with comorbid ASD (high functioning) and TS demonstrated no EF differences. Another study found that children with ASD alone were impaired in flexibility, while the TS group revealed no impairment when compared to controls.<sup>207</sup> A more recent study comparing children with TS, ADHD and ASD found that children with TS were more impaired in emotional control (EC) as measured by the BRIEF scale, children with ASD were more impaired in flexibility (Shift subscale). Children with ADHD were more impaired in inhibition and behavioural regulation.<sup>208</sup> Openneer and colleagues<sup>209</sup> extend our understanding of EF in TS and comorbidities, with results indicating that children with TS and ADHD had impaired cognitive control (also executive control)

performance. Studies reviewing EF performance in FASD and ADHD reveal overall EF deficits<sup>210</sup> as well as unique patterns of impairment. A meta-analysis by Kingdon and colleagues<sup>146</sup> found children with FASD were found to have unique impairments in the areas of planning, fluency and flexibility (set-shifting) when compared to controls and working memory impairments when compared to children with ADHD.<sup>146</sup> The neurodevelopmental research highlights the highly nuanced EF profiles of these NDCs with the co-occurrence of NDCs being a norm rather than the exception.<sup>211</sup> Studies looking at LD and TS are few, as they often co-occur in the presence of ASD or ADHD. When LD and TS do co-occur with ASD or ADHD, their presence often adds to their overall functional impairments.<sup>211</sup> These findings highlight the condition specific impairments are prevalent when discrete conditions are compared and also highlight that interactive EF effects emerge when NDCs co-occur, signalling the distinctive impact of EF and its expression in NDCs. These distinctive profiles within NDCs herald the potential for EF to provide a detailed and nuanced neuropsychological indicator of functioning.

# 1.6. Executive Function as a Cognitive Endophenotype in Neurodevelopmental Conditions: A Focus on Key Cross-Condition Comparisons

The current DSM iteration (DSM-5-TR)<sup>133</sup> largely utilises behavioural expressions of NDCs. New and emerging research is highlighting the capacity of other markers to guide diagnosis, with some references to cognitive markers. EF, a cognitive marker, has the potential to guide diagnoses in an array of NDCs. EF when considered as an endophenotype can appropriately guide the supports and assessment of NDCs. Endophenotypes or intermediate phenotypes are markers (they can be biological, cognitive or behavioural in nature), that are suggestive of causal indicators such as genetics in the manifestation of condition which include NDCs<sup>133</sup> (i.e., the link between genes and behavioural psychopathology). For instance, in

dyslexia a prominent cognitive endophenotype which indicates the presence of this variant of SLD, is the impairment in phonological awareness attributed to this condition.<sup>212</sup> Endophenotypes have the potential to identify the genetical liability and further our understanding of genetic components linked with observable psychopathology.<sup>213</sup>

Research to date, has explored the cognitive endophenotypes that may be present in NDCs such as ASD and ADHD.<sup>196,214</sup> Rommelse and colleagues (2011) argue that ASD and ADHD are pleiotropic endophenotypes (conditions that are manifestations from a common gene).<sup>215</sup> Their review highlights neural and behavioural markers of these conditions and addresses a key pattern of comorbidity which is now on the rise. They address the high genetic link to these conditions and their increasing prevalence<sup>186,215</sup> and highlight emerging literature on familial studies and heritability with this NDC group.<sup>216,217</sup> As summarised in the prior sections of this thesis, the EF literature across NDCs such as ASD and ADHD allude to the presence of overall EF similarities<sup>166,218-220</sup> and some differences, with dissociable difference inhibition, cognitive flexibility, planning and variants of WM.<sup>221-223</sup> In comorbid in presentations, the literature is both mixed and limited. Some research suggests no differences between single NDCs and comorbid presentations of ASD and ADHD<sup>224</sup> whereas others highlight an additive deficit<sup>225</sup> when looking at inhibitory control and others suggesting the comorbid group presents with elevated impairment in this area of EF.<sup>226</sup> Studies on other NDCs reveal endophenotypic patterns that make links between different NDCs such as TS and ADHD.<sup>227</sup> Studies on TS suggest that flexibility is a unique endophenotype for this condition.<sup>228</sup> Other studies evaluating TS in comparison to ADHD and obsessive compulsive disorder (OCD) found executive control (with references to disinhibition) to be a prominent endophenotype implicated in this condition.<sup>209,227,229</sup> In a meta-analysis, looking at comorbid TS and ADHD, the EF pattern of increased inhibitory deficits appeared to be a specific marker

of executive control in this comorbid group, however this endophenotype was also present in the TS alone.<sup>182</sup> The pattern of EF across NDCs is pivotal in illustrating cognitive patterns which predict adaptive and behavioural responses to the world. Children with TS may exhibit impaired inhibitory control which may manifest behaviourally (i.e., vocal or motor tics) and children with ADHD may experience this EF with difficulty in emotional as well as behavioural regulatory mechanisms (e.g., response inhibition and working memory). Further, the pattern of NDCs in comorbid groups is proving a window into the complexity of EF in these groups and enhances our understanding of these neurodevelopmental presentations. Such presentations, therefore, exist in a complex continuum of EF unique to each condition.<sup>230</sup> EF serves as a transdiagnostic marker of neurodevelopmental delay, representing a key cognitive endophenotype that spans various conditions.<sup>196,214,231</sup> This cognitive endophenotype provides a window into shared underlying mechanisms prevalent in an array of NDCs, offering an enhanced understanding of the role of genetics and the etiological and developmental manifestations of such conditions.<sup>215,232,233</sup>

# 1.7 Transdiagnostic Perspectives on Executive Functioning: Theoretical and Practical Implications

The evaluation of EF performance within NDCs herald a new method of examining and understanding the impact of conditions within children. EFs within NDCs have historically been constrained by disorder-specific paradigms. However, recent advances advocate for a transdiagnostic approach, acknowledging the shared cognitive impairments across various NDCs.<sup>215,230</sup> This thesis posits that understanding the transdiagnostic overlap in EFs is pivotal, offering insights into the universal mechanisms that underpin diverse NDCs. The recognition of EF overlap across NDCs illustrates that shared cognitive substrates transcend diagnostic boundaries. This perspective challenges more traditional, phenotypic diagnostic nosologies,

suggesting that a more nuanced understanding of cognitive processes is necessary for elucidating the aetiology and expression of NDCs. The transdiagnostic viewpoint disrupts traditional, siloed approaches to studying NDCs, advocating for an integrative model that considers the complexity of cognitive functioning, and how EF can better shape our understanding. A transdiagnostic theoretical framework thus illustrates the potential for refining diagnostic criteria and enhancing intervention strategies, thereby fostering a more holistic approach to child neurodevelopment research and practice. Such models promise to reconcile the discrepancies between isolated condition frameworks and the empirical realities of overlapping executive performance in NDCs.<sup>188,189</sup> From a practical standpoint, the transdiagnostic approach to EFs proposes a paradigm shift in assessment, intervention, and educational practices. By focusing on common EF deficits rather than condition-specific symptoms, practitioners can devise more personalised and effective strategies. This encompasses the development of interventions that are applicable across a spectrum of NDCs and the implementation of pedagogical techniques that support EF development in diverse paediatric populations.<sup>234</sup>

#### 1.8. Research Aims

The objective of this project is to facilitate an integrated understanding of EF as a pertinent, endophenotype in the assessment and management of NDCs in children. This objective serves to establish an evidence-based understanding of EF profiles across various NDCs utilising validated tools. To achieve this, the research project is structured around three main aims. The first aim is to systematically review the broad literature on EF in children with prominent NDCs in children and better conceptualise an understanding of EF profiles and the factors contributing to variations across different conditions within this population. The second aim is to examine EF profiles in children with prominent comorbid NDCs, particularly focusing on the variability and severity of EF impairments in relation to the comorbidity of these

conditions. The final aim of this project is to explore the role of caregiver evaluation in children with a range of NDCs and the association between their developmental strengths and weaknesses with EF outcomes. Overall, this project aims to comprehensively assess EF performance transdiagnostically and to evaluate EF performance in NDCs within paediatric clinical settings.

# **1.9. Project Hypotheses**

Following a broad review of the literature in this field, the following core hypotheses regarding EF and NDCs in children will be examined:

- I. EF Delays in Children with NDCs:
  - Children diagnosed with NDCs will exhibit significant delays in EF compared to controls.
  - The severity of EF impairments will show variance depending on the assessment method utilised and gender differences may play a role in the manifestation of these impairments.
  - Distinct differences in EF profiles will be observed across various NDCs, highlighting specific sub-domain impairments unique to each condition.
- II. Variances in EF profiles, among children with different NDCs:
  - Variations in EF profiles, as assessed by the BRIEF, will be evident among children with different NDCs such as ASD, SLD, and ADHD.
  - Greater impairments in cognitive flexibility and inhibition will be observed in children with comorbid conditions, particularly those with ASD and ADHD, compared to those with a single NDC.

- An increase in the number of comorbidities will be associated with more pronounced overall EF deficits, suggesting an additive or interactive effect on EF.
- III. Association between DSM diagnoses, caregiver concerns, and EF delays:
  - A higher number of DSM diagnoses and caregiver-reported concerns in children will be correlated with elevated EF deficits, as measured by the BRIEF.
  - Conversely, a greater number of caregiver-reported strengths will correspond to lower EF difficulties, indicating a potential protective factor against executive delay.
  - Specific challenges in social abilities, behaviour, and caregiver concerns related to NDCs (such as ASD, ADHD, SLD) will be linked with impaired BRIEF Global Executive Composite (GEC) and domainspecific scores, highlighting the interplay between EF delays and clinical symptomatology.

## 1.10. Research Program

To address the main objectives of this research project on EF in NDCs, this thesis is further divided into three interrelated internal chapters. These chapters address issues such as comorbidity within NDCs and developmental strengths and weakness in relation to EF, which are key objectives in this field of research.

Chapter 2 of the thesis is a comprehensive systematic review and meta-analysis focusing on the role of EF as a transdiagnostic endophenotype in NDCs such as ASD and ADHD, along with other prominent NDCs affecting children up to the age of 18. This Chapter explores seven identified EF constructs: attention, fluency, set shifting, set switching, response inhibition, planning, and working memory. The analysis investigates the EF profiles across various NDCs, considering the impact of assessment type (informant-based vs. performance-based) and demographic factors (age, gender) on these profiles.

In Chapter 3, the focus shifts to examining EF profiles in children aged 5 to 18 years diagnosed with NDCs such as ASD, ADHD or SLD were examined. Utilising the BRIEF measure, this chapter compares EF profiles among participants with single versus multiple NDCs. Additionally, it discusses the degree of EF severity in relation to specific diagnoses, shedding light on how comorbidities may influence EF outcomes.

In Chapter 4, the relationship between EF and caregiver reported strengths and challenges in children with developmental concerns, was explored using the BRIEF measure for a comprehensive EF assessment. Spanning a diverse age range of 2-16 years, the research primarily focuses on the correlation between EF profiles and parental reports of strengths and challenges encompassing behaviour, social skills, play capabilities, and cognitive abilities.

In Chapter 5, a comprehensive discussion is provided, incorporating the findings from each empirical chapter, and highlighting their contributions to both research and clinical practice. The detailed discussion integrates the thesis's primary findings, addresses any limitations encountered during the research project and explores potential avenues for future research in the field.

# Chapter 2: Executive Function in Children with Autism, ADHD and other Neurodevelopmental Conditions: A Systematic Review and Meta-Analysis. Study Objectives:

This review sought to:

- (a) Review forty-two years of literature on EF in NDCs among paediatric population, with a specific focus on ASD, ADHD, while also considering how these NDCs compare to other conditions in their EF performance within the same population.
- (b) Evaluate differences in EF profiles across various NDCs and compare these profiles to those observed in neurotypical population.
- (c) Assess moderating influence that contribute to our overall understanding of EF in children with NDCs; with a particular emphasis on age and type of measures utilised for EF assessment.

Executive function in children with Autism, ADHD and other neurodevelopmental conditions: A systematic review and meta-analysis.

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Abstract Word: 408

# Body Word Count: 4513

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#### Data availability

The data used to undertake this systematic review and meta-analysis are freely available upon request to authors.

# **Conflict of Interest**

There are no conflicts of interest to report as part of this review.

Acknowledgements: The authors acknowledge the technical assistance provided by the Sydney Informatics Hub, a Core Research Facility of the University of Sydney. Of note, we wish to thank Jim Mathews, Gordan McDonald, Januar Harianto and Timothy Wong for their statistical guidance. AS is a PhD student at the University of Sydney and was kindly supported by the Cerebral Palsy Alliance Scholarship program. AS had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

#### 2.1. Abstract

Executive function (EF) impairments have been found in many child neurodevelopmental conditions (NDCs). These impairments, such as challenges with task initiation and attention, have been well-documented in NDCs such as ASD, ADHD and SLD when explored individually however there are many contradictory findings making it difficult to ascertain how salient their results are. The influence of key demographic and measurement variables, such as gender, age and type of EF measure utilised are also not well understood. To examine moderators of this effect, and to test differentiating EF impairments between key NDCs, a systematic review and meta-analysis of EF across paediatric NDCs was conducted. Studies with children with at least one of ASD or ADHD compared to an independent sample with an NDC were evaluated. In line with PRISMA guidelines, a systematic literature review was carried out in MEDLINE, EMBASE and PsychInfo using a selection of relevant terms and the search covered the period of January 1980 to April 2022. The review was registered with PROSPERO (CRD42020210785). Of 175 identified studies, 105 met selection criteria. Two independent reviewers conducted study screening and assessed against the inclusion criteria. This included all studies that measured EF using established tests in participants under 18 years of age and describing populations comparing ASD and ADHD with a NDC group. Methods followed PRISMA guidelines. Extraction and risk of bias assessment was conducted by two independent reviewers. Data was pooled using a random-effects model. Outcomes across seven EF domains included attention, fluency, set shifting, set switching, response inhibition, planning and working memory. Analyses of individual EF domains were conducted for each comparison (i.e., ASD vs ADHD). Main outcomes included scores on performance and informant-based EF measures. The moderator effects (i.e., age and type of measure) of EF domains were analysed. Analyses was conducted using the metafor package in R. A moderate effect size of EF impairment across all NDCs was found (g=0.63), in comparison to control. Children with ADHD showed greater problems with attention and response inhibition, children with autism showed larger impairments in set-shifting, while children with learning disorders showed evidence of greater impairments in set-switching. Informant measures overall showed larger effects sizes of EF impairment, in comparison to performance-based measures. EF impairment is a transdiagnostic feature of key NDCs that is likely underpinned by accompanying divergence in brain structure, activation, connectivity, and chemical signalling. Findings support the prioritisation of transdiagnostic approaches to EF delay in prominent NDCs to improve life outcomes for these children.

*Keywords:* Neurodevelopment, paediatric developmental conditions, autism, ADHD, biomarkers

#### 2.2. Introduction

Executive function (EF) is an umbrella term used to conceptualise a range of cognitive processes including planning, working memory, attention, inhibition, self-monitoring, , and initiation.<sup>1,2</sup> EF encompasses a network of functional cognitive abilities that allow for realworld engagement, which are the refined during key developmental periods.<sup>1,4</sup> Impairments in EF can include difficulties in sustaining attention, impulsivity, and an inability to transition between, and flexibly manage, multiple tasks.<sup>2,33,136-139</sup> The presence of EF impairments may also signal divergence in brain development with a role in both causal and maintaining factors in neurodevelopmental conditions (NDCs).<sup>26,235</sup> EF processes are believed to be involved in a range of emotional, behavioural and social functions. EF research has been able to formulate numerous models to explain this complex network of cognitive systems. EF research led to the formulation of numerous models to explain this complex network of cognitive systems. Miyake and colleagues<sup>24</sup> and Diamond<sup>46</sup> postulate theories that conceptualise EF with core faculties (including attention) which set the foundation for higher order, more complex faculties to develop. These models are informed and supported by a substantial amount of EF research and clinical data<sup>43,236</sup> and set the groundwork for this review. This review aims to investigate both higher order and more foundational domains within the paediatric population. EF research demonstrates considerable debate on how EF domains are considered to overlap, or present as separate faculties. Further, the literature attempts to capture these faculties through the use of various EF measures. Considering the body of literature in this area, this review will focus on attention, set shifting, set switching, fluency, planning, working memory and response inhibition. Not only will this allow for a comprehensive EF developmental trajectory review but encompasses EF domains that have been found to be linked to functional outcomes. For example, although attention is a contentious domain in EF theoretical literature,<sup>1</sup> it is nonetheless comprehensively measured and found to be considerably impaired in NDCs such as ADHD<sup>237</sup>. Impairments in EF are believed to impact quality of life in children<sup>238</sup> and can contribute to lifelong challenges.<sup>2,4</sup> These impairments are thought to be moderated by variables such as sex, type of EF measure, and age.<sup>232</sup> For example, some studies have suggested that EF difficulties may increase during adolescence,<sup>239</sup> while others do not.<sup>52,240,241</sup> Overall, deficits in EF could be considered to represent a broad transdiagnostic cognitive phenotype of NDCs. There has, however, been limited research examining the transdiagnostic endophenotype across neurodevelopmental conditions.

EF impairments have traditionally been studied within specific NDCs.<sup>145,146</sup> Paediatric EF studies have generally focused on emerging core EF domains of inhibition, working memory, and cognitive flexibility.<sup>24,242</sup> These domains are believed to serve foundational cognitive faculties that allow for the development of higher order EF functions, such as planning and problem solving.<sup>24</sup> Impairments in each of these domains have been reported in children with NDCs from their first years of life.<sup>2,4</sup> To date, age based effects have also been examined within disorders. For example, deficits in working memory (WM) are well-documented in children with Attention-deficit/hyperactivity disorder (ADHD) and Learning disorders (LD).<sup>114,243,244</sup> Although research of executive function capacities between NDCs exists, it often lacks a transdiagnostic lens with emerging research attempting to capture this viewpoint. <sup>245</sup>

Cross-condition studies<sup>146,186</sup> further show that there may be some differences in subdomain EF outcomes based on the disorder specific phenotype. In support, some studies comparing children diagnosed with Autism (ASD) or ADHD show that children with ASD show marked impairments in cognitive flexibility and planning, while children with ADHD may be more likely to show impairments in inhibition and working memory.<sup>246-249</sup> Other studies<sup>166</sup> have reported stronger impairments in response inhibition, cognitive flexibility/switching, and WM for children with ASD in comparison to those with ADHD.<sup>166</sup> Such comparisons are important for understanding the causal and maintaining features that differentiate clinical profiles of conditions. Further, they could be used to screen for diagnoses, confirm co-occurring NDCs and assess clinical severity. These profiles can subsequently inform assessment practices and the educational and therapeutic supports children receive for different conditions.

#### 2.2.1. Prominent Neurodevelopmental Conditions: ASD and ADHD

ASD and ADHD are two of the most prominent NDCs in the paediatric literature with high comorbidity and prevalence rates.<sup>250,251</sup> Recent prevalence studies indicate that 0.6% of children are diagnosed with ASD,252,253 and 5.6% to 7.6% of children are diagnosed with ADHD globally.<sup>254</sup> A recent meta-analysis on the co-occurrence of both ASD and ADHD found current and lifetime prevalence to stand at 38.5% to 40.2%.<sup>187</sup> These figures currently capture the co-occurrence of these conditions, given it was only after 2013 that DSM iterations acknowledged their comorbidity. Reviews have largely focused on EF processes across single NDCs<sup>145,255</sup> with emerging research capturing the presence of multiple NDCs in children. Recently, a meta-analysis by Townes and colleagues<sup>256</sup> (2023) compared EF profiles of children with ASD or ADHD, with results indicating no significant differences between these two NDCs across domains of attention, flexibility, visuospatial abilities, working memory, processing speed, and response inhibition. Systematic reviews that study comorbid presentations of ASD and ADHD find that the co-occurrence of these presentations are found to demonstrate increased executive delay compared to those with single conditions. <sup>189,188</sup> The literature has, to date, reviewed the significance of executive delay that exist within these conditions. However, a nuanced exploration through a meta-analysis of how these prominent NDCs perform in relation to other, less prevalent NDCs across EF is yet to be explored. In light of an increase in prevalence rates and increased comorbidity, EF performance of key NDCs in
comparison to other NDCs can assist in providing a transdiagnostic neurodevelopmental evaluation of EF in children.

#### **2.2.2. Executive Function Measures in the Paediatric Population**

Assessments of EF include both performance and informant-based measures. Performance EF tasks typically involve practical tasks of EF capacities (e.g., errors on a computer-based response inhibition task; placing objects in an instructed order) and are purported to objectively tap into discrete EF domains. There is, however, a high degree of overlap between EF domains and their underlying neurobiology, raising questions about their functional indpendence.<sup>139</sup> As such, many measures of EF likely tap multiple domains. For example, tasks that measure set-shifting such as the WCST (Wisconsin Card Sorting test) may also be impacted by a WM component<sup>257</sup>. Other measures such as informant-based measures are proposed to possess greater ecological validity given their reliance on the reporting of observed everyday behaviours.<sup>2</sup> Informant-based measures often describe how a child's EF profile directly relates to their daily functioning, often encompassing greater reported functional deficits<sup>145,232</sup> suggesting greater ecological validity but come at a cost of reduced objective reliability.<sup>114,243,244</sup> The debate between the utility and reliability of these measures has been long-standing and mixed. For example, some authors have argued performance-based measures may provide more objective scaling of EF performance, with others have pointed to the utility of informant and self-report measures to predict functional outcomes. Nonetheless, each measurement approach provides unique clinical utility in a range of paediatric contexts<sup>258-</sup> 260

# 2.3 Study Aims

There is a lack of research addressing the role of EF as a transdiagnostic endophenotype in NDCs in children. This meta-analysis aims to synthesise the existing literature on EF in NDCs, with a focus on ASD and ADHD. It reviews seven EF constructs identified in paediatric literature (attention, fluency, set shifting, set switching, response inhibition, planning and working memory). Given that EF is a component of cognition across neurodevelopment, it is critical to evaluate its discriminating and/or shared profile across NDCs. This systematic review and meta-analysis aimed to review studies that investigated EF measures in populations with ASD or ADHD and other NDCs. Studies were required to have two or more NDCs in children with or without a control comparison. Further, this study aimed to consider how type of assessment measure (informant or performance based) and demographic factors (age, gender) influenced the results of the primary analysis. We predicted that:

- 1) All neurodevelopmental conditions would be associated with significant impairments across EF domains, when compared to controls.
- Effect size of impairment would be moderated by type of assessment and sex, such that informant-based measures and a higher percentage of males captured in studies would be associated with larger effect sizes.
- Comparisons between EF profiles between NDCs would show differences in the severity of impairment in sub-domains of impairment.

# 2.4. Methods and Materials

This review adheres to the Preferred Reporting Items for Systematic Reviews and Metaanalyses (PRISMA) guidelines.<sup>261,262</sup> The review was registered with PROSPERO (CRD42020210785).

# 2.4.1. Study Selection

The review included peer-reviewed English language studies published from 1980 to April 2022 (see Figure 2.1 for data extraction diagram). Studies were considered if they included children under 18 years of age and reported on at least two comparison groups, with ASD and ADHD being key comparative groups. The search employed a focus on articles that reviewed ASD with other NDCs, and ADHD with other NDCs. That is, these two groups were each compared to other NDCs. Participant NDC diagnosis needed to be assessed with reliable diagnostic measures (see Supplementary Table 1 for search strategy in Appendix A). NDCs were identified if they were listed within the DSM-V as an NDC. Each NDC then needed sufficient data to be included to inform key NDC groups for further analysis (i.e., ASD vs ADHD). The search strategy captured information such as whether the diagnosis was made through a clinical interview, DSM criteria, standardised measures or other mode of classification. Effort was made to ensure all captured studies used best practice clinical measures.

Studies must have included outcome measures including informant measures and/or performance measures of EF (see Supplementary Table 1 in Appendix A). Outcome measures may include one or more measures derived from psychometric tests, experimental tasks and/or self/informant measures.



# 2.4.2. Search strategy and study variables

The literature search was conducted through Medline, Embase and PsychINFO databases using a detailed search criteria of EF measures (i.e., "BRIEF", "Wisconsin Card Sorting Test", "Go-no-Go task" "Stroop test") and a full range of paediatric NDCs (e.g., "Autism" "Autism Spectrum Disorders", "ADHD", "Tourette's Syndrome", see supplementary information for more detailed descriptions of extracted studies). The first author (AS) screened results for initial eligibility based on title and abstract using Covidence.<sup>263</sup> Full-text versions of eligible studies were screened with a second reviewer (CS). A third reviewer addressed any disagreements (EAD). Reported EF measure outcomes (i.e., reaction times, commissions or omissions errors in a task like Go-No-Go), were extracted as mean values and standard deviation scores for each group at a single time point. To manage selective data extraction, all relevant EF outcomes were extracted. This assumed that within assessment measures are at least moderately correlated, and to avoid selective data reporting. Where there was missing data, efforts were made to contact authors regarding missing data, however no author was able to address the authors' request. In addition, authors contacted all study authors for unpublished data to mitigate 'the file drawer effect'. One author was able to address this request with two studies and their data is included in the results.

#### 2.4.3. Quality assessment

Quality review of studies was completed by two assessors using the Checklist for Cross Sectional and Cohort Studies within the JBI Critical Appraisal Tools.<sup>264</sup> Studies were rated "fair" to "good".

#### 2.4.4. Data items

Group level summary data (e.g., sample size, means, standard deviations, F-values) was extracted for all measures reporting outcomes for executive function. All meta-analyses results were conducted and obtained using the metafor package in R.<sup>265,266</sup> The analytical approach used was a multilevel analysis using the random-effects model. The unit of analysis utilised within this model was the standardised mean difference (calculated as Hedges' g) on each measure between NDCs. When making group comparisons, a positive effect size indicated that the control group performed better than the NDC group. Within the cross-condition analysis (i.e., ADHD versus SLD), the positive effect size indicated that one comparison group was performing better than its comparison group, (i.e. ADHD vs. ASD). The data analysis was planned a priori and was completed in four stages. The initial analysis combined all EF outcomes to assess the overall EF effect size in NDCs when compared to controls (i.e., typically developing children). The second analysis examined subgroup comparison of the individual EF domains. The third analysis examined the estimated effect size of difference for each NDC in comparison to control conditions. The next step involved examining between study variability and moderator impact for overall EF and individual EF domains, this includes 'Type of Measure', 'Gender', 'Age' and 'DSM edition' which was assessed as a covariate in metaregression analyses. The final step involved the analyses of individual EF domains which were conducted for each comparison (i.e., that is ADHD vs SLD etc.). The effect size measure of Hedges'  $g \leq 0.30$ , >0.30 and <0.60 and  $\geq 0.60$  are described as small, moderate or large. Heterogeneity was assessed using several statistical measures. The degree of variation between-studies was reported using the  $\tau^2$ . Where applicable, heterogeneity across studies was assessed and reported using the  $l^2$  statistic with 95% confidence intervals (CIs). The  $l^2$  values of 25, 50 and 75% define small, moderate and large heterogeneity.

#### 2.5. Results

# 2.5.1. Primary Outcome: Neurodevelopmental Groups and Controls

An overall meta-analysis comparing eligible studies that compared at least two NDCs with controls was completed (see Figure 2.2 and Supplementary Table 2, Appendix A for study

characteristics). The neurodevelopmental groups showed significant impairment in their overall EF (n=88, k=1573, g=0.60, 95% CI=0.53 to 0.65, p < 0.001;  $\tau^2=0.18$ ;  $I^2=75\%$ ; prediction interval 0.56 to 0.69). Following data screening, four studies were removed as they contributed to plot asymmetry. Separate meta-analyses for single neurodevelopmental conditions and their controls were compiled. These meta-analyses were conducted for ADHD, ASD, Tourette's Syndrome (TS), LD and Williams Syndrome revealed significant impairments in overall EF for all neurodevelopmental groups ( $p \le 0.048$ ).



Note: *N* refers to the number of EF comparisons made within the meta-analysis and not the number of studies. *Figure 2.2. Hedges' g for EF in NDCs versus Controls* 

Funnel plot asymmetry was detected, indicating possible small-study effect ( $\beta$ = 0.105; one-tailed *p*=0.002; see Supplementary Figure 1 in Appendix A). A trim and fill analysis imputed one study; the adjusted effect size suggested minor small-study bias (*g*=0.60; 95% CI= 0.54 to 0.67; *p*<0.001), see Supplementary Figure 2 in Appendix A. Sensitivity analyses comparing a hierarchal (*g*=0.58; 95% CI= 0.53 to 0.64; *p*<0.01;  $\Omega^2$ =0.07;  $\tau^2$ =0.05) to a

correlational model as well as correlation assumptions revealed the model assumptions of the main analysis to be robust.

#### 2.5.2. Moderator Analysis

Further moderator analyses as part of the multivariate meta-analysis revealed the contribution of performance measure (n=88, k=1573 g=0.97, CI = 0.82 to 1.11, p<0.001) was significant when compared to informant measures (n=88, k=1573 g=0.40, CI = 0.26 to 0.54, p<0.001;  $Q_{(1,1571)}=30.18$ , p<0.001,  $R^2=14\%$ ). For gender, the higher the percentage of males, the more significantly they contribute to the overall effect size, however, this was just significant and accounted for a negligible degree of variance, (n=65, k=1237, g=0.008, 95% CI = 0.000 to 0.015, p=0.049;  $Q_{(1,1235)}=3.881$ , p=0.05,  $R^2=0\%$ ). The effect of age was not significant with younger children (n=86, k=1538, g=-0.126, 95% CI = -0.244 to -0.007, p=0.03;  $Q_{(1,1536)}=1.91$ , p=0.167,  $R^2=0\%$ ), showing an insignificant contribution to the overall effect size than their older counterparts, (n=86, k=1538, g=-0.044, 95% CI = -0.107 to -0.019, p=0.167). Further, DSM editions used in each study had no significant moderating effect (n=75, k=1263, g=0.12, 95% CI = -0.081 to 0.321, p=0.12 to 0.15).

## 2.5.3. Differences in EF Profiles according to specific neurodevelopmental conditions.

The next set of analyses examined whether the observed impairment found in EF differed according to the neurodevelopmental diagnosis (see Figure 2.3). To address this question, we conducted a series of analyses between each NDC using studies that provided enough power. This was informed by the presence of underlying heterogeneity as well as sufficient number and balance of studies within subgroups that allowed for these cross-condition analyses to take place within each cell.



Figure 2.3. Effect Sizes for Seven Areas of EF across Primary NDC comparisons.

*Autism Spectrum Disorder and ADHD:* Findings from 30 studies comparing ADHD and ASD showed that there were no significant differences of overall EF between conditions  $(n=29, k=208, g = 0.024, \text{CI} = -0.065 \text{ to } 0.112, p = 0.60, \tau^2=0.20; l^2=75\%$ ; prediction interval - 0.086 to 0.119). On sub-domains, however, significant differences were found between comparison groups in set shifting  $(n=14, k=34, g= 0.30, 95\% \text{ CI} = 0.10 \text{ to } 0.51, p=0.004, \tau^2=0.12)$ . Children with ADHD performed better on measures of set shifting compared to children with ASD.

We then compared the effect of EF on informant or performance-based measures for this population to determine whether the effects observed persisted. There were too few studies to test this on informant measures. For performance measures, after informant measure outcomes were removed, only the attention domain was significant, as shown in Figure 4 (n=8, k=32, g=-0.19, 95% CI = -0.34 to -0.05, p = 0.007,  $\tau^2=0.02$ ), where children with ASD performed better on measures of attention than children with ADHD.



Figure 2.4. Effect Sizes for Seven Areas of EF across primary NDC comparisons with performance only measures.

*Tourette's Syndrome and ADHD:* There was a significant effect for overall EF domain differences (n=15, k=70, g = -0.27, 95% CI = -0.50 to 0.05, p = 0.018,  $\tau^2=0.21$ ;  $l^2=73\%$ ; prediction interval -0.55 to -0.03) across 15 studies, suggesting poorer EF performance for ADHD compared to TS. Sub-domain meta-analyses for individual EF domains showed unique differences in response inhibition across 15 group comparisons (n=7, k=15, g= -0.19, 95% CI = -0.32 to -0.05, p = 0.005,  $\tau^2=0.00$ ) where children with Tourette's syndrome (TS) performed better than children with ADHD. The sub-domain analysis for attention was also significant favouring TS (n=7, k=18, g= -0.403, 95% CI = -0.76 to -0.039, p = 0.03,  $\tau^2= 0.20$ ), across 18 group comparisons. Findings were similar when informant measures were removed from the analysis.

*Learning disorders and ADHD:* Findings from 38 studies comparing learning disorders (LD) and ADHD showed no significant results for a combined EF effect (n=38, k=208, g = -0.16, 95% CI = -0.37 to 0.05, p=0.13,  $\tau^2=0.94$ ;  $l^2=92\%$ ). As shown in Figure 2, subdomain analysis revealed an effect size direction that ADHD children had better performance in the set switching domain across 4 group comparisons (n=4, k=4, g=0.21, 95% CI = 0.034 to 0.387, p = 0.02,  $\tau^2=0.00$ ), and LD children in set shifting across 21 comparisons (n=13, k=21, g= -0.46, 95% CI = -0.82 to -0.12, p = 0.008,  $\tau^2=0.34$ ) and attention domain across 24 comparisons (n=10, k=24, g= -0.37, 95% CI = -0.72 to -0.02, p = 0.036,  $\tau^2=0.26$ ). When informant measures were removed only set switching (n=4, k=4, g=0.21, 95% CI = 0.034 to 0.387, p = 0.02,  $\tau^2=0.00$ ) and attention (n=10, k=24, g= -0.37, 95% CI = -0.72 to -0.02, p = 0.036,  $\tau^2=0.26$ ). When informant measures were removed only set switching (n=4, k=4, g=0.21, 95% CI = 0.036,  $\tau^2=0.26$ ) remained attention (n=10, k=24, g= -0.37, 95% CI = -0.72 to -0.02, p = 0.036,  $\tau^2=0.26$ ) remained significant, where children with ADHD had impaired attention but better set switching.

**ASD and TS:** Cross disorder meta-analysis results with the TS and ASD cohort were not significant (n=2, k=11, g=-0.10, 95% CI = -0.30 to 0.09, p = 0.30,  $\tau^2=0.06$ ;  $l^2=33\%$ ), following a review of 2 studies. No significant results were found with subdomain analysis within these groups. *Learning Disorders and ASD:* A review of 6 studies comparing children with ASD and LD revealed no significant differences in their combined EF effect (n=6, k=27, g=0.39, 95% CI = -0.008 to 0.79, p = 0.055,  $\tau^2=0.27$ ;  $I^2=78\%$ ). No significant results were found with subdomain analysis.

# 2.6. Discussion

Our results suggest that EF is a transdiagnostic feature across key NDCs, showing an overall moderate effect size of impairment that did not differ markedly across NDCs. Results also supported the value of cross-condition research, with some condition specific impairments in EF sub-domains. Children with ADHD showed greater impairments in attention and response inhibition, children with ASD showed greater impairments in set shifting tests and children with LD showed poorer set-switching. Overall, informant-based measures of EF, relative to performance-based measures, showed larger effects, that is, informant measures had a larger contribution to the overall effect size. The effect size of EF impairment increased with the percentage of males in each study, but the contribution of gender to the effect size was marginal. There was no influence of age. The results here show that EF impairments are a transdiagnostic feature of NDCs and that some NDCs are associated with greater EF impairments in specific domains.

The findings of this study suggests a broad EF impairment across prominent NDCs with little evidence that specific NDCs were associated with greater overall EF impairments. There has long been speculation that EF may be a transdiagnostic feature of neurodevelopmental delay. The executive system is believed to be the most recently evolved brain system that operates as a control centre, managing many other cognitive abilities (e.g., attention, learning, social development, and memory).<sup>2,4</sup> This system facilitates flexibility and adaptability<sup>267</sup> to both novel and complex situations.<sup>268,269</sup> While the executive system circuitry is facilitated by

the pre-frontal cortex, it is highly connected and reliant on other brain circuiry.<sup>33</sup> It follows then, that any divergence in brain development is likely to impact this interconnected system. Indeed, research has shown how genetic,<sup>270</sup> neurochemical, <sup>271</sup> and environmental<sup>272,273</sup> factors linked to NDCs, as well as critical periods of neurodevelopment,<sup>274</sup> may all influence EF maturation. A transdiagnostic NDC research framework is needed to further evaluate modifiers of EF across child development. This will pave the way for a better understanding of EF and its impact on neurodevelopmental divergence broadly.<sup>275,276</sup>

Assessment type had a significant contribution to the overall effect. Findings of larger EF impairments when using performance versus informant-based measures has also been supported by prior literature.<sup>145,260</sup> The administration of performance-based measures evaluates EF in cumulative scores that tap into accuracy of individual cognitive domains, whereas informant-based measures are often based on reported deficits which are correlated with functionality or real-world behavioural performance of the individual. It is noted that within EF literature, a large number of studies utilise performance-based measures, which allows for EF domains to be siloed and measures tend to capture.<sup>260</sup> On the other hand, some research has shown that informant EF measures may be better at differentiating those with a clinical diagnosis as it captures the degree of impairments in everyday life.<sup>145</sup> Taken together, these findings suggest research is needed to delineate the use of informant and performance-based measures across development and their utility to understand when informant or performance measures are best utilised, with some research suggesting the increased efficacy of combined use.<sup>260</sup>

While there was broad support for a transdiagnostic approach to overall EF impairment, there was also evidence of some disorder-specific effects on EF. For ADHD, the overall effect size of EF impairment was small in contrast to the moderate effect size of impairment for other conditions. Despite this, results repeatedly demonstrated that children with ADHD showed worse outcomes on attention sub-domain measures in comparison to many other NDCs. Attentional disruption is core to the diagnostic criteria of ADHD<sup>277</sup> and the results here further reinforce this through the use of both informant and performance measures. They also offer support to the specificity of attention-based models of ADHD<sup>237,278,279</sup> that highlight brain regions (such as the dorsal anterior cingular cortex) involving selective and sustained attention. There was some evidence of impairments on sub-domains of response inhibition and cognitive flexibility (set shifting and set switching), for comparisons with TS and ADHD, and LD and ADHD, respectively. According to the supervisory attentional system<sup>278</sup> impaired attention can cause challenges in disengaging from habitual behaviour and exerting novel responses, which in turn implicates response inhibition and set shifting.<sup>14</sup> Such models allude to the unique role attention holds within the EF network and its multi-layered nature.<sup>1,82</sup> Other models take a multifactorial approach and highlight the trajectory EF domains take from simple to complex of EF networks.<sup>24,33</sup> These models emphasise the interconnected relationship attention has with other key EF domain areas as EF networks become more mature.<sup>280</sup> In regards to other conditions, children with ASD were more impaired on tests of set-shifting (also known as concept formation) in comparison to their ADHD counterparts.<sup>145,188</sup> This impairment has been linked to the phenotype of rigidity and repetitive behaviours, as well difficulties in processing stimuli and social information in complex environments.<sup>281,282</sup> Children with LD also showed poorer set-switching in comparison to ADHD. This can manifest as challenges with the capacity to switch between mental processes in response to changing demands and such challenges have been outlined in students with different forms of LDs.<sup>283-285</sup> Taken together, these findings inform our understanding that while neurodevelopmental conditions share an overall transdiagnostic EF profile,<sup>199,230</sup> nuanced atypicalities across neurodevelopment can also lead to distinct cognitive profiles and different levels of impairment.<sup>145,166,188,276,286</sup>

# 2.6.1. Limitations

Although a large body of neurodevelopmental literature controls for IQ, we did not include IQ as a primary covariate in our analysis given the overlap between IQ and EF domains. <sup>287</sup> We also note the low number of studies used to identify EF patterns in lesser investigated NDCs (i.e., Tourette's syndrome with learning disorders). This meta-analysis focused on NDC comparisons with key NDCs, ASD and ADHD and is limited by the existing literature and the absence of broad investigations of neurodevelopment and cross-disorder comparisons. This study highlights the urgent need for future work to address these gaps in cross-disorder and transdiagnostic developmental research. In addition, a statistically sufficient amount of data outcomes were captured for performance only measures. Subsequently, the results can therefore be more applicable to studies that have investigated performance-based measures and hence more generalisable based on the parameters set out by these test conditions Further research into informant-based measures and their transdiagnostic EF evaluation will continue to inform this area of research. We also note that for ADHD studies, singe-condition metaanalyses have reported moderate effect sizes of impairment overall (e.g., hedges g =0.54).<sup>249,286,288</sup> Inspection of such meta-analyses, however, reveal that they focus largely on tests of attention, working memory, set shifting and response inhibition. The results here shows that when a cross-condition evaluation of EF domains is applied, it leads to a more nuanced understanding of the EF impairment across sub-domains and overall. Considering this review was limited by the number of studies captured within a particular NDC, we note generalisability to lesser investigated NDCs such as cerebral palsy is limited. The generalisability of findings

to long term outcomes is also limited as our review did not capture a comprehensive list various experimental methods such as longitudinal studies. Finally, we acknowledge that many of the included studies did not control for comorbidity and the changing criteria in DSM iterations is a limitation given the changes to discrete diagnostic classifications over time. This review highlights the urgent need for well characterised studies that both address condition specific and transdiagnostic comparisons of NDCs.

# 2.6.2. Conclusion

The conclusions drawn here demonstrate that EF impairment is a transdiagnostic feature of paediatric NDCs, particularly for ASD and ADHD. Future research should target transdiagnostic and distinct EF profiles across the developmental trajectory with a focus on determinants of the EF endophenotype, such as gene profiles, neurobiological underpinnings (e.g., functional brain connectivity, neurotransmission) and environmental factors that moderate outcomes across time. EF profiles may provide one of the best transdiagnostic markers for neurodevelopmental delays for use in both research and clinical practice. In addition, subtle differences observed here between key NDCs offer potential for a precision medicine approach that may lead to better supports for learning, cognition, and daily living.<sup>289-291</sup>

# Chapter 3: Executive Function Profiles across Neurodevelopmental Conditions: A Focus on Comorbidities in Autism, ADHD and Specific Learning Disorders in Children. Study Objectives:

This study sought to:

- a) Explore the degree of EF severity in increasing NDC comorbidities.
- b) Examine executive delay profiles in children with NDCs (ASD, SLD, and ADHD) and their comorbid groups using the BRIEF measure.

Executive Function Profiles Across Neurodevelopmental Conditions: A Focus on Comorbidities in Autism, ADHD and Specific Learning Disorders in Children.

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Abstract Word Count: 219 Body Word Count: 3936 words Tables/Figures: 4 Target Journal: Autism Research

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Abbreviated Title: Executive Function Profiles in Comorbid Neurodevelopmental

Conditions

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**Funding**: This research was funded by author's postgraduate scholarship funded by the CP Alliance.

Data availability statement: Data are available upon reasonable request.

**Ethical statement:** The study was approved by the Sydney Children's Hospital Network Human Research Ethics Committee (LNR/17/SCHN/293; Child Development Registry).

# 3.1. Abstract

Children with neurodevelopmental conditions (NDCs) typically show executive function delays. They also frequently present with comorbidities, including other NDCs, which contribute to functional challenges. How co-occurring neurodevelopmental presentations influence EF profiles is not well understood. This study addressed this gap by evaluating data from a sample of 170 participants aged 7 to 17 years and assessed EF profiles measured through parent Behavior Rating Inventory of Executive Function (BRIEF) questionnaire responses. Participants were diagnosed with Autism (ASD) (n=47), Autism and Attentiondeficit/hyperactivity disorder (ADHD) (n=32), ADHD and specific learning disorders (SLD) (n=67) and Autism, ADHD and SLD (n=24). Results revealed greater EF delays in children with the most diagnosed comorbidity, that is Autism, ADHD and SLD, with specific delays in cognitive flexibility and working memory. In fact, children diagnosed with both Autism and ADHD, or Autism, ADHD and SLD, showed greater delays in comparison to children with ADHD and SLD. EF profiles for the BRIEF Inhibit, Shift, Emotional Control and Working Memory domains revealed comorbid Autism and ADHD was associated with significant executive delay compared to ADHD and SLD. Our findings demonstrate the impact of comorbid diagnoses on functional executive abilities and portray the distinct EF domains impacted based on diagnostic profiles. Findings highlight the role EF serves as a useful marker for understanding the severity and type of neurodevelopmental delay.

*Keywords:* Neurodevelopmental Conditions, Executive Function, Autism and Comorbid Conditions, Developmental Conditions

# **3.2. Introduction**

Executive function (EF) refers to a constellation of cognitive abilities that facilitate goal-oriented behavior and adaptive engagement with complex real-world scenarios.<sup>3</sup> Executive functioning abilities support behvaioural regulation<sup>292</sup> and everyday functional skills.<sup>293</sup> For example, executive functioning abilities allow for problem-solving of simple to complex problems.<sup>293</sup> This can include the ability to recall items, inhibit a desired response and plan tasks.<sup>33,294</sup> These are refined throughout key developmental periods<sup>1,4</sup> starting with some simple executive functions that develop first in children (i.e. holding in mind, inhibiting a response,) which then set the groundwork for complex functions, such as cognitive flexibility and planning.<sup>235,295</sup> Impairments in the typical developmental trajectory of executive function have been well-established in neurodevelopmental conditions such as autism<sup>145</sup> (ASD), Attention-deficit/hyperactivity disorder<sup>249</sup> (ADHD) and specific learning disorders<sup>296</sup> (SLD). The patterns of deficits for ADHD implicate behavioural inhibition as part of Barkley's theory of EF,<sup>22</sup> with subsequent impairment to working memory and self-monitoring.<sup>141</sup> Studies in people diagnosed with ASD show a pattern of EF delays that implicates flexibility<sup>297</sup>, response inhibition, working memory (WM), planning, and attention.<sup>298</sup> A recent meta-analysis found generalised impairment across EF subdomains with moderate effect sizes in ASD.<sup>145</sup> SLD is found to implicate planning and selective attention in young children.<sup>299</sup> These findings have paved the way for condition specific EF patterns, with each condition demonstrating a higher degree of impairments in some EF domains than others. The profiles of executive function in some neurodevelopmental conditions (NDCs) are well understood<sup>232</sup>, however such studies often focus on single disorders.<sup>145,249,300</sup> Such research findings do not reflect the more common real-life occurances where comorbidity in NDCs is the "rule rather than the exception".<sup>301</sup> Past studies have shown that the presence of two or more conditions are often associated with more adpative and behavioural impairments.<sup>302</sup> In light of this, there is a need to undestand whether increased NDC comorbidity is also associated with a greater severity of EF delay.

## 3.2.1. Comorbidity and Executive Function Neurodevelopmental Conditions

The literature exploring executive functioning in comorbid NDCs offers interesting insights into executive functioning patterns. Some studies suggest similar executive impairments between different comorbid groups<sup>189</sup> and others show poorer executive skills with additional comorbid diagnoses.<sup>303</sup> For example, Benallie and colleagues<sup>189</sup> conducted a systematic review on ASD and either ADHD or ID (intellectual disability) as a comorbid presentation, and found deficits in flexbility, inhibition and attention in the ASD and ADHD group and more impaired planning, regulation, flexibility and attention in the ASD and ID group. Further, another review by Craig and colleagues<sup>188</sup> reviewed EF profiles of children with ASD, ADHD and ASD+ADHD, with results showing that comorbidity was associated with greater impairments in response inhibition, flexibility and planning. A more recent review adds that although children with both ASD and ADHD have similar impairments in domains such as attention, response inhibition, working memory and flexibility, and add that they did not show impairments in planning abilities.<sup>191</sup> Emerging research has begun to examine EF profiles of comorbid NDCs with findings that allude to cumulative deficits and others to domain differences withint he same NDC group.<sup>189,191</sup>

EF as a endophenotype can, through EF subdomain performance, reveal EF strengths and weaknesses for children with NDCs. A recent review found that children with ASD were more impaired in working memory and flexibility when compared to children with children with ADHD with no difference in planning and attention amongst both clinical groups.<sup>188</sup> Another study found that children with ADHD were more impaired than children with SLD in inhibition, cognitive flexibility and working memory.<sup>165</sup> SLD is often prevalent in comobidty to ADHD, and is found to be implicted in visuospatial updating.<sup>199</sup> Further, the addition of another NDC appears to impair a larger number of EF domains <sup>188,304</sup> indicating a cumulative effect on cognitive functioning.

Developing research on comorbid NDCs has alluded to more nuanced patterns of EF profiles. A recent systematic review on comorbid NDCs examined ASD and ADHD and found that this comorbid group revealed a specific pattern of EF deficits specific to working memory, flexibility, and planning than children with a single disorder ASD, who are often found to be impaired in flexibility and planning, alone.<sup>189</sup> These results indicate the combination of these NDCs have an interactive impact, with planning being impacted uniquly in addition to working memory and flexibility.<sup>188,189</sup> The study of ADHD and SLD and their pattern of EF defiicts is by comparison often more nuanced, with the type of SLD dictating unique EF impairments. Some studies indicate that inhibition and lexical decision was uniquely impacted in ADHD<sup>305</sup> and those with reading disorder, and other studies suggest that visuospatial updating<sup>199</sup> and working memory<sup>306</sup> is uniquely effected in the ADHD and SLD group. This pattern of research findings highlights that emerging EF profiles in comorbid NDCs are idiosyncratic and suggests that some comorbid groups exhibit cumulative impairments, while others show additive impairments in executive functions. These results highlight the nuances of EF profiles in NDCs, which is crucial for developing targeted interventions and educational strategies.<sup>33</sup> This can allow for greater use of EF as a diganostic tool allowing better identification of the functional challenges of NDCs.

# 3.2.2. Paediatric Measure of Executive Function: the BRIEF Questionnaire

There are a number of methods used to assess EF in children and adolescents. One of the most common is the use of informant measures, such as the BRIEF-2.<sup>109</sup> Informant measures are simple to administer, prove to be an efficient when examing vulernable

populations and correlate with academic achievement<sup>307</sup> as well as other functional domains.<sup>131</sup> Moreover, these informant report measures can predict clinical symptoms and show sensitivity to different theorised sub-domains of EF. These sub-domains include inhibition, cognitive flexibility (shift), emotional control, initiation, working memory, planning, and organisation. To illustrate, inhibition is described as the ability to exert restraint or 'inhibit' automatic or common responses.<sup>22</sup> When assessed by the BRIEF, studies have shown that the Inhibit subscale in addition to the Working Memory, and Organisation of Materials scales could discriminate children with ADHD from those that were typically developing.<sup>308</sup> Similarly, shift is defined as a measure of cognitive flexibility and the ability to transition between tasks or mental operations. It measures response time or accuracy and often manifests in children's ability to problem solve, move between topics and respond to change in the environment<sup>5</sup>. When assessed by the BRIEF, studies have shown the Shift subscale is correlated with impairments in NDCs such as ASD.<sup>309</sup> Further, studies that have examined comorbid NDCs using the BRIEF-2 have found that children with ADHD and SLD had elevated scores on the Inhibition, Working Memory, and Planning subscales.<sup>310</sup> Other BRIEF-2 subscales include, Emotional Control,<sup>311</sup> Organisation of Materials and Initiate, which provide insights into other EF areas when investigating mental health, adaptive functioning and other psychiatric illnesses.<sup>109,120,312,313</sup> Research to date, is yet to explore a number of comorbid groups together with a single NDC to examine their EF peformance, through informant measures such as the BRIEF-2.

# 3.3. Objectives

To date, few studies have captured the trandiagnostic quality of EF when investigating comorbid NDCs in children in a tertiary setting. The current study aims to fill this gap and proposes that as the complexity and comorbidity of NDCs emerge so do the degree of EF impairments, as measured by the BRIEF measure.

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The study aims to explore the EF profile of children with neurodevelopmental conditions attending a tertiary clinic. Tertiary clinics capture the occurrence of NDCs in the community and provide ecologically valid information of their presence. It is predicted that specific differences in their EF profiles will be found, and that the presence of comorbidity will significantly impair EF. Further, it is predicted greater impairment in overall EF scores in the co-occurring ASD and other NDC groups when compared to the ASD condition group alone. This will allow for a comparative examination of EF profiles for a single condition and multiple conditions.

# 3.3.1 Study Aim

To explore EF profiles captured by the BRIEF, of children with NDCs attending a tertiary assessment clinic with different comorbid diagnoses relating to ASD, SLD, and ADHD.

## **3.3.2.** Hypotheses

- In review of the literature on EF and comorbid NDCs as well as the findings of study one, there will be significant differences in BRIEF EF profiles across children with different NDCs. Specifically, it is predicted that:
  - a. Children with ASD alone will demonstrate increased impairments in cognitive flexibility (Shift scores in the BRIEF) compared to children with either ADHD or SLD.
  - b. Children with ASD and comorbid ADHD will have more impairments in cognitive flexibility (Shift scores in the BRIEF) and working memory when compared to children with ADHD or SLD.

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- c. It is also anticipated that the ADHD and SLD group will have increased difficulties with inhibition (related to response inhibition) than the ASD only clinical group.
- Children with increasing number of comorbidities will display poorer EF (BRIEF profiles).
  - a. Children with comorbidities will demonstrate increased EF profile impairment compared to the ASD only group. That is children with two or three comorbidities will have more overall impairments in their Global Executive Composite (GEC) score in the BRIEF.

#### 3.4. Methods

# 3.4.1. Participants

Participants were 157 children aged between 6 and 17 years of age who were recruited for a Child Development Study by the Child Development Assessment Service at Westmead and the Clinic for Autism and Neurodevelopmental Research at the University of Sydney between 2017 and 2022. Inclusion criteria for this study were 1) children aged 6 or above 2) met diagnostic criteria for ASD, ADHD or SLD and 3) had caregivers who completed the BRIEF-2. Younger children were excluded because they typically did not complete the BRIEF-2, were not at school and were unlikely to present with ADHD or SLD. Younger children were more likely to be diagnosed with ASD earlier, with other NDC diagnosis such as ADHD and SLD typically diagnosed for school-age children. This age cut-off was utilised based on studies on the same service (See Boulton and colleagues).<sup>314</sup> Children aged 6 and above were select to avoid misrepresentation of diagnosis favouring ASD. Children who presented to this research study for assessment met criteria for ASD (N=35), ASD and ADHD (N=32), ADHD and SLD (N=66) and ASD, ADHD and SLD (N=24). Prior to being selected for this study, children had previously been formally diagnosed through tertiary level clinics for assessment of NDCs and comorbidities using standardised assessments (e.g., ADOS-2<sup>315</sup>), in conjunction with a thorough developmental history and standardised measures from qualified clinicians.

# 3.4.2. Measure of Executive Functioning

To examine executive function abilities, children were administered the Behaviour Rating Inventory of Executive Functioning Second Version, Parent Form (BRIEF-2<sup>109</sup>). The BRIEF-2 is 63-item questionnaire administered to parents of children from the ages of 5-18 years and purports to tap into key areas of executive functioning. Both versions are reported to have sound internal consistency<sup>109</sup> and validity<sup>316</sup>. This measure has nine clinical scales (inhibit, self-monitor, shift, emotional control, initiate, working memory, plan/organise, task-monitor, and organisation of materials) and these scales comprise of three indices: the Behaviour Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index. These indices provide a summary executive function score, the Global Executive Composite Score (GEC).

# Combining BRIEF data

Data from the BRIEF-2 and BRIEF were pooled and are referred to as BRIEF data to maximise the analytical capacity within our paediatric sample. Raw scores can be translated into T-scores for each clinical scale, where larger scores denote higher levels of executive dysfunction. T-scores can also be broken down into four categories: T-scores up to 59 indicate a normal level of functioning; 60 to 64 indicate mildly elevated levels of dysfunction; 65 to 69 indicate potentially clinically elevated levels; and at or above 70 indicate clinically elevated levels. T-scores were utilised (instead of raw scores) for analysis as the number of items linked to each subscale varied between the BRIEF-2 and BRIEF. For the purposes of this research, the scales Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organise,

Organisation of materials, Behaviour Regulation Index (BRI) and the GEC were used, as they map onto consistent indices across the two versions of the BRIEF.

#### 3.4.3. Procedure

Families were sent the BRIEF questionnaire via the Research Enterprise Data Capture platform, RedCap an online data collection system endorsed by the University of Sydney. Families received an email reminder to complete the protocol one week prior to their appointment, and those who did not do so before their appointment completed it on the day of appointment.<sup>317</sup> Statistical analysis was conducted in SPSS (i.e., Chi-Square and ANOVA) and appropriate statistical corrections using the Bonferroni method were implemented as relevant within our analysis.<sup>318</sup> Post hoc tests were conducted following the use of ANOVA. To mitigate the risk of encountering a Type I error (incorrectly rejecting a true null hypothesis), the Bonferroni adjustment addresses this issue by reducing the alpha level (significance threshold) for each individual test, thereby maintaining the overall Type I error rate at a predetermined level, typically 0.05. this was automatically applied when conducting analyses. <sup>319</sup>

## 3.5. Results

#### 3.5.1. Demographics

Demographic and clinical data for 157 children (M=9.9, SD=2.3, 68% male) with clinical diagnoses of ASD, and comorbid ADHD, ASD, SLD subgroups are summarised in Table 3.1. Across the main analysis in the paper, further analysis was repeated to explore the differences in age across the group. Specifically, children with ASD alone were younger than the other comorbid groups. Follow-up analysis revealed that age did not moderate the results.

	ASD	ASD and ADHD	ADHD and SLD	ASD, SLD and ADHD
N	35	32	66	24
Gender (% Male)	66%	84%	70%	63%
Age (Mean Years,	8.7 (2.6)	9.4(2.8)	10.5(1.7)	9.9(1.2)
SD)				

Table 3.1 A Comparison of Demographic Information Between NDCs for 6-17 yr olds

# 3.5.2. Executive Function Across Developmental Conditions

A categorical analysis was performed using a two-way chi-square and revealed a significant relationship between the number of elevated BRIEF GEC scores and diagnostic groups,  $\chi^2(3, N=157) = 12.52$ , p=.006. See Table 3.2 for statistical information and Figure 3.1 for graph on the percentage of normal, borderline clinical and elevated scores across four NDC groups.

Table 3. 2. Chi-Square: Proportion of Combined Borderline Clinical and Elevated BRIEF Scoresacross NDC Groups.

BRIEF Domain T scores	ASD only	ASD and ADHD	ADHD and SLD	ASD+ADHD+SLD
	N(%)	N(%)	N(%)	N(%)
No. Elevated GEC	31(88.6)	28(87.5)	47(71.2)	24(100)



Figure 3.1. Composite GEC BRIEF Scores across NDC groups.

Note: Scores equal to 60 and under were categorised as normal. Scores of 61 and 69 were categorised as borderline clinical and scores of 70 and above were elevated.

# 3.5.3. Executive Function Across Comorbid Developmental Conditions

To investigate between-group differences across the neurodevelopmental groups, a oneway analysis of variance was conducted (ANOVA) initially on the total score of the BRIEF GEC scores. These results showed a significant effect on the GEC total score by group, F(3,156) = 9.13, p <.001,  $\eta_p^2 = .15$ . Results revealed that there was a significant difference on all BRIEF subdomain T scores and developmental groups. There was a significant main effect for Inhibit T-scores, F(3,156) = 4.85, p = 0.003,  $\eta_p^2 = .08$ , Shift T-scores, F(3,156) = 11.30, p =<.001,  $\eta_p^2 = .18$ . Emotional Control T -score, F(3,156) = 9.68, p < 0.001,  $\eta_p^2 = .16$ , Initiate Tscores, F(3,156) = 3.75, p = 0.012,  $\eta_p^2 = .07$ , Working Memory T-scores, F(3,156) = 6.94, p =<.001,  $\eta_p^2 = .12$ , Plan/Organise T scores, F(3,155) = 4.13, p = 0.03,  $\eta_p^2 = .07$ , Organisation of Materials T-scores, F(3,155) = 3.07, p = 0.03,  $\eta_p^2 = .06$ , and Behavioral Regulation Index (BRI) T scores F(3,166) = 5.75, p <.001,  $\eta_p^2 = .10$ . Post-hoc tests were conducted on subdomains of the BRIEF to include two analyses; the first analysis included composite domain score of the BRIEF (GEC) and the second analysis was conducted on the individual subdomains of the BRIEF (Inhibit, Shift, Emotional Control, Initiate, Working Memory, Plan/Organise, Organisation of Materials, Behaviour Regulation Index (BRI)). Statistical corrections using the Bonferroni method was used. Results of this analysis are detailed in Table 3.3. Further information on mean differences are provided in Appendix B.

Combined BRIEF	<b>ASD</b> <sup>a</sup>	ASD and ADHD <sup>b</sup>	ADHD and	ASD, SLD and
		M(SD)	SLD <sup>c</sup>	<b>ADHD</b> <sup>d</sup>
<b>T-scores</b>	M(SD)		M(SD)	M(SD)
Inhibit (Inhibitory	65.85(10.99)	68.43(11.55) ** <sup>b&gt;c</sup>	60.92(10.19)	68.37(12.31) * <sup>d&gt;c</sup>
Control)				
Shift (Flexibility)	73.14(10.94)*** <sup>a&gt;c</sup>	72.96(12.83) *** <sup>b&gt;c</sup>	63.01(11.38)	75.33(10.14) *** <sup>d&gt;c</sup>
Emotional Control	67.4(11.91) *** <sup>a&gt;c</sup>	66.75(12.18) ** <sup>b&gt;c</sup>	57.93(10.88)	69.79(11.79) *** <sup>d&gt;c</sup>
(self-regulation)				
Initiate	64.11(9.10)	67.06(9.54)	62.48(8.61)	68.58(7.91) * <sup>d&gt;c</sup>
Working Memory	66.25(11.89)	72.81(9.22) * <sup>b&gt;a</sup>	65.39(8.04)	72.41(7.43) ** <sup>d&gt;c</sup>
Plan/Organise	63.20(11.57)	68.12(9.09)	63.65(8.13)	69.37(5.77) * <sup>d&gt;c</sup>
Organisation of	57.62(10.61)	63.35(8.99)	59.33(9.66)	63.54(8.61)
Materials				
Behaviour	67.28(10.87) * <sup>a&gt;c</sup>	68.84(11.41) ** <sup>b&gt;c</sup>	61.21(9.98)	68.91(11.08) * <sup>d&gt;c</sup>
<b>Regulation Index</b>				
(BRI)				
GEC	68.74(10.85)	73.43(10.47) * <sup>b&gt;c</sup>	65.16(8.46)	74.87(8.10) ** <sup>d&gt;c</sup>

Table 3.3. Results of BRIEF Data Across NDC Groups

ADHD=attention deficit/hyperactivity disorders; ASD=autism spectrum disorders; SLD=specific learning disorders; M=Mean; SD=standard deviation. Data are presented as Mean (SD). *Note:* \*p < .05; \*\*p < .01, \*\*p < 0.001.

These results showed that GEC scores were significantly different between the ADHD and SLD group when compared to the ASD and ADHD cohort ( $M_{diff}$ =8.27, SE=2.02) and the ASD, ADHD and SLD cohort ( $M_{diff}$ =9.70, SE=2.24). Further, the BRI index was significantly elevated when the ADHD and SLD group was compared to the ASD and ADHD group ( $M_{diff}$ =7.63, SE=2.29) and also when it was compared to the ASD, SLD and ADHD comorbid groups ( $M_{diff}$ =7.70, SE=2.53). ASD alone when compared to ADHD with comorbid SLD revealed a small but significant difference, ( $M_{diff}$ = 6.07, SE=2.22).

## 3.5.4 Domain Specific Difference Across Comorbid Conditions

Subdomain analyses revealed further NDC group differences. For the Inhibit (inhibitory control) domain ( $M_{diff}$ =7.51, SE=2.36), Shift ( $M_{diff}$ =9.95, SE=2.46), Emotional Control ( $M_{diff}$ =8.81, SE=2.48) and Working Memory ( $M_{diff}$ =7.41, SE=1.97) subdomains, the ASD and ADHD comorbidity group had significantly elevated scores when compared to the ADHD and SLD group was compared to the ASD, SLD and ADHD group, with significant elevation for children with ASD, SLD and ADHD in inhibition ( $M_{diff}$ =7.45, SE=2.62), shift ( $M_{diff}$ =12.31, SE=2.72), emotional control ( $M_{diff}$ =11.85, SE=2.74), initiate ( $M_{diff}$ =6.09, SE=2.10), and working memory ( $M_{diff}$ = 7.02, SE=2.19). The shift and emotional control domain results revealed further differences between the ASD only and ADHD and SLD group, with ASD alone revealing significant evaluation [( $M_{diff}$ =10.12, SE=2.38) and ( $M_{diff}$ =9.46, SE=2.40) respectively.] Lastly. the working memory revealed significant differences between ASD and ADHD when compared to ASD, where children with ASD and ADHD had significantly higher scores than children with ASD alone ( $M_{diff}$ =6.55, SE=2.24).

# 3.6. Discussion

The current study sought to explore EF profiles captured by the BRIEF-2 questionnaire in children with NDCs, with a focus on single as well as comorbid NDC presentations. As expected, all children with three NDC presentations (ASD, SLD and ADHD) showed elevated EF impairments as measured by the BRIEF-2.<sup>166,320-322</sup> Additionally, the results also showed that as comorbidity increased, the delays in EF became more severe. These findings are among the first to examine profiles of EF in an increasing number of NDCs and illuminate the cumulative impact of NDC diagnosis on everyday EF in children. In line with previous research, ASD presents with unique EF deficits in flexibility,<sup>323,188</sup> however, these findings add that children who presented with ASD and comorbidities of ADHD or SLD, and then ASD, ADHD and also SLD, had poorer EF in comparison to those without ASD. This was found across the total score and the subdomains of Inhibition, Shift, Emotional Control and Working Memory. Working memory scores were better in the ASD group when compared to the ASD and ADHD group. Of note, the ADHD and SLD group did not reveal significantly elevated executive scores when compared to other NDC groups. These findings highlight the cumulative relationship between diagnoses and EF impairments.

The addition of ASD to diagnostic groupings (ADHD and SLD) led to an increased number of delays on a number of EF domains, suggesting that a diagnosis of ASD is associated with specific executive delays for children. ASD appears to cumulatively exacerbate executive delays in NDCs. This is consistent with findings by Sinzig and colleagues (2008)<sup>324</sup> that suggest ASD is linked with greater delays in flexibility, working memory and inhibition and the current findings extend to this, with greater impairments in comorbid conditions in children that included an ASD diagnosis. Such findings add to growing literature which highlights increasing impairment in children with ASD and other diagnostic and psychiatric comorbidties.<sup>325,326</sup> Subdomains impacted by the addition of ASD highlight that there appears to be a cumulative impact of executive delay, in addition to flexibility and emotional control concerns which are often a hallmark feature of ASD. Additional domains such as inhibition, and working memory are further implicated. This aligns with research which implicates attention and inhibition with ASD not ADHD.<sup>327</sup> Studies examining cognitive remediation support often provide further evidence for this link. Studies examining children with high

executive delay with ASD and ADHD, who have undergone an emotional regulation program, revealed significantly improved outcomes<sup>245</sup>, subsequently impacting EF abilities.<sup>328</sup>

Studies on NDC brain divergence show distinct patterns of neural biomarkers in ASD when compared to other NDCs<sup>329</sup> and the addition of ASD to other NDCs may increase neuropathology.<sup>330</sup> The neural biomarkers in co-occurring conditions are distinct and more widespread compared with single diagnosis despite having similarities to them. For example, a study examining the differences between children with ASD and those with ADHD found unique patterns of altered activation in the rich-club region, a region in the brain that is influential in structure and function as well as integrated and relaying high order information.<sup>331</sup>

EF abilities within the planning or organisational domain and initiate domain revealed that the three comorbid NDC group (ASD, ADHD and SLD) had significantly more reported challenges in these domains when compared to ADHD and SLD. These findings contribute to and implicate the addition of SLD to the growing literature on ADHD and ASD<sup>218,332</sup> which suggests impairment in planning in when SLD is present with other NDCs diagnoses.<sup>333</sup> Further, initiation, a higher order EF is also implicated in executive delay findings in children with ASD.<sup>334</sup> These findings also add to the literature with this NDC group on planning deficits using performance measures,<sup>188</sup> and is consistent with EF models<sup>33</sup> that posit that EF domains such as planning or organisational abilities are higher-order EF abilities that extend on domains of working memory, inhibitory control, and cognitive flexibility. As such, these findings add to the literature with NDCs. These findings contribute to the literature which links an array of EF domains in children with ASD and ADHD<sup>191</sup>, when compared with controls.

Evidence for EF as a cognitive endophenotype is increasingly pertinent<sup>215,233</sup> and can inform the degree of diagnostic impairment, with these results showing that as children increase in the number of diagnosed conditions, their EF impairment increases. These results suggest a unique pattern of impairment with ASD when present in addition to other NDCs like SLD and ADHD can significantly impact a child's executive delay, with EF profiles that accumulate in domains and severity (i.e. additive effect of NDCs).<sup>189,245</sup> Findings add to theoretical models, <sup>18,24</sup> and provide patterns of cognitive functioning that can be seen to be distinct when NDCs are compared for their degree of EF impairments.

## 3.6.1. Strengths and Limitations

The current study contributes to the literature and our understanding of comorbid NDC presentations in children with a direct exploration of specific EF domains and specific profiles of executive delay, with unique findings for ASD. There were differences in ages across the four NDCs. Notably, children diagnosed solely with ASD were younger than those in other comorbid groups. Subsequent analyses indicated that age did not influence the outcomes. The study conducted data collection through a tertiary community sample, consisting of individuals who opted to participate in research. Within this sample, children are flagged for ASD sooner through early intervention pathways, while ADHD is typically diagnosed later, often once the child starts school. Further, our study did not capture an ADHD only group, there was limited number of children with ADHD alone, due to high rates of community comorbidity. Future studies could use this group to capture EF in this group compared to other comorbid presentations. Although parent reported performance is useful in capturing overall EF functioning, our study did not capture EF functioning in the schooling arena, which can often provide a unique EF lens as reported by educators.<sup>335</sup> Future studies could capture teacher reported EF performance for a more comprehensive EF evaluation.
#### 3.6.2. Conclusion

In summary, children that have ASD in comorbid presentation with ADHD and SLD show significant impairments reported by parents in a number of key EF domains, including working memory, emotional control, cognitive flexibility and inhibition. This effect is stronger the more comorbidities' children with ASD present with. This highlights the significant and cumulative challenges parents of children with neurodevelopmental comorbidities likely face, particularly in relation to patterns of executive delay as identified in children with ASD and other NDCs. Further, an increasing number of comorbid NDC presentations signals increasing reported levels of executive delay. Findings provide evidence to support the notion that EF serves as a transdiagnostic endophenotype with relevance for identifying and targeting vulnerabilities of executive delay across NDCs in children.

# Chapter 4: How Caregiver Reported Strengths and Challenges Relate to Delays in

# **Executive Function Performance.**

### **Study Objectives:**

Following a nuanced understanding of how comorbidities contribute to executive delay in NDCs, this study sought to examine underpinnings of behavioural and developmental delay that could contribute to executive delay in young children. As such this study sought to:

a) Explore the degree of EF severity in increasing number of DSM diagnoses.

b) Examine caregiver-reported concerns and executive delays in children as measured by the BRIEF.

c) Examine caregiver-reported strengths and executive performance as measured by the BRIEF.

# How Caregiver Reported Strengths and Challenges Relate to EF Delays in Children with Neurodevelopmental Conditions.

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Abstract Word Count: 302

# Body Word Count: 4852 words

# Tables/Figures: 4

# Target Journal: Autism Research

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## Acknowledgments

The authors would like to thank all of the families that have contributed to the Sydney Child Neurodevelopment Research Registry and the staff from the Child Development Unit that have contributed to data collection. We would also like to extend our gratitude to the Cerebral Palsy Alliance who have provided funding to support this research.

# Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

**Funding**: This research was funded by author's postgraduate scholarship funded by the CP Alliance.

**Ethical statement:** The study was approved by the Sydney Children's Hospital Network Human Research Ethics Committee (LNR/17/SCHN/293; Child Development Registry).

#### 4.1. Abstract

Children with significant developmental concerns and behavioural challenges often receive diagnostic assessments to guide supports and interventions. Diagnoses can then account for the functional and cognitive deficits transdiagnostically, which often emerge early in childhood. Executive function (EF), a marker of high order thinking and functioning, is instrumental in better understanding cognitive and developmental impact. Evaluating EF performance in assessment is key to establishing functional strengths and weakness that inform diagnostic trajectory in children. Certain EF measures can provide informant based clinical information on executive abilities of children, with caregivers of children providing clinically pertinent markers of functioning in children. This study is the first to examine the interplay between children's EF profiles and parent-reported strengths and concerns. This study examined 127 children aged between 2 years and 16 years who attended a developmental diagnostic and assessment service. We examined the relationship between caregiver-reported EF abilities on the Behavior Rating Inventory of Executive Function (BRIEF-2) and parentreported concerns (e.g., behaviour, social and play skills) and strengths (e.g., intelligence and social cognition). Overall, findings showed distinct EF patterns associated with various parental concerns and strengths. Elevated inhibition scores were correlated with behavioural and social/play concerns, while children with behavioural issues exhibit broader EF deficits. Children with specific diagnostic concerns also showed deficits across multiple EF domains, including inhibition, emotional control, working memory, and planning. Conversely, children identified with social and interpersonal strengths displayed better EF performance in inhibition, flexibility, and emotional control. Together, these findings demonstrate that parental input on specific developmental concerns and strengths can be a valuable addition to childhood developmental assessments, with certain domains of concerns and strengths corresponding to specific EF profiles. These outcomes provide the basis for individualised plans and treatment guides and elucidate our understanding of how best to synthesise parental evaluations in the context of formal developmental assessments.

*Keywords:* Neurodevelopmental Conditions, Executive Function, Autism and Comorbid Conditions, Developmental Conditions, Parent Concerns, BRIEF.

#### 4.2. Introduction

Executive function (EF) refers to a set of higher order cognitive skills that are essential for goal-directed activity, problem-solving, and adapting to new situations.<sup>1</sup> These skills are foundational for academic success, social relationships, and overall well-being.<sup>293,336,337</sup> In the context of neurodevelopmental conditions (NDCs), EF reflects the cognitive neurobiological processes underlying these conditions. This recognition is grounded in extensive research that illustrates the link between EF deficits and a range of NDCs.<sup>188,189,199,338</sup> EF is now increasingly recognised as a key endophenotype in NDCs and can significantly influence children's development and wellbeing. <sup>2</sup> EF performance across various neurodevelopmental disorders from a transdiagnostic perspective has revealed both shared and distinct cognitive profiles. Research comparing EF across different NDCs, such as Attention-deficit/hyperactivity disorder (ADHD), Autism Spectrum Disorders (ASD), Tourette's syndrome (TS) and learning disabilities (e.g., dyslexia), has consistently found EF deficits to be a common feature across these conditions.<sup>2,188</sup> However, the specific nature and extent of these deficits vary. For example, while both children with ADHD and ASD show deficits in inhibitory control, those with ADHD may exhibit more pronounced difficulties in this area.<sup>339</sup> Notably, certain EF deficits seem to be more characteristic of specific disorders. For instance, difficulties in cognitive flexibility is more pronounced in ASD, while ADHD is more strongly associated with problems in inhibitory control and working memory.<sup>166</sup> As a consequence, EF specific profiles pave the way for strengths and challenges that children can present with based on diagnosis.<sup>340-342</sup> Such disorder-specific EF profiles can provide critical diagnostic insights and guide tailored interventions for children with an array of NDCs.

Caregiver evaluations have played a crucial role in identifying EF delays in children, especially in the context of developmental delays. Caregiver observations and reports have

been instrumental in distinguishing between typical developmental variations and potential indicators of underlying neurodevelopmental disorders. For instance, studies are showing that caregiver reports of EF problems in preschool children are predictive of later ADHD diagnosis.<sup>343</sup> Corroborating caregiver open-ended general developmental evaluations with questionnaire-based results is important for amalgamating qualitative information from caregivers and results from outcome-based measures, which seek to quantify information based on cognitive and behavioural domains of child behaviour. For example, a recent study by Hutchison, Müller and Iarocci1 (2020)<sup>344</sup> found through caregiver evaluation that elevated scores on an EF measure (Behavior Rating Inventory of Executive Function, second Edition; BRIEF-2) was predictive of functional language abilities. This in turn, accurately predicted impairments in functional language in children with autism and subsequently was key guiding treatment planning and recommendations. Caregiver evaluations and the integration of their information in measures and other diagnostic tools can allow for a more comprehensive and tailored treatment plan.

Evaluations often provide a bias to capturing behavioural challenges in children with NDCs experience, strengths-based perspectives emphasise the need to capture both strengths and weaknesses in a child's developmental functioning. There is, however, limited research applying strengths-based perspectives to real world clinical contexts for paediatric neurodevelopment. This means that it remains unclear how best to apply strengths-based perspective to a clinical context. One study by Khan<sup>345</sup> (2023) found EF domains such as cognitive regulation predicted interpersonal strengths (active listening and emotional maturity) and family support in neurotypical adolescents. Conversely, studies have found associations between poor emotional regulation and compromised competency in social behaviour in young children.<sup>346,347</sup> There is, nonetheless, limited research directly exploring parental strengths in children flagged for developmental delays and their relationship to their diagnostic outcomes

or specific executive abilities. Given the recent focus on adopting a strengths-based approach when conducting diagnostic assessments,<sup>348</sup> a better understanding of how caregiver-reported strengths may relate to outcomes, such as EF, is warranted.

EF has long been linked with social, emotional, and behavioural delays in children with developmental delays. Slot and colleagues<sup>349</sup> (2017) found that EF abilities showed a significant relationship between emotional self-regulation in pre-schoolers. Slot and colleagues also found that the quality of pretend play was associated with cognitive and emotional self-Another study found planning deficits were linked with poor adaptive regulation. communication abilities and social abilities in children with NDCs (i.e., ADHD and CD/ODD).<sup>350</sup> These results also extend to other areas of EF, for example, better response inhibition abilities were associated with lower externalising behaviour in a sample of typically developing five to six year old children.<sup>351</sup> Further, social challenges have been linked with NDCs and EF performance. A study by Miranda and colleagues<sup>352</sup> (2017) found that processes of behavioural regulation, (i.e., inhibition and emotional control) revealed a greater correlation with social cognition in children with ADHD. Further, initiation and planning, were found to be more closely linked to social cognition in autistic children with low support needs. Such evidence adds to our understanding of EF specific difficulties and associated links to behavioural and social weaknesses in children.

Holistic caregiver appraisals guide the diagnostic journey as they allow clinicians to fine tune information into appropriate diagnostic and intervention pathways.<sup>353</sup> These reports further allow clinicians to substantiate the level of functional support a child may require post their diagnoses, providing a neuro-affirming framework.<sup>354</sup> Behavioural measures such as the BRIEF-2 rely on caregiver report and capture observable EF impairments based on child behaviour made over the space of years. Although research has been able to identify the importance of caregiver evaluations, little is known about how these holistic evaluations

(reviewing both strengths and weaknesses) perform with informant measures of executive functioning, through a transdiagnostic lens. This study is the first to provide an assessment of key concerns and strengths, and their relationship to specific domains of EF at a tertiary developmental service.

#### 4.2.2. Study Aims:

- The first aim was to examine relationships between EF symptoms using the BRIEF, caregiver-reported strengths and concerns, and the number of DSM diagnoses received. In particular, and based on the literature to date, we predicted that a higher number of diagnoses and caregiver-reported concerns would be associated with elevated EF difficulties, while a higher number of caregiver-reported strengths would be associated with decreased EF difficulties.
- 2) The second aim was to examine the proportion of children with elevated BRIEF T scores on different variables of strengths and concerns. Recent research has shown that regulation is linked with interpersonal skill, and we predicted that caregiver reported strengths in social and interpersonal strengths would be associated with lower scores on subscales of emotional control and inhibition.
- 3) The final aim was to evaluate how concerns and strengths effect various EF domains. Research to date links emotional regulatory strategies to social behaviour, as such we predict that caregiver reported challenges with social and play skills will be associated with impairments in Inhibit and Emotional Control T scores. Further, impairments in these subscales will extend to concerns for NDCs, following literature that associates NDCs with EF deficits.

#### 4.3. Methods

#### 4.3.1. Participants and Setting

Participants were 127 children aged between 2 years and 16 years (M=8.60 years, SD=3.70, Median=8.9 years), who attended the Child Development Unit (CDU) at the Children's Hospital Westmead, Sydney, Australia between 2019 and 2023. The CDU is part of the publicly funded Sydney Children's Hospital Network which provides developmental and diagnostic assessment services to children. Referrals made to this service are for assessment of complex neurodevelopmental impairments, including autism, intellectual disability, global developmental delay, speech and language delays, and other difficulties with adaptive and/or cognitive functioning. Following referral, children receive comprehensive assessments conducted by a multidisciplinary team. Following assessments, a diagnosis is made, and families receive feedback and recommendations. The CDU, in collaboration with the Clinic for Autism and Neurodevelopmental (CAN) Research at the University of Sydney have an integrated research registry, the Sydney Child Neurodevelopment Research Registry. Boulton and colleagues<sup>355</sup> conducted research on this registry and a detailed explanation and of the clinic cohort and integrated research registry is available, see citation. The study was approved by the Sydney Children's Hospital Network Human Research Ethics Committee (LNR/17/SCHN/293; Child Development Registry). All families participated in this study using opt-out consent procedures.

#### 4.3.2. Measures

#### 4.3.2.1 Parent Carer Questionnaire

The Parent Carer Questionnaire (PCQ) is a six-page questionnaire, developed by the CDU clinical team to collect clinically relevant information on children and families before their appointment. (see Appendix B, Figure 1). The PCQ is completed by the primary caregiver of the child being assessed, and collects demographic information, family history and child

developmental history. This questionnaire evaluates developmental functioning and largely elicits open responses from caregivers. Caregiver-reported concerns were grouped into nine categories based on the categories outlined in Munro and colleagues<sup>356</sup> (2023). Strengths were grouped into six categories based on themes identified in a qualitative analysis of the larger registry, described in Hankin and colleagues<sup>357</sup> (under review). These categories are detailed in appendix C Supplementary Table 1 and summarised in Table 4.2. These categories were formed through reflexive thematic analysis and each category was subsequently dichotomously coded (i.e., scored as being present or absent in the PCQ).<sup>357</sup>

#### 4.3.2.2 Behaviour Rating Inventory of Executive Functioning Measure,

## **Parent Form**

To examine executive function abilities, children were administered the Behaviour Rating Inventory of Executive Functioning Second Version, Parent Form (BRIEF-2<sup>109</sup>) and the BRIEF-P. The BRIEF-2 is 63-item questionnaire administered to parents of children from the ages of 5-18 years and purports to tap into key areas of executive functioning. This measure has nine clinical scales (inhibit, self-monitor, shift, emotional control, initiate, working memory, plan/organise, task-monitor, and organisation of materials) and these scales comprise of three indices: the Behaviour Regulation Index, Emotion Regulation Index, and Cognitive Regulation Index. These indices provide a summary executive function score, the Global Executive Composite Score (GEC). The Behavior Rating Inventory of Executive Function Preschool Version (BRIEF-P<sup>244</sup>) is utilised for children between 2 and 5 years and has five overlapping subscales with the BRIEF-2, which contribute to three indices (Inhibitory Self-Control Index, Flexibility Index and Emergent Metacognition Index) as well as an overall composite, the GEC. Shared subscales across both versions of the BRIEF measure were used as part of analysis; Inhibit, Shift, Emotional Control, Working Memory and Plan/Organise. Parents report EF impairments across key areas of thinking faculties. Raw scores can be translated into T-scores for each clinical scale, where higher scores denote higher levels of executive dysfunction. T-scores can also be broken down into four categories: T-scores up to 59 indicate a normal level of functioning; 60 to 64 indicate mildly elevated levels of dysfunction; 65 to 69 indicate potentially clinically elevated levels; and at or above 70 indicate clinically elevated levels. T-scores were utilised (instead of raw scores) for analysis and scores above 60 were regarded as elevated in this study

#### 4.3.3. Procedures

One month prior to their assessment at the CDU families were sent the PCQ electronically via the Research Enterprise Data Capture (REDCap) platform, an online data collection system endorsed by the University of Sydney. Families received an email reminder to complete the questionnaire one week prior to their appointment as outlined by Boulton and Colleagues.<sup>355</sup>

#### 4.3.3.1. Statistical Analysis

Statistical analyses were performed with IBM SPSS Statistics for Windows, version 27. To examine the correlation between GEC scores, DSM diagnoses, strengths, and concerns, a series of correlation analyses were conducted. Further, a chi-square analysis was undertaken to examine the proportion of children with elevated GEC scores (>60) and caregiver reported strengths and weaknesses. Our examination of which domains of EF are associated with various caregiver-reported concerns and strengths were exploratory. A one-way between subjects' multivariate analysis of variance (MANOVA) was employed. That is, caregiver reported concerns and strengths within this model and their association to EF domains (dependant variables) is being explored. Appropriate statistical corrections using the Bonferroni method within SPSS were implemented as relevant within our analysis. Analyses were conducted on parent reported strengths and concerns that had a minimum sample size of thirty (N= 30).

Assumptions of normality, homogeneity of variance-covariance were largely met. Mahalanobis distance was used to assess multivariate outliers; the critical value of 13.82 was not met. Item-total correlations were evaluated using Pearson's product–moment correlation coefficients (r). Items with correlations 0.5 were considered strong<sup>358</sup>. The association between the dependant variables is not significant, r(126) = 2.52, p = .051 for the category, play and social concerns (see appendix B, Table 1). This association was significant for behavioural and diagnostic concerns category as well as social and interpersonal strengths. Data screening and diagnostics were conducted and they revealed that correlation coefficient was less than .9; thus, multicollinearity is not a concern<sup>359</sup>. Singularity is not a concern. Further, the assumption of homogeneity and variance-covariance is tenable [Box's test *M*=16.98, *F*(21, 17277.59) = .754, *p* =.779]. Levene's test of equality of error provided evidence that the assumption of homogeneity of variance across groups is also tenable for most BRIEF T scores, all *p* > 0.34, with the exception of BRIEF Working memory T scores, *p* > 0.04 in play and social concerns.

#### 4.4. Results

#### 4.4.1. Demographics

Demographic characteristics are presented in Table 4.1. The majority of participants were male, and over 50% of participants received a diagnosis of ASD. On average, children had 1.83 DSM diagnoses (SD=1.11). Most children (80%) demonstrated elevated levels of executive function difficulties, denoted by T scores of 60 or higher.

Table 4.1. Demographic Information, Diagnostic Characteristics within PCQ

	Mean (SD)	N	%
Total Participants	-	127	-
Gender (% Male)	-	83	65.4
Age (Mean Years)	8.6 (3.7)	-	-

# **DSM Diagnosis**

66	52
52	40.9
35	27.6
31	24.4
28	22
10	7.9
9	7
1	0.8
1	0.8
	66 52 35 31 28 10 9 1 1

Table 4.2 displays caregiver-reported concerns and strengths. The most commonly reported concerns related to learning and cognition, while the most commonly occurring strengths were those relating to character and personality, and cognitive and intellectual skills. On average, caregivers reported 3.07 concerns (SD=1.96) and 1.96 strengths (SD=0.82).

Table 4.2. Reported Concerns and Strengths Within PCQ

Parent Reported Concerns	N	%	
Learning and Cognition	73	57.5	
Behavioural Issues (Internalising & Externalising & Sensory & RRB)	45	35.4	
Speech and Language Concerns	45	35.4	
Developmental Concerns	44	34.6	
Play and Social Skills	36	28.3	

Query NDCs (ASD, ADHD, SLD)	34	26.8
Medical Concerns	25	19.4
School Readiness	20	15.7
Attention and Focus	18	14.2
Parent Reported Strengths		
Character and Personality	44	34.6
Cognitive and Intellectual Skills	43	33.9
Hobbies and Passions	40	31.5
Social and Interpersonal	34	26.7
Physical and Motor Skills	31	24.4
Behavioural	21	16.5

#### 4.4.2. Correlation Between Elevated EF Scores and Diagnoses, Strengths and Concerns

The relationship between overall scores on the BRIEF (GEC T scores) and number of DSM diagnoses was explored. There was a moderate, positive relationship between BRIEF scores and the number of diagnoses, r(125) = .330, p<.001, such that increased EF difficulties were associated with a higher number of DSM diagnoses.

The relationship between overall scores on the BRIEF (GEC T scores) and the total number of caregiver-reported concerns and strengths was explored. There was a small, positive correlation between BRIEF GEC T scores and the number of concerns reported by parents, r(125) = .216, p=.015, that is, a higher BRIEF score was associated with an increased number of concerns as reported by caregivers on the PCQ. The correlation between BRIEF T scores and total number of caregiver-reported strengths did not reach statistical significance, r(108) = ..137, p = ..154.

# 4.4.3. Proportion of Elevated EF Scores and Caregiver-Reported Concerns and Strengths

The proportion of children with elevated BRIEF scores and their caregiver reported concerns and strengths were calculated. Table 4.3 reports the odds ratios and percentage of children with elevated T scores whose parents also reported concerns or strengths across various categories. Chi-square results indicated that children with elevated GEC T scores were five times more likely to have behavioural challenges reported by caregivers on the PCQ,  $\chi^2$  (1, *N*=127) = 7.47, *p* = .006. Further, those children with caregiver-reported behavioural concerns (N = 45/127) were also four times more likely to have elevated scores in other executive function domains such as inhibition,  $\chi^2$  (1, *N*=127) = 11.75, *p* = .001, twice as likely to have emotional control challenges,  $\chi^2$  (1, *N*=127) = 18.50, *p* = .001. Children with elevated inhibition T scores were twice as likely to have concerns in their social and play abilities (N=36/127),  $\chi^2$  (1, *N*=127) = 6.31, *p* = .012. Children with elevated emotional control T scores were two and a half times more likely to be flagged for diagnostic concerns (N=34/1270,  $\chi^2$  (1, *N*=127) = 4.95, *p* = .026 and those with elevated planning scores were three times more likely to have been flagged for diagnostic concerns,  $\chi^2$  (1, *N*=127) = 5.45, *p* = .020.

Considering associations between caregiver-reported strengths and BRIEF scores, findings were specific to the inhibition domain. Children who did not have elevated scores on the inhibition domain (that is, T scores less than 60), were twice times more likely to have cognitive and intellectual strengths reported by caregivers on the PCQ (N=43/110),  $\chi^2$  (1, N=110) = 4.30, p = .038. Similarly, those children were also more likely to have social and interpersonal strengths reported by caregivers (N=34/110),  $\chi^2$  (1, N=110) = 12.51, p = <.001.

Table 4.3. Elevated T scores for Reported Concerns or Strengths across Various Categories.

PCQ Concerns							PCQ Strengths					
BRIEF Domains	Speech and Language Concerns	Learning and Cognition	Play/Social Concerns	All Behavioural Concerns	Developme ntal Concerns	Diagnostic Concerns (ASD, SLD and ADHD)	Character and Personality	Cognitive and Intellectual Skills	Hobbies and Passions	Physical and Motor Skills	Social and Interpersona I Strengths	
CEC T scores	(80%), 1,45	(76.7%),	(86.1%),	(93.3%),	(81.8%),	(91.2%), 3.20	(77.3%),	(81.4%),	(85%),	(77.4%),	(73.5%), 0.57	
GEC I SCORES	(00,0), 0000	0.57	1.74	5.13**	1.16	(*******	0.75	1.15	1.67	0.80	(13.370), 0.37	
Inhibit T gaarag	(64.4%),	(50.7%),	(75%),	(77.8%),	(61.4%),	(70.6%) 2.15	(56.8%),	(72.1%),	(57.5%),	(54.8%),	(35.3%),	
minut 1 scores	1.56	0.51	2.9**	4.05***	1.27	(70.070), 2.15	0.80	2.36*	0.85	0.74	0.22***	
	(57.8%),	(63%) 1 17	(72.2%),	(75.6%),	(63.6%),	(72.5%) 2.00	(54.5%),	(67.4%),	(55%),	(61.3%),	(47.1%), 0.46	
Shift I scores	0.79	(0570), 1.17	1.95	2.66*	1.15	(73.370), 2.09	0.68	1.68	68 0.72	1.07		
Emotional	0.93,	(47.9%),	(63.9%),	(80%),	(59.1%),	(70.6%),	(500()) 0.70	(62.8%),	(57.5%),	(64.5%),	(44.10()) 0.51	
Control T scores	(53.3%)	0.54	1.73	5.94***	1.34	2.56*	(50%), 0.70	1.63	1.14	1.68	(44.1%), 0.51	
Working	(82.2%),	(76.7%),	(750() 0.80	(73.3%),	(79.5%),	(82.40/) 1.44	(70.5%),	(69.8%),	(80%),	(74.2%),	(70, 00) = 0, 0, 0	
Memory T scores	1.50	0.84	(75%), 0.80	0.66	1.15	(82.4%), 1.44	0.53	0.50	1.30	0.78	(70.6%), 0.60	
Plan/Organise	(66.7%),	(65.8%),	(75%) 179	(71.1%),	(70,5%), 1,5	(82.4%),	(68.2%),	(65.1%),	(65.5%),	(61.3%),	(55.9%) 0.51	
T scores	1.03	0.96	(13/0), 1.79	1.42	(10.570), 1.5	3.08*	1.14	0.91	1.08	0.733	(33.9%), 0.31	

Note: \*Denotes significance at p<0.05, \*\*Denotes significance at p<0.01, \*\*\*Denotes significance at p<0.001. The % denotes the percentage of children with elevated T

scores who also were marked as having the aforementioned concerns and strengths by caregivers. The odds ratio value has been calculated from the chi-square analyses.

#### 4.4.4. PCQ Concerns and Strengths and EF Domains

An ANOVA was first conducted with GEC T scores as the outcome variable to determine which caregiver-reported concerns and strengths were associated with GEC scores. As shown in Table 4.4, for caregiver-reported concerns, GEC scores significantly differed by learning and cognition, F(1, 125) = 5.07, p = .026;  $\eta_p^2 = 0.04$ , play/social concerns F(1, 125) = 5.94, p = .016;  $\eta_p^2 = 0.045$ , behavioural concerns, F(1, 125) = 11.64, p = <.001;  $\eta_p^2 = 0.085$ , as well as diagnostic concerns, F(1, 125) = 10.67, p = .001;  $\eta_p^2 = 0.08$ . For caregiver-reported social and interpersonal strengths, GEC scores significantly differed by F(1, 108) = 7.28, p = .008;  $\eta_p^2 = 0.063$ . The remainder of strengths were non-significant, p > .202.

A multivariate analysis of variance (MANOVA) was conducted to investigate whether caregiver-reported concerns and strengths (IVs) were differentially associated with EF domains (DVs; Inhibit, Shift, Emotional Control, Working Memory and Plan/Organise), with results shown in Table 4.4. With respect to play and social concerns, MANOVA results indicated Inhibit and Shift differed as a function of this concern, with children demonstrating significantly increased EF difficulties in these domains when caregivers reported play and social concerns. For behavioural concerns, Inhibit, Shift as well as Emotional Control differed as a in relation to this concern. For diagnostic concerns, all BRIEF domains were implicated within this concern with the exception of Shift, which was not significant. The MANOVA results for strengths categories indicated that 'Cognitive and Intellectual Skills' and 'Social and Interpersonal Strengths' produced significant domain results, where Emotional Control was implicated in both categories. That is, better EF skills (lower scores) were associated with these aforementioned strengths. Additionally, lower Inhibit and Shift scores were also associated with social and interpersonal strengths.

Table 4.4. Significant	<b>BRIEF T Scores</b>	Based on	Caregiver-	Reported	Concerns a	nd Strengths.

			PCQ C	Concerns		PCQ Strengths						
BRIEF Domains	Speech and Language Concerns	Learning and Cognition	Play/Social Concerns	All Behavioural Concerns	Development al Concerns	Diagnostic Concerns (ASD, SLD and ADHD)	Character and Personality	Cognitive and Intellectual Skills	Hobbies and Passions	Physical and Motor Skills	Social and Interpersonal Strengths	
Inhibit T scores	.894	3.03	8.61**	9.35*	.061	11.23***	.372	2.90	.887	.538	11.97***	
Shift T scores	.043	.006	4.92*	6.10*	1.34	2.57	.614	0.28	.255	.139	5.94*	
Emotional Control T scores	.102	3.14	2.07	31.85***	.310	10.19**	.284	4.26*	.404	.216	4.57*	
Working Memory T scores	2.40	1.68	3.25	1.52	2.16	4.60*	1.38	.656	.007	1.55	.858	
Plan/Organise T scores	.111	1.62	1.50	2.70	1.25	5.17*	.184	.633	.016	.036	1.78	
GEC T scores	1.50	5.07*	5.94*	11.64***	1.65	10.67***	1.38	1.65	.009	.161	7.28**	

Note: \*Denotes significance at p<0.05, \*\*Denotes significance at p<0.01, \*\*\*Denotes significance at p<0.001. The F statistic is based on the ANOVA and MANOVA results is reported here.

#### 4.5. Discussion

This study explored caregiver-identified concerns and strengths and their association with observed EF. The results of this study showed larger EF delays were associated with a greater number of diagnoses and concerns for their child. Moreover, caregivers of children with greater EF delays identified fewer positive strengths generally. Caregivers with a greater number of concerns, play/social, behaviour and diagnostic concerns, showed greater EF delay, with subdomains of inhibition, shift (flexibility) and emotional control also showing associations. A pattern of caregiver-identified strengths revealed unique insights. Children with reported social and interpersonal strengths demonstrated higher levels of inhibition, flexibility and emotional control. Of note, the study showed there was no association between reported strengths and number of diagnoses. Children with greater delays in inhibition and flexibility exhibited significant concerns in play, social engagement, and behaviour (both internalising and externalising) as well as behaviours warranting diagnostic investigation NDCs. Additionally, impairments in emotional control were linked to general behavioural concerns and patterns indicative of NDCs. Inhibition, flexibility and emotional control (regulatory skills) play a key role in the adaptability of children's behaviour and development.<sup>3</sup> These key domains are in part, consistent with executive function models proposed by Miyake and colleagues<sup>26,31</sup> (2000; 2012) who implicate flexibility and inhibition in contributing uniquely to cognitive processes and behavioural regulation. Together, these findings reveal a pattern of EF performance in the inhibit, shift and emotional control domains which are linked with observable caregiver identified concerns and strengths in children. Caregiver evaluations on certain behavioural performance can directly inform our understanding of patterns of differential EF performance.

. Inhibition plays a key role in learning, play and social interaction in children, and so it stands that children with impaired inhibition scores are more perceived by the caregivers to have fewer problems and hence more strengths in play.<sup>360</sup> These skills are essential for engaging in complex social play, which is often challenging for children with NDCs. Of note, studies have established the key role that inhibition can have in play.<sup>361-363</sup> Findings also add to our understanding of poor inhibitory control and the occurrence of challenging behaviour such as aggression<sup>364,365</sup> in both typically developing children and those with NDCs. This relationship is particularly pronounced in children with NDCs, where inhibition deficits can exacerbate behavioural challenges.<sup>366</sup> Further, studies have found inhibitory control is linked to risk-taking behaviours in young children.<sup>367-369</sup> Domains such as flexibility and emotional control were also implicated in the study's findings.

Flexibility is essential in play, social interaction, and social cognition. Children with reduced flexibility (measured by the shift domain), were reported to have significant concerns about their play, social engagement and behaviour. Children with higher cognitive flexibility tend to engage more effectively in imaginative play and are better able to understand and adapt to the rules of games, which are crucial skills for social learning and interaction.<sup>370</sup> Inflexible behaviours can often lead to frustration, behavioural outbursts or rigidity<sup>371</sup> which is often pronounced in children with NDCs where difficulties in inflexible thinking and behaviour often result in increased behavioural challenges. Children with caregiver reported difficulties in emotional control were reported to demonstrate significant challenges with behaviour and often these behaviours were signalling the presence of a NDC for caregivers. Emotional control allows children the ability to modulate or regulate their emotional responses and is often a key behavioural phenotype for

children with autism<sup>372</sup> and ADHD<sup>373</sup> who often display poor emotional control, contributing to impulsivity, increased emotional reactivity to social situations and non-compliance.<sup>374</sup>

Children with difficulties in EF skills were five times more likely to have behavioural concerns noted by parents as part of their early developmental screening. When reviewing their EF profile, these same children with behavioural concerns raised also were four times more likely to have impaired inhibition, two times more likely to have impaired flexibility and five times more likely to demonstrate emotional dysregulation. Further analyses support these findings with children with elevated results in inhibition, flexibility and emotional control more likely to have reported early behavioural markers including sensory, restrictive, internalising and externalising behaviour. These findings are consistent with research that has established the link between poor EF and impaired externalising behaviour, <sup>375</sup> emotional regulation<sup>376</sup> and flexibility in thinking and in behaviour<sup>377,378</sup>. As predicted, children with social concerns did present with executive delay, and this was a pattern that effected their inhibition, and flexibility. Specifically, children with elevated inhibition scores where nearly three times more likely to show caregiver-reported concerns for social and play behaviour. This adds to our results and enhances our understanding of EF and social development whereby inhibitory skills are often at the core when reviewing EF abilities and social play behaviour.<sup>379</sup> These finding align with models of developmental executive growth whereby regulating the self and one's own behaviour would translate into interpersonal regulation.<sup>26</sup>

In addition to the aforementioned concerns, children with impaired emotional regulation abilities and impaired planning were up to three times more likely to have caregiver-reported concerns about specific NDCs. Diagnostic markers are often described using behavioural phenotypes (i.e., hyperactivity in ADHD and inflexibility in Autism). When reviewing early behavioural concerns, these results suggest that emotional outbursts and impaired planning are often a key behavioural marker implicated by parents in diagnostic investigations for ASD, ADHD and SLD<sup>222</sup>. Further, inhibition and working memory was also implicated in diagnostic concerns. Behavioural inhibition has been implicated in NDCs such as ADHD and working memory is often a key impaired EF in NDCs such as SLD<sup>380</sup>. Interestingly, concerns pertaining to NDCs were found to have more impairments in their EF profile. This is a well-established finding where children with NDCs are found to have significant impairments in a range of EF abilities. <sup>145,189</sup>

The relationship between caregiver reported social strengths and differential EF performance provided a unique lens in understanding the role of emotional control, inhibition, and flexibility in fostering interpersonal skills and social development. Children whose caregivers reported social/interpersonal strengths had better EF domain performance. This pattern of EF strengths was found to extend to inhibition, shift (flexibility) and emotional control. These findings concur with the results of studies that establish a link between EF performance and social competence.<sup>292,381,382</sup> For example, Benavides-Nieto and colleagues<sup>381</sup> (2017) found that young children with better EF were correlated with high social competence. Emotional regulation and flexibility account for interpersonal problem-solving allowing an individual to perceive changes in others, detect emotional cues (verbal and non-verbal) in others, adjust one's own response and implement an socially appropriate interpersonal response.<sup>383,384</sup> Emotional control, inhibition and

flexibility hence, play a key role in interpersonal skill and social development.<sup>370,385</sup> Social strengths captured within this study could be viewed conversely to the play and social engagement concerns reported by caregivers, It is possible this question on strengths elicited positive aspects of a child's functioning highlighting the importance of holistic, more neuro-affirming diagnostic lens in developmental assessments. Emerging research acknowledges that socially appropriate responses are based on social norms that are largely driven by research based on a more medical and deficit focused lens.<sup>386</sup> Interestingly, children with more impaired inhibition were two times more likely to have been flagged for cognitive strengths. These results could also suggest despite some significant EF impairments, parents and caregivers were able to recognise key cognitive strengths in these children despite some inhibitory challenges. Capturing strengths in addition to weaknesses, can support early intervention that can enhance existing strengths while mitigating challenges which can have a profound impact on a child's developmental trajectory,<sup>387</sup> overall well-being and school functioning.

#### 4.5.1. Strengths and Limitations

This research study has links patterns of EF performance to caregiver-identified concerns and strengths in a sample of children attending a tertiary service, providing unique insights into a clinically relevant sample. However, this study is not without limitations. We did not have access to data on cognitive ability or symptom severity for children. It is possible that some of our findings may have been impacted by differences in these areas. Another limitation of this study is that a measure of strengths was not utilised. The incorporation of such a measure could enable further quantification of functional strengths. Although we note measures reviewing childhood strengths in the absence of difficulties are difficult to find, with measures such as the Strengths and Difficulties questionnaire only assessing a few questions based on strengths and focus on psychosocial difficulties.<sup>388</sup> Specific validated measures capturing child strengths do not exist yet, however provide an important avenue for future research in capturing developmental strengths in children. We acknowledge the lack of statistical correction for the number of concerns and strengths examined and positioned this in the context of the exploratory nature of our study. Our study utilised shared method variance, where the child's caregivers' reports were evaluated. Further research could also evaluate educator reported evaluations and their subsequent performance on teacher-rated EF measures. Educational evaluations can provide information pertaining to a child's learning performance as EF can manifest in many areas of learning and school difficulties.<sup>389</sup>

#### 4.5.2. Conclusions

This study provides novel insights into how caregiver evaluations, encompassing both strengths and concerns, correlate with children's EF performance. Notable findings of the study establish that a unique pattern of EF impairments are significantly associated with caregiver-reported behavioural concerns, with particular deficits observed in inhibition, flexibility, and emotional control domains. Conversely, children identified with social and interpersonal strengths exhibited enhanced performance in these EF domains. These findings highlight the importance of incorporating caregiver insights into children's developmental assessments, as well as how best to utilise these evaluations into the child's assessment. Further, a focus on caregiver identified strengths stressed the need for holistic, neuro-affirming approaches in developmental evaluations, which illuminates how individual strengths can be meaningfully incorporated as part of the child's treatment report and guide intervention This research not only deepens our understanding of the intricate relationship between EF and social development in children but also emphasises the value

of a strengths-based perspective in early intervention strategies, which can significantly influence children's developmental trajectories, ameliorate disease burden and improve overall well-being.

#### **Chapter 5 Objectives:**

In review of the chapters within this thesis, the following chapter is a synthesis of all the studies that have been conducted in the exploration of EF in the area of transdiagnostic neurodevelopmental research. This chapter seeks to provide a detailed discussion on key findings across thesis chapters, summarise implications, limitations and future direction. This chapter contains the following sections:

- a) General Thesis Discussion
- b) Thesis Summary
- c) Transdiagnostic Nature of EF Impairment: Cross-Condition EF Examination
- d) Comorbidity in Neurodevelopmental Conditions and Executive Function Profiles
- e) Parental Evaluations in Understanding Executive Functioning in Children
- f) Integrating Models on Executive Function in Neurodevelopmental Conditions
- g) Clinical and Research Implications
- h) Limitations and Future Research Directions
- i) General Conclusion: Integrating Perspectives on Executive Function in

Neurodevelopmental Conditions

#### 5. General Thesis Discussion

This thesis highlights the pervasive nature of EF impairments across different NDCs in children, showcasing their transdiagnostic impact. Our findings across three empirical studies consistently indicate moderate EF impairments across NDCs, with important subtleties between NDCs. NDCs are significantly more impaired across EF domains when compared to controls. In addition, there was disparity in EF impairments as measured by performance-based versus informant-based assessments. However, gender did not prove to indicate significant contribution to the overall effect. The percentage of males versus females did not inform the overall effect size, with both genders being equally impacted. This disparity suggests the need for a nuanced approach to EF evaluation, combining both objective and subjective measures to capture a more complete profile of EF in children with prominent NDCs.

A second significant aspect of our findings was the association of comorbidities on EF profiles. Particularly, the presence of ASD in conjunction with other conditions like ADHD and SLD. Caregiver reports, reflecting both the challenges and strengths of children with NDCs, highlight the necessity for interventions that are both comprehensive and tailored to holistic individual needs. With regard to specific EF delays, particularly in inhibition, flexibility, and emotional control, we observed significant associations with distinct behavioural and functional challenges. These deficits, crucial in areas such as learning and social interaction, highlight the need for targeted support. Moreover, the strong correlation between these EF deficits and caregiver-reported behavioural concerns emphasises the importance of early and accurate EF assessment.

The potential for condition specific intervention strategies is further emphasised by our findings. These strategies should account for the unique EF profiles and comorbidities of each child, incorporating a strengths-based approach as indicated in caregiver reports. Such an approach ensures that support programs are not only remedial but also empowering. In summary, this thesis reinforces the utility of EF as a transdiagnostic element in paediatric NDCs. The nuanced EF profiles identified offer valuable markers for neurodevelopmental delays and present significant opportunities for advancing both research and clinical practice in this area. Our findings highlight the potential of EF profiles as a cornerstone for developing precision medicine approaches in the management of NDCs, enhancing the quality of life and functional outcomes for affected children.

#### 5.1. Thesis Summary

The second chapter within this thesis presented a systematic review and meta-analysis to examine EF impairments across different conditions, with a focused comparison of NDCs with ASD and ADHD, in children under 18 years of age. The study reveals that EF impairments are a common feature across various NDCs, with some condition-specific deficits in certain EF domains. Detailed findings include specific EF deficits in these conditions, with a focus on differential EF performance in children with ADHD who displayed greater problems with attention and response inhibition, and children with ASD showed larger impairments in set-shifting, while children with learning disorders showed greater impairments in set-switching. The chapter also highlighted how the type of measures utilised revealed a large effect on the size of EF impairment, when informant measures were compared to performance-based measures. The findings emphasised the value of a transdiagnostic approach to understand and support children with NDCs, suggesting the need for targeted interventions that consider the unique and overlapping aspects of EF impairments across these conditions. This research is vital for clinical applications, suggesting a nuanced approach to interventions and supporting the need for EF remediation therapies tailored to individual profiles within NDCs. The study underscores the importance of understanding the complexities of EF in child development and neurodevelopmental disorders, offering insights for both research and clinical practice.

The third chapter within this thesis investigated the EF profiles in children with NDCs, with a specific focus on ASD, ADHD, and SLD, occurring in comorbidity, within a clinically relevant sample of children under the age of 18. The results highlighted the significant disease burden of comorbid NDCs. Specifically, children with comorbid ASD and ADHD or ASD, ADHD, and SLD exhibited more significant EF deficits compared to children with ADHD and comorbid SLD. These deficits are particularly notable in response inhibition, flexibility, emotional control and working memory, while deficits in initiation and planning/organisation only affect the three comorbid group (i.e., ASD, ADHD, SLD). The study illuminates the cumulative effect of comorbid NDCs on EF and highlights the importance of considering these overlapping impairments in clinical and educational strategies. It supports the hypothesis that while ASD and ADHD are distinct disorders, they share underlying mechanisms affecting EF,<sup>256</sup> and their co-occurrence has a significant impact on the executive abilities of the affected child. This has implications for diagnosis, intervention, and understanding the broader context of EF impairments in child development.

The fourth and final chapter within this thesis examined EF performance in children attending a tertiary developmental service, following caregiver-identified concerns and strengths.

Findings provided unique insights into the link between reported developmental concerns and their EF performance. Children identified with behavioural concerns by caregivers showed significant deficits in EF domains, especially in inhibition, flexibility, and emotional control. Conversely, children with caregiver-reported social and interpersonal strengths displayed better EF performance in these areas.

The thesis unveils enlightening data on the EF profiles within the spectrum of NDCs affecting children, shedding light on the pervasive challenges faced by those with NDCs. Such results provide evidence to support that EF is an endophenotype within NDCs.<sup>230</sup> Further, conceptualising EF under a transdiagnostic lens involves understanding these cognitive processes as underlying dimensions that cut across traditional behavioural-latent diagnostic categories. This perspective is particularly valuable in NDCs, where there is considerable overlap in EF deficits. For example, a child with a primary diagnosis of ADHD might also exhibit EF deficits typical of ASD, suggesting shared underlying neurocognitive processes as suggested by EF models.<sup>22,24</sup> This transdiagnostic approach can lead to more comprehensive and individualised treatment strategies. The transdiagnostic perspective on EF in NDCs encourages a shift from a disorder-specific focus to a more holistic understanding of cognitive processes. This approach not only enhances our understanding of the aetiology and development of these conditions but also provides nuanced cross-condition interventions targeting EF. For instance, interventions designed to improve working memory could benefit a range of conditions beyond their primary targets.<sup>390</sup>

#### 5.2 Transdiagnostic Nature of EF Impairment: Cross-Condition EF Examination

The synthesis of Chapter 2's findings across multiple studies on EF within NDCs in children reveals a nuanced, transdiagnostic landscape of impairments. Notably, a significant, moderate EF impairment was present across NDCs when compared to typically developing children. This reinforces the notion that EF difficulties are not condition-specific but rather indicative of a broader neurodevelopmental profile. Variables that contribute to this significant finding include children's sex and the type of assessment utilised to capture EF delay. Males are found to be impacted more significantly by NDCs; a finding consistent with a recent meta-analysis indicating a higher rate of diagnosis in males than females.<sup>391</sup> The tendency for larger EF impairments to be identified by informant-based measures compared to performance-based measures raises questions about the most appropriate methods for assessing EF in clinical and research settings. It suggests a potential underestimation of EF impairments when relying solely on performance-based reports, which may not capture the full extent of EF challenges faced by children with NDCs. Performance and informant-based measures are thought to measure distinct constructs with performance-based measures providing a measure of cognitive efficiency, typically addressing cold constructs of EF, and informant-based measures tap into everyday EF challenges encompassing both hot and cold measures of EF.<sup>260</sup> Further, consistent across the studies is the differentiation of EF impairments among various conditions. Children with ADHD display pronounced challenges in attention and response inhibition, aligning with core diagnostic criteria and supporting attention-based models of the condition.<sup>22,118</sup> Meanwhile, children with ASD were more severely impacted in set-shifting abilities, a finding that aligns with the literature and is responsible for the behavioural phenotype characteristic of rigidity and repetitive patterns of behaviour.<sup>188</sup> Furthermore, SLDs are notably associated with set-switching difficulties,

emphasising the nuanced impact of cognitive flexibility impacting these children.<sup>199</sup> EF has the potential to serve as a transdiagnostic indicator of everyday functional challenges in children, which in addition to behavioural challenges provides nuanced cognitive proficiencies that are impaired across NDCs. These findings highlight the advantage of including EF in furthering our understanding of traditional behavioural diagnostic criteria in better understanding and diagnosing NDCs in children.<sup>230</sup>

#### 5.3 Comorbidity in Neurodevelopmental Conditions and Executive Function Profiles

The impact of comorbidities, particularly the presence of ASD in conjunction with ADHD and SLD is profound and associated with greater EF impairment. This finding is pivotal as it highlights the cumulative effect of multiple NDCs on a child's EF and calls for a nuanced understanding of these children's needs. The complexity of EF profiles associated with comorbid conditions warrants individualised approaches to intervention, highlighting the need for tailored intervention within the paediatric neurodevelopmental field. More specifically, comorbid presentations are associated with delays in EF domains such as inhibitory control, flexibility, emotional control, working memory, and initiation. The additive component of NDCs, whereby a child has more than one NDC leads to increased functional delays<sup>392</sup> and greater support needs. The addition of a second NDC attenuates to the child's executive capacity, where multiple, cumulative EF deficits are observed.

A key finding of the second empirical paper, when examining comorbidities, was the significant impact of ASD on the severity of EF impairments. Studies have demonstrated that children and adults with ASD are significantly impacted by homotypic (within the NDC

classification) and heterotypic (outside the NDC classification) comorbid conditions with a significant impact on overall wellbeing<sup>393,394</sup> Research examining NDC brain divergence reveals distinct patterns of neural biomarkers unique to ASD when compared to other NDCs.<sup>329</sup> The co-occurrence of ASD with other NDCs is likely to increase neuropathology,<sup>330</sup> that is, the neural markers found in conditions that co-occur are unique and more extensive than in cases with a single diagnosis, despite sharing some similarities.

The EF domains of inhibition, flexibility, working memory and emotional control are implicated in a wide array of everyday behaviours such as social engagement, play, and challenging behaviours<sup>370</sup> and are consistent with developmental EF models by Diamond<sup>33</sup> and Miyake.<sup>26,31</sup> A recent systematic review implicated unique EF deficits to ASD co-occurring with ADHD which extended to flexibility, inhibition and attention.<sup>189</sup> The findings of this thesis extends these findings and explore how EF is cumulatively impaired across key EF domains as measured by the BRIEF questionnaire. Children with comorbid NDCs, such as ADHD, ASD, and LD exhibit distinctive patterns of inhibitory control, 395,396 flexibility, 247,397 working memory, 398-400 and emotional regulatory abilities<sup>372,373,401</sup> transdiagnostically.<sup>402,403</sup> Flexibility is a key EF skill involved in learning and social engagement; an impairment in this skill manifests as behavioural outbursts or rigidity, and when not ameliorated can exacerbate social interaction, academic success, and overall well-being.<sup>404</sup> Working memory capacity supports complex cognitive tasks like problem-solving, language comprehension, and academic achievement, is crucial for day-to-day social, personal and academic engagement. In NDCs, such as ADHD, ASD and SLD working memory impairments are well established<sup>405</sup> and its impact in comorbid presentations appears to be cumulative.<sup>166</sup> Emotional control, a key hot EF ability responsible for healthy environmental adaption as well as academic and mental health outcomes in children.<sup>406,407</sup> In children with NDCs,

these outcomes are compromised and lead to increased aggression, non-compliance, and other externalising behaviours. Understanding and supporting the development of emotional control is therefore essential for promoting positive outcomes in children with NDCs. Cognitive remediation programs that offer amelioration of condition specific delay are best placed to target key EF domains outlined by this empirical study, <sup>408</sup> and may subsequently, promote EF development, thereby facilitating increased participation in social activities, and promoting adaptive behaviour.<sup>409</sup>

#### 5.4. Parental Evaluations in Understanding Executive Functioning in Children

This third empirical study delves into the relationship between EF and parental evaluations in children with developmental concerns, utilising the BRIEF-2 measure for a comprehensive EF assessment. Key aims for this study primarily focused on the correlation between EF profiles and parental reports of strengths and challenges encompassing behaviour, social skills, play capabilities, and cognitive abilities. A notable aspect of the study is the identification of distinct EF patterns that emerge in relation to various parental concerns. This is particularly evident in cases where elevated inhibition scores were observed, which closely correlated with parental reports of behavioural difficulties and challenges in social interactions and play. Furthermore, the study uncovered that children facing behavioural issues demonstrate broader executive deficits across multiple EF domains, emphasising the complexity and interrelated nature of EF components. Interestingly, the research also shed light on the EF profiles of children with specific diagnostic concerns, revealing deficits in key areas such as inhibition, emotional control, working memory, and planning. This insight is pivotal in understanding the multifaceted nature of developmental concerns and the integral role of EF in these concerns. Conversely, the study
highlighted a positive correlation between children identified with social and interpersonal strengths and their performance in EF domains, particularly in inhibition, flexibility, and emotional control. This finding highlights the importance of EF in fostering social competence and adaptability in children with NDCs.

Developmental evaluations completed by caregivers revealed that learning, play and social, behaviour and diagnostic concerns were found to be associated with impaired EF within specific domains, namely, inhibition, shift (flexibility) and emotional control. Developmental concerns for play and social engagement, challenging behaviour and concerns pertaining to the diagnosis of NDCs were associated with delays in inhibition. A consistent profile was found for flexibility where delays within this domain also showed significant concerns in play and social and behavioural concerns. Impairments in emotional control also indicated those children had general behavioural concerns as well as behaviours indicative of an NDC reported by caregivers. Play, social engagement and challenging behaviours were consistently linked to EF delay. These findings align with recent reviews on early behavioural markers of NDCs in the first years of life whereby, delays in motor and language development, atypical play and social engagement, as well as unusual sensory processing markers signal the necessity of early detection of NDCs.<sup>410</sup> Further, research also links executive delays as a precursor to developmental conditions such as ASD and ADHD.<sup>411</sup> Interestingly, a unique pattern of caregiver-identified strengths revealed children with reported social and interpersonal strengths also had better inhibit, flexibility and emotional control. This finding is consistent with a recent meta-analysis exploring the relationship between EF, emotion regulation and affective abilities in children with NDCs (with a focus on ASD).<sup>412</sup> Findings revealed that children with fewer EF deficits experience fewer emotional or behavioural

challenges. This relationship highlights how EF abilities are intertwined with observable behaviours and capabilities as reported by caregivers.

Caregivers play a crucial role in the identification and management of EF impairments. Their perspectives reveal an association between the number of diagnoses a child has and the severity of reported EF delays, further influencing the perception of a child's strengths.<sup>413</sup> This emphasises the importance of involving caregivers in the assessment process and considering their insights when planning tailored interventions.<sup>414</sup> Further, a comprehensive developmental evaluation (encompassing both strengths and weakness) at the diagnostic level can appropriately guide academic as well as daily living support.<sup>415</sup> The importance of evaluating both strengths and weaknesses in children with developmental delays is increasingly recognised in both research and practice.<sup>355,416</sup> This comprehensive approach not only enhances our understanding of the child's abilities and needs but also informs the development of more effective, personalised interventions. The study's findings emphasise the crucial role of caregiver input in the developmental assessment of children. By integrating parental perspectives, the study stresses the importance of capturing early markers of concern and strengths, paving the way for more individualised and effective diagnostic and treatment plans.<sup>411</sup> These findings contribute significantly to the understanding of EF in childhood development, offering valuable insights for clinicians, educators, and parents in supporting children with developmental challenges and guiding their diagnostic trajectory.

#### 5.5. Integrating Models on Executive Function in Neurodevelopmental Conditions

In synthesising the empirical findings of this thesis on EF impairments across various NDCs unveils a complex landscape that both supports and extends existing theoretical frameworks. The models presented Miyake and colleagues<sup>26,31</sup> and Diamond<sup>33</sup> offer foundational perspectives on EF's multifaceted nature, including updating, shifting, and inhibiting processes, as well as its developmental progression. These models serve as a benchmark against which the results of this thesis can be juxtaposed. The findings here, which delineate specific patterns of EF delays, do not merely validate the dimensional construct of EF proposed by these frameworks but also spotlight the transdiagnostic prevalence of EF impairments across a diverse range of NDCs. This revelation highlights the imperative for a theoretical expansion that encompasses the nuanced manifestations of EF impairments observed in this study.

Furthermore, the project findings navigate through the intricate interplay between the established models and novel insights garnered from this research. The thesis reveals areas where the traditional models align with the empirical evidence gathered, as well as domains where the findings challenge or refine these conceptualisations. For instance, the pervasive nature of certain EF impairments across NDCs suggests a more integrated, perhaps even universal, aspect of executive delay than previously accounted for by the segmented approach of earlier models such as the attentional model proposed by Posner.<sup>29</sup> Other models are also informative in enhancing our understanding of the project findings however offer perspectives to extend our understanding of the EF framework. Integrating Barkley's EF model<sup>22,417,418</sup>, which emphasises self-regulation, inhibitory control, and the foundational role of EF in goal-directed behaviour and future-oriented tasks, with the findings of this thesis reveals a profound alignment and potential areas for extension. The data presented herein, demonstrating pervasive EF impairments across a variety of NDCs not only corroborate Barkley's assertions regarding the centrality of inhibition and self-regulation in child development but also suggest the necessity of broadening the model to

encompass additional EF components identified as critical across NDCs identified within this project. This synthesis iterates the potential for Barkley's framework to guide targeted interventions that enhance inhibitory control, planning, and self-regulation, offering a theoretical and empirical foundation for future research aimed at optimising therapeutic strategies for children with NDCs, thus enriching our understanding and intervention approaches within the field of NDCs.

Further, Anderson's model of EF<sup>6</sup> within the context of this thesis highlights how his framework, which delineates EF into distinct yet interrelated components such as cognitive flexibility, goal setting, and information processing, aligns with the observed EF impairments across NDCs. The thesis findings enrich Anderson's model by demonstrating these components' variability and their collective impact on the functional outcomes in children with NDCs. In a review of theoretical models of EF, the project findings assert that multifactorial models proposed by Miyake<sup>26,31</sup> and Anderson<sup>6</sup> provide a more integrative perspective of the EF framework and align with the overall project findings. This integration conceptualises how single conditions and comorbid conditions map on the EF framework. This integrated perspective holds the promise of fostering more effective, holistic strategies for supporting children with NDCs, marking a pivotal step forward in both research and clinical practice.

In view of the EF delays exhibited across NDCs within this thesis, and the theoretical basis of EF research, the project findings add some support for the potential for EF to serve as a cognitive endophenotype not just for single conditions but for NDCs as a whole. EF can be viewed as a cognitive intermediatory when investigating transdiagnostic EF delay in children, its specific impact on NDCs and its link to developmental and behavioural outcomes examined within this project. Current NDC research continues to examine the potential for EF to present as an intermediatory endophenotype and is gaining traction with studies compiling evidence for this in ASD, ADHD and SLD.<sup>196,215,227</sup> More recent exploratory studies examine EF as an endophenotype through research on parents thus exploring a genetic link,<sup>419</sup> and others have examined transdiagnostic brain mapping,<sup>420</sup> with increasing evidence to support a transdiagnostic evaluation of EF in the context of NDCs to foster enhanced assessment and intervention.<sup>230,421</sup> The findings of this thesis cumulatively contribute to this emerging body of research on endophenotypes, and highlight the role EF can play in better understanding condition presentation transdiagnostically. An integrative transdiagnostic map of EF delays is depicted in Figure 5.1, based on thesis findings and theoretical models.



Figure 5.1. An Integrated Transdiagnostic Map of EF Delays

### 5.6 Clinical and Research Implications

In review of project findings, the thesis has several clinical and research implications which will be outlined. The results within this thesis project contribute to a growing consensus that EF impairments serve as a transdiagnostic endophenotype for many NDCs.<sup>230,232,419,422</sup> Studies examining the potential for ASD and ADHD to present as a endophenotype examine genetics, neurobiological processes as well as observable behaviours. Of note, research examines the link between neurobiological underpinnings of executive performance and its impact on children with NDCs.<sup>8,196,232</sup> They highlight the potential utility of EF profiles as markers for neurodevelopmental delays, which can guide both research and clinical practice in treatment children with NDCs. DSM

iterations have a focus on behavioural phenotypes, new literature posits theories on cognitive phenotypes as diagnostic markers in better understanding NDCs.<sup>192,196,232</sup> An enhanced perspective on the diagnostic markers of NDCs can contribute to finetuning diagnosis in young children who may have differential functioning or may not meet full behavioural diagnostic criteria however still experience significant cognitive functional challenges as part of their NDCs.<sup>423,424</sup> Our findings add to this new body of literature, and provide evidence to explore EF as a key, informative diagnostic marker.

The thesis findings also reveal that subtle differences in EF between NDCs can inform a precision medicine and intervention approach, potentially leading to improved support for learning, cognition, and daily living. For example, in children with ASD and another comorbid NDC, increased EF delay in inhibition, flexibility and emotional regulation can have significant implications across home and school contexts.<sup>425,426</sup> Deficits in both contexts that pertain to domains such as inhibition, flexibility and regulation, have serious implications for a child's functioning. Programs that remediate these areas then offer several clinical implications, namely, improvements in these EF areas could result in improved social, play and behavioural functioning.<sup>427,428</sup> Such implications offer to delineate a child from an otherwise disadvantageous trajectory that could have serious psychosocial functioning implications.<sup>429,430</sup> For example, studies on neuroplasticity and brain development emphasise the importance of early detection and intervention of NDCs.<sup>429</sup> Further, EF profiles may serve as cognitive markers that can inform individualised support programs for particular NDCs, for example EF remediation programs may target individualised EF domains in children with ASD.<sup>431</sup> Consequently, further research is needed in these areas, particularly on the subtle EF differences across other lesser prevalent NDCs.

This includes exploring EF profiles in NDCs such as Rett's Syndrome, cerebral palsy or Williams syndrome. There is a need for further cross-condition research in such NDCs and how their EF profiles can further inform personalised medicine or intervention models in order to mitigate these impairments.

Another component of the diagnostic journey taken is early recognition of NDCs by caregivers and clinicians. Early detection is pivotal in ameliorating condition trajectory with research findings suggesting that early intervention support can show efficacy and ameliorate impairments in children with ASD and ADHD.<sup>431-433</sup> As such, caregiver evaluations plays a pivotal role in shaping the early diagnostic journey taken. The literature has ample support for the recognition of deficits in the cognitive, behavioural and socio-emotional functioning arena of children with NDCs.<sup>432-434</sup> As outlined in chapter 4, the key areas of developmental concerns were behavioural and social/play concerns, as well as children with caregiver concerns for neurodevelopmental diagnosis. These areas have established links in the literature to NDCs, 435-437 however how these links are connected to EF domain specific severity is a new finding. These findings provide important information on how developmental concerns unfold and how executive delays in inhibition, flexibility and emotional control can contribute to our understanding of these developmental concerns. Such findings have clinical and research implications on how to interpret captured delays when examined by EF measures, and subsequently can guide various intervention and support pathways for children attending a developmental service for assessment.

Notwithstanding the importance of identifying weakness in a child's early development, the findings in this thesis project illustrate the importance of assessing for developmental strengths

as well. Encompassing both strengths and weaknesses facilitate better collaboration between families and schools. This collaborative approach is essential for creating supportive environments that accommodate the child's needs.<sup>438</sup> Focusing on a child's strengths, alongside weaknesses, has been linked to more positive outcomes in children with developmental delays. Research suggests that children who receive support that builds on their strengths exhibit better self-esteem, resilience, and overall well-being.<sup>439</sup> In addition, the early identification of strengths, in addition to weaknesses, can lead to earlier and more effective support.<sup>416,440</sup> Early interventions that focus on enhancing existing strengths while mitigating challenges can have long-term positive effects on the child's developmental trajectory.<sup>387,441</sup> The research in exploring neuro-affirming or strengthsbased diagnostic methods trails behind research on deficits that influence delays in NDCs, particularly with the ASD research field.<sup>442,443</sup> Further research could examine further areas of developmental strengths that contribute to EF performance in children with focus on variables that may mitigate this outcome. Such variables could include the influence of social factors, genes, sex, age and mental health factors. In turn, such explorations can further our understanding of areas of strengths as well as challenges in children's EF performance, providing a more holistic neurodevelopmental profile.

#### 5.7. Limitations and Future Research Directions

The thesis project offers several meaningful results; however, these findings are not without limitations. Firstly, while the meta-analysis captured key NDCs, a more comprehensive analysis could be achieved by conducting detailed cross-conditions searches to include a broader range of NDCs and explore their EF performance. Secondly, the reviewed studies were controlled for comorbidities, future research could expand on this and conduct enhanced systemic reviews on comorbidities in across all NDC and explore the impact of EF in children. Additionally, only informant measures were used in the two empirical studies within this project. Broader research suggests there is minimal correlation between informant and performance measures indicating they are likely to be measuring different underlying mental constructs.<sup>116</sup> Although, informant measures offer unique insights into a child's overall executive functioning, the use of performance measures can provide unique into a child's EF performance within each domain under structured settings, and allows for high task purity.<sup>116</sup>

Furthermore, NDC groups within empirical paper two were largely informed by THE prevalence of the individual conditions<sup>185</sup> (i.e. ADHD more likely to co-occur with SLD in a tertiary developmental service). This meant single disorder comparisons such as ADHD or SLD alone, were less prevalent and subsequently not possible to obtain as part of this thesis project. This is consistent with literature on prevalence rates of NDCs,<sup>444-446</sup> and thus limits the generalisability of findings to populations with single diagnoses. Future research could further enhance our understanding of EF profiles across single and comorbid presentations of less prevalent NDCs. The BRIEF parent evaluations were a critical measure within this project and provided an overall evaluation of a child's EF abilities within the home environment. Future research could augment this project's findings and utilise teacher reported EF performance to address gaps in our understanding of cross-condition comparisons within the academic arena. In addition, future research paradigms could encompass the use of prospective data and encompass DSM changes over time. The empirical studies make associations to EF domains within NDCs, and this link is not causal. Further, we note the project's quality of clinical data and assessments used on NDCs populations were limited by the CDU developmental service's use of tools often

directed by clinician within the team. An example of this is the empirical chapters utilised informant-based EF measures over performance-based EF measures. This limited the bounds of the empirical studies within this project however the project research aims, and method employed were formulated with considerations made on this. Lastly, empirical studies within this project utilised cross-sectional data, to establish the stability of these findings, further research could employ longitudinal data to establish the stability of EF and the impact of time or age on EF performance within NDC cohorts.<sup>447,448</sup>

# 5.8. General Conclusion: Integrating Perspectives on Executive Function in Neurodevelopmental Conditions

This thesis has elucidated the complex landscape of EF impairments across NDCs, adopting a transdiagnostic perspective that underscores both shared and unique aspects of these impairments among children with highly prevalent NDCs such as ASD, ADHD, and SLD. Through systematic review, meta-analysis, and empirical studies, this work highlights the moderate to significant impairments in EF that underpin these conditions, revealing the critical role of comorbidities and caregiver insights in understanding and assessing EF. The findings advocate for a nuanced approach to the evaluation and intervention of EF impairments, stressing the importance of considering the individual profiles and comorbidities of children.

Chapter two's systematic review and meta-analysis identified that children with ADHD exhibit significant difficulties related to attention and response inhibition, while ASD is more closely associated with challenges in flexibility. Moreover, specific learning disorders were linked to difficulties in working memory and task switching. In chapter three, the impact of comorbidities on EF profiles was further delineated, revealing that children with additional comorbid ASD alongside other NDCs, such as ADHD and SLD, face more pronounced EF deficits than those with a single diagnosis of ASD alone, particularly in domains like inhibition, flexibility, emotional control and working memory. This suggests how specific diagnostic comorbidities exacerbate EF challenges, highlighting the need for tailored intervention strategies that address the compounded difficulties faced by these children. Chapter four's focus on caregiver-reported strengths and challenges concerning EF performance underscored the importance of considering real-world implications of EF impairments. Insights provided by caregivers revealed that behavioural, social, and learning challenges often corresponded with specific EF deficits, such as inhibition, flexibility, and emotional control. Conversely, strengths identified by caregivers in areas like social interaction and interpersonal skills were linked to more favourable EF outcomes in those same domains. These disorder-specific findings shed light on the complexity of EF impairments in NDCs and the need for a nuanced understanding that accounts for the variability within and across conditions. They advocate for the development of specialised assessment and intervention strategies that are sensitive to the distinct EF profiles and comorbidities present in children with NDCs. Furthermore, the inclusion of caregiver perspectives not only enriches the assessment of EF but also paves the way for more personalised and holistic intervention strategies that leverage the strengths of children alongside addressing their challenges. Future research should aim to broaden the understanding of EF impairments by incorporating diverse assessment tools, including educator reports, and exploring longitudinal studies to track the development of EF over time in children with NDCs. Additionally, further exploration into the integration of neurobiological, genetic, and environmental factors could offer deeper insights into the aetiology and progression of EF impairments.

To conclude, this thesis contributes significantly to the field of paediatric neurodevelopmental literature by offering a comprehensive and integrative view of EF impairments across key NDCs. The insights garnered highlight the importance of a transdiagnostic approach in enhancing diagnostic accuracy, tailoring interventions, and ultimately improving the quality of life and functional outcomes for children with NDCs. It also provides a foundation for developing individualised, evidence-based interventions that consider the unique EF profiles and strengths of children with NDCs. As the field moves forward, a collaborative approach involving caregivers, educators, and clinicians will be essential in addressing the multifaceted challenges presented by EF impairments in NDCs.

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## Appendix A. Chapter 2: Supplementary Tables/Figures

## Supplementary Table 1 – Search Strategy

1.	executive dysfunction.mp.
2.	cognitive flexibility.mp.
3.	mental flexibility.mp.
4.	set switching.mp.
5.	task switching.mp.
6.	set shifting.mp.
7.	exp short term memory/
8.	working memory.mp.
9.	Attention/ or Memory, Short-Term/ or Brain/ or cognitive
updating	g.mp. or mental updating.mp.
10.	fluency.mp. or exp Verbal Fluency/
11.	planning.mp.
12.	cognitive planning.mp.
13.	(central executive or inhibitory control).mp.
14.	response inhibition.mp. or exp Response Inhibition/
15.	exp neuropsychological assessment/ or halstead reitan
neurops	ychological battery/ or luria nebraska neuropsychological
battery/	or task switching/ or wisconsin card sorting test/
16.	neuropsychological assessment.mp.
17.	BRIEF.mp.
18.	behavior rating inventory of executive function.mp.
19.	BRIEF-P.mp.
20.	Tower of london.mp.
21.	exp Stroop Color Word Test/ or stroop test.mp.
22.	delis-kaplan executive function system.mp.
23.	trail making test.mp.
24.	exp Luria Nebraska Neuropsychological Battery/ or luria-
nebraska	a neuropsychological battery.mp.
25.	task shifting.mp.
26.	Go no-go task.mp.
27.	*planning/

#### Medline\_NDC Search

28. Wisconsin Card	l Sorting Test.mp.
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- 29. (delis-kaplan executive function system or DKEFS).mp.
- 30. Tower of london.mp.
- 31. Affective decision making.mp.
- 32. Childrens gambling task.mp.
- 33. Iowa gambling task.mp.
- 34. Sandbox task.mp.
- 35. (Cambridge Neuropsychological Test Automated Battery or

CANTAB).mp.

- 36. Cambridge Gambling Task.mp.
- 37. Information Sampling Task.mp.
- 38. Tower of Hanoi.mp.
- 39. Hayling test.mp.
- 40. Eriksen flanker test.mp.
- 41. Color-Word interference test.mp.
- 42. NIH toolbox cognition battery.mp.
- 43. (Flanker Inhibitory Control and Attention test).mp.
- 44. List Sorting Working Memory Test.mp.
- 45. exp \*Wechsler Memory Scale/ or wechsler memory

scale.mp.

- 46. Digits backwards.mp.
- 47. n-back test.mp.
- 48. Letter Sequencing task.mp.
- 49. Intra-extra Dimensional Set Shift.mp.
- 50. (Stop Signal Task and Stroop Stepping Test).mp.
- 51. Spatial Working Memory Test.mp.
- 52. Dimensional Change Card Sort Test.mp.
- 53. Flexible Item Selection Task.mp.
- 54. (Barkley Deficits in Executive Functioning Scale or

#### BDEFS).mp.

- 55. (Controlled Oral Word Association Test or COWAT).mp.
- 56. (Behavioural Assessment of the Dysexecutive Syndrome or

BADS).mp.

- 57. Dysexecutive Questionnaire.mp.
- 58. (Autism Spectrum disorder or ASD).mp.

59. exp autism spe	ectrum disorders/
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- 60. Asperger Syndrome.mp.
- 61. Pervasive developmental Disorder.mp.
- 62. 58 or 59 or 60 or 61
- 63. tic disorder.mp.
- 64. tourette's syndrome.mp.
- 65. Tourettes disease.mp.
- 66. cerebral palsy.mp. or \*Cerebral Palsy/
- 67. Down syndrome.mp. or exp Down's Syndrome/
- 68. Trisomy 21 syndrome.mp.
- 69. \*Fragile X Syndrome/ or fragile X syndrome.mp.
- 70. Martin-Bell syndrome.mp.
- 71. \*williams syndrome/
- 72. (williams beuren syndrome or Williams syndrome).mp.
- 73. \*Prader Willi Syndrome/ or Prader Willi syndrome.mp.
- 74. Angelman syndrome.mp.
- 75. happy puppet syndrome.mp.
- 76. \*Rett Syndrome/ or Rett syndrome.mp.
- 77. \*Turners Syndrome/ or Turner syndrome.mp.
- 78. Smith-Magenis syndrome.mp.
- 79. \*"Sclerosis (Nervous System)"/ or Tuberous sclerosis.mp.
- 80. DiGeorge syndrome.mp.
- 81. velocardiofacial syndrome.mp.
- 82. 22q11 deletion syndrome.mp.
- 83. dyslexia.mp. or \*Dyslexia/
- 84. dyscalculia.mp. or exp Acalculia/
- 85. exp Learning Disorders/ or Specific learning disorders.mp.

86. (executive adj2 function\*).mp. [mp=title, book title,

abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]

87. concept formation.mp. or concept formation/

88.	(fluency or verba	l fluency or non	verbal fluency).mp.
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- 89. "Delay of Gratification"/ or delayed gratification.mp.
- 90. Attention/
- 91. Cognition/
- 92. exp Memory/
- 93. Problem Solving/
- 94. Attention Deficit Hyperactivity Disorder.mp.
- 95. "attention deficit and disruptive behavior disorders"/ or exp

attention deficit disorder with hyperactivity/ or ADHD.mp.

- 96. 94 or 95
- 97. Fetal Alcohol Spectrum Disorders/ or FASD.mp. or foetal alcohol spectrum disorder.mp.
- 98. task switching/
- 99. executive function/
- 100. set shifting/
- 101. task switching/
- 102. executive functioning measures/

103. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 10 or 11 or 12 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 62 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 99 or 100 or 101 or 102

- 104. 62 and 103
- 105. 96 and 103
- 106. 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or
- 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or
- 85
- 107. 104 and 106
- 108. 105 and 106
- 109. 107 or 108
- 110. limit 109 to yr="1980 2023"
- 111. limit 110 to (childhood or adolescence <13 to 17 years>)

Study No.	Study Name & Vear	Diagnostic Group	EF Domains Analysed	Hedges' g, (95% CL)	Control Sample	Age Range	Gender	JBI Quality
	i cui		maryseu		size		(% of	1155055110110
							Males)	
1	Bayliss, 2000	ADHD (n=15) and LD $(n=12)$	Set Shifting	0.42 (-0.56,	15	8-12 years	70	Good
		(II-12)	Inhibition	0.90)				
			Attention					
2	Bental, 2007	ADHD (n=13),	Fluency	0.34 (-0.36,	23	7.9-11.7 years	100	Good
		ADHD+RD	Planning	0.88)				
		(n=27) and RD (n=17)	Response					
			Inhibition					
			working Memory					
3	Brandimonte,	ASD (n=10) and ADHD	Response	0.66 (-0.22,	10	6-12 years	81	Good
	2011	(n=10)	Inhibition	1.56)				
4	Coles, 1997	FASD (n=15) and	Set Shifting	0.36 (-0.27,	26	7-8.8 years	Not reported	Good
		ADHD (n=17)	Attention	0.98)				
	Corbett, 2009	ASD (n=18) and ADHD	Set Shifting	0.73 (0.06, 1.40)	18	7-12 years	Not reported	Good
		(n=18)	Fluency					
			Planning					
			Inhibition					
			Working Memory					
			Attention					
6	Crippa, 2015	ADHD (n=11), ADHD	Set Shifting	1.28 (0.63, 1.93)	71	7-12 years	75	Good
		+RD (n=13)	Planning					

## Supplementary Table 2. Characteristics of Final Included Studies with a Neurodevelopmental Group versus Controls

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
			Response					
			Inhibition					
			Attention					
7	G : : 0001		D	0.07 (0.25, 1.20)	40	0.14		
/	Crisci, 2021	ADHD ( $n=18$ ) and LD	Response	0.87 (0.35, 1.38)	48	8-14 years		Good
		(n=18)	innibition					
0	Cricci &	$\Delta SD (n-50)$ and $\Delta DUD$	Attention	0.01 (0.57, 1.27)	04	9 16 years	Not reported	Esia
0	Mammaralla	(n-64)	Attention	0.91 (0.37, 1.27)	94	o-10 years	Not reported	Fall
	(Unpub)	(11-04)						
9	Fernandez-	ADHD (n=35) Dyslexia	Set Shifting	1.08 (0.57, 1.58)	35	8-10 years	48 57	Good
,	Andres, 2019	(n=35), ADHD+Dyslexia	Planning	1.00 (0.57, 1.50)	55	o io years	10.57	0000
	1110100, 2019	(n=35)	Response					
		( )	Inhibition					
			Working Memory					
10	Fernandez-	Dyslexia (n=35),	Response	1.21 (0.69, 1.72)	35	8-10 years	51.43	Good
	Andres et al,	ADHD (n=35),	Inhibition					
	2021	ADHD+Dyslexia (n=35)	Set Shifting					
			Working Memory					
			Planning					
			Attention					
11	Geurts, 2004	ASD (n=41) and ADHD	Set Shifting	0.53 (0.11, 0.96)	41	6-13 years	Not reported	Good
		(n=54)	Fluency					
			Planning					
			Response					
			Inhibition					
			Working Memory					
			Attention					

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
12	Gioia (2002)	RD (n=34), ADHD-I	Response	1.50 (1.15, 1.85)	208	Not reported	72	Good
		(n=27), ADHD-C (n=26)	Inhibition					
		and ASD (n=54)	Planning					
			Set Shifting					
			Working Memory					
13	Glass, 2013	FASD (n=38) and	Fluency	0.81 (0.44, 1.07)	136	8-16 years	136	Good
		ADHD (n=80)	Planning					
			Set Shifting					
			Response					
			Inhibition					
			Working Memory					
14	Goldberg, 2005	ASD (n=17) and ADHD	Set Shifting	0.30 (-0.27,	32	8-12 years	75	Good
		(n=21)	Planning	0.86)				
			Response					
			Inhibition					
			Working Memory					
15	Gooch, 2011	Dyslexia (n=17),	Response	0.29 (-0.26,	35	5-14 years	61	Good
		ADHD+Dyslexia (n=24)	Inhibition	0.86)				
		and ADHD (n=17)	Attention					
16	Greimel, 2011	ADHD (n=23), TS	Set Shifting	0.26 (-0.37,	27	Up to 17 years	78.1	Good
		(n=21) and ADHD+TS	Response	0.74)				
		(n=25)	Inhibition					
			Attention					
17	Greimel, 2008	ADHD (n=20) and	Set Shifting	0.23 (-0.26,	20	8-15 years	50	Good
		ADHD+TS (n=20)	Attention	0.97)				
18	Hall, 1997	ADHD (n=14) and RD	Attention	0.59 (-0.06,	28	6-13 years	67	Good
		(n=17)		1.24)				
19	Happé, 2006	ASD (n=32) and ADHD	Set Shifting	0.44 (-0.06,	32	8-16 years	100	Good
		(n=30)	Fluency	0.93)				

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
			Response					
			Inhibition					
			Set Shifting					
			Planning					
			Response					
			Inhibition					
			Set switching					
			Working Memory					
			Attention					
20	Hovik, 2016	TS (n=19) and ADHD	Response	0.38 (-0.03,	50	8-17 years	60	Good
		(79)	Inhibition	0.87)				
			Attention					
21	Hovik, 2015	ADHD (n=33) and TS	Attention	0.42 (-0.06,	50	Not reported	66	Good
		(n=19)		0.91)				
22	Huang, 2016	ADHD (n=391) and	Set Shifting	0.29 (0.11, 0.46)	188	6-14 years	Not reported	Good
		ADHD+LD (n=380)	Response					
			Inhibition					
23	Hwang-Gu,	ASD (n=221),	Attention	0.46 (0.24, 0.68)	249	8-15 years	60	Good
	2019	ASD+ADHD (n=97) and						
		ADHD (n=8)						
24	Kado, 2020	ASD (n=69) and	Set Shifting	0.38 (0.02, 0.74)	69	5-15 years	72	Good
		ADHD+ASD (n=43)						
25	Kado, 2012	PDD (n=52) and ADHD	Set Shifting	0.41 (0.02, 0.81)	52	5-15 years	78	Good
		(n=46)						
26	Kibby, 2008	ADHD (n=30),	Working Memory	0.86 (0.32, 1.40)	30	6-15 years	Not reported	Good
		ADHD+RD (n=30) and						
		RD (n=23)						
27	Kooistra, 2011	ADHD (n=47) and	Attention	0.20 (-0.26,	38	7-10 years	51	Good
		FASD (n=28)		0.65)				

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
28	Kuhn, 2016	Dyscalculia (n=33) and	Set Shifting	0.51 (-0.01,	40	Not reported	40	Good
		ADHD (n=16)	Working Memory	1.04)				
			Attention					
29	Lievore &	ASD (n=60) and	Set Shifting	0.27 (-0.01,	150	8-16 years	Not reported	Fair
	Mammarella	Learning Disorders		0.56)				
	(Unpub)	(n=80)						
30	Lundervold,	ASD (n=9),	Attention	0.41 (-0.16,	134	8-10 years	66	Fair
	2016	ASD+ADHD (n=11) and		0.98)				
		ADHD (n=38)						
31	Maehler, 2016	Dyslexia (n=31),	Set Shifting	0.48 (-0.04,	31	Not reported	54	Good
		Dyslexia+ADHD (n=37),	Fluency	1.00)				
		Dyscalculia (n=18),	Planning					
		Dyscalculia+ADHD (n=	Response					
		21), ADHD (n=34)	Inhibition					
			Set switching					
			Working Memory					
			Attention					
32	Maghsoodloonej	ADHD (n=36) and LD	Response	1.05 (0.59, 1.52)	43	7-12 years	Not reported	Fair
	ad, 2017	(n=47)	Inhibition					
			Attention					
33	Mammarella,	ASD (n=17) and LD	Planning	0.59 (-0.10,	17	8-18 years	Not reported	Good
	2019	(n=17)	Working Memory	1.28)				
34	Martinussen,	ADHD (n=60), LD	Set Shifting	0.98 (0.44, 1.53)	34	Not reported	58	Good
	2006	(n=14) and ADHD+LD	Fluency					
		(n=28)	Planning					
			Response					
			Inhibition					
			Set switching					
			Working Memory					
			Attention					

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
35	Marzocchi, 2008	ADHD ( $n=35$ ) and RD	Set Shifting	0.50 (-	30	7-12 years	86	Good
		(n=22)	Fluency	0.02,1.03)				
			Response					
			Inhibition					
			Working Memory					
			6 9					
36	Matsuura, 2014	ASD (n=11) and ADHD	Working Memory	0.40 (-0.30,	19	Not reported	80	Good
		(n=15)	Attention	1.10)				
37	Maziero, 2020	Dyslexia (n=47),	Working Memory	0.98 (0.48, 1.50)	42	7-12 years	Not reported	Good
		Coordination Disorder,						
		DCD (n=22) and						
		Dyslexia+DCD (n=27)						
38	Mohl 2015	ADHD(n-14)	Attention	0.76 (-0.06	14	Not reported	100	Good
50	Wolli, 2015	ADHD $(n=14)$ , ADHD+RD $(n=10)$	Attention	1.57)	14	Not reported	100	Good
39	Moura, 2017	ADHD (n=32), Dyslexia	Fluency	0.76 (0.23, 1.29)	34	8-10 years	69	Good
		(n=32), Dyslexia+ADHD	Planning			-		
		(n=18)	Set switching					
			Working Memory					
40	Narhi 1995	RD (n=21), ADHD+RD	Set switching	0.35 (-0.39,	10	8-12 years	Not reported	Good
		(n=25) and ADHD		1.09)				
4.1	Nudan 1000	(n=17)	Sat Shifting	0.86 ( 0.04	10	6 19 10000	100	Cood
41	Nyden, 1999	Asperger's $(n=10)$ , ADHD $(n=10)$ BD/WD	Bernonso	0.80 (-0.04,	10	0-18 years	100	Good
		(n=10) (n=10), KD/WD	Inhibition	1.75)				
		(	Working Memory					
			6					

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
42	Openneer, 2020	TS (n=34), TS+ADHD	Set Shifting	0.23 (-0.18,	60	8-12 years	Not reported	Good
		(n=26) and ADHD	Response	0.65)				
		(n=54)	Inhibition					
			Working Memory					
43	Operto 2021	ASD-HF ( $n = 19$ ) ADHD	Working Memory	0.96 (0.31, 1.61)	20	years	72	Good
		(n = 21), SLD (n = 22)						
44	Ozonoff, 1994	TS (n=14) and ASD	Set switching	0.23 (-0.50,	14	8-16 years	83	Good
		(n=14)		0.95)				
45	Ozonoff, 1999	ASD (n=40), TS (n=30)	Set Shifting	0.40 (-0.11,	29	8-17 years	Not reported	Good
		and ADHD (n=24)	Planning	0.91)				
46	Passolunghi,	ADHD (n=10) and LD	Working Memory	0.92 (0.03, 1.80)	10	9-11 years	Not reported	Good
	2005	(n=10)						
47	Pennington,	ADHD (n=16) and RD	Set Shifting	0.39 (-0.25,	23	7-10 years	100	Good
	1993	(n=15)	Planning	1.04)				
			Attention					
48	Pereira, 2020	ADHD (n=11), RD	Fluency	0.61 (0.02, 1.21)	33	8-11 years	48	Good
		(n=45) and ADHD/RD	Planning					
		(n=15)	Response					
			Inhibition					
			Set switching					
			Working Memory					
49	Pitzianti, 2016	ASD (n=13),	Planning	1.51 (0.62, 2.40)	13	8-15 years	92	Good
		ASD+ADHD (n=12) and	Response					
		ADHD (n=13)	Inhibition					
			Working Memory					
50	Poon, 2014	ADHD (n=27), RD	Planning	0.67 (0.11, 1.23)	25	12-18yr	100	Good
		(n=22) and ADHD+RD	Response					
		(n=34)	Inhibition					

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
			Working Memory					
51	Pride, 2012	ADHD+NF1 (n=60) and	Set Shifting	0.57 (0.22, 0.93)	52	6-16 years	54	Good
		NF1 (n=132)	Fluency					
			Planning					
			Attention					
52	Purvis, 2000	ADHD (n=17),	Response	1.50 (-0.03,	17	7-11 years	72	Good
		ADHD+RD (n=17) and	Inhibition	1.33)				
		RD (n=17)	Attention					
53	Roessner, 2007	TS (n=22), TD+ADHD	Set Shifting	0.35 (-0.27,	22	Not reported	100	Good
		(n=14) and ADHD	Attention	0.97)				
		(n=19)						
54	Rhodes, 2011	ADHD (n=24) and WS	Working Memory	1.64 (0.83, 2.45)	19	7-14 years	87.8	Fair
		(n=20)	Planning					
55	Saito, 2019	ASD+ADHD (n=10) and	Attention	0.95 (0.05, 1.86)	9	Not reported	71	Good
		ADHD (n=11)						
56	Samyn, 2015	ADHD (n=30) and ASD	Set Shifting	0.20 (-0.19,	148	10-15 years	Not reported	Good
		(n=31)	Response	0.59)				
			Inhibition					
			Attention					
				0.04/0.05	21	10.15		<u> </u>
57	Samyn, 2014	ADHD ( $n=24$ ) and ASD	Response	0.34 (-0.25,	21	10-15 years	Not reported	Good
		(n=20)	Inhibition	0.94)				
58	Schuchardt	Dyscalculia (n-17)	Working Memory	0.74 (0.17, 1.32)	30	7-10 years	51	Good
50	2008	Dyscalculia+Dyslexia	working weiliory	0.71 (0.17, 1.32)	50	7 To years	51	0000
	2000	(n=20)						
		and Dyslexia $(n=30)$						
59	Schuerholz,	ADHD+TS (n=19) and	Fluency	0.50 (-0.09.	27	6-14 years	86	Good
	1996	TS (n=21)	Planning	1.08)		2		

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control Sample	Age Range	Gender	JBI Quality
	1041		Anaryseu	()5 /0 (1)	size		(% of	Assessment
							Males)	
			Attention					
60	Schuerholz,	ADHD (n=39),	Fluency	0.76 (0.23, 1.29)	36	6-16 years	44	Good
	1998	TS+ADHD (n=23) and TS (n=18)	Attention					
61	Seidman, 2001	ADHD (n=79), Dyslexia	Set Shifting	0.51 (0.08, 0.94)	127	6-17 years	100	Good
		(n=16), Dyscalculia	Planning					
		(n=32), Dyslexia+	Response					
		Dyscalculia (n=21)	Inhibition					
			Working Memory					
			Attention					
62	Semrud-	ADHD (n=39) and LD	Planning	0.28 (-0.23,	39	9-15 years	Not reported	Good
	Clikeman, 2008	(n=16)	Attention	0.80)				
63	Semrud-	ASD (n=50), ADHD	Planning	0.84 (0.30, 1.37)	113	9-16 years	70	Good
	Clikeman, 2010	(n=156) and NVLD						
		(n=26)						
64	Semrud-	ASD (n=15) and ADHD	Set Shifting	0.89 (0.32, 1.45)	32	9-16.5 years	60	Good
	Clikeman et al	(n=49)	Planning					
	2010a		Response					
			Inhibition					
			Set switching					
			working Memory					
65	Semrud-	ASD (n=37), NVLD	Set Shifting	0.71 (0.24, 1.18)	40	8-17.5 years	74	Good
	Clikeman, 2014	(n=31)	Fluency					
			Planning					
			Set switching					
			Working Memory					

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of Males)	
66	Shalev, 2019	Williams syndrome	Attention	0.59 (0.11, 1.07)	99	3-7 years	Not reported	Good
		(n=25) and Downs						
		Syndrome (n=18)						
67	Shanahan, 2006	ADHD (n=105),	Set switching	0.69 (0.40, 0.98)	144	Not reported	51	Good
		ADHD+RD (n=51) and						
		RD (n=95)						
68	Shin, 2001	ADHD (n=21) and TS	Set switching	1.08 (0.41, 1.75)	22	6-18 years	Not reported	Good
		(n=16)	Attention					~ .
69	Shin, 2003	ADHD (n=15), LD	Planning	0.21 (-0.45,	20	6-13 years	Not reported	Good
		(n=13), ADHD+LD		0.88)				
70	<u>a:</u> : 2000	(n=15) and TS $(n=15)$	<b>D</b>		20	6.10	07	
70	Sinzig, 2008	ASD (n=20),	Response	0.32 (-0.22,	30	6-18 years	85	Good
		ASD+ADHD $(n=21)$ and ADUD $(n=20)$	Innibition	0.87)				
		ADHD (n=50)	Attention					
71	Sinzig, 2008a	ASD (n=20),	Set Shifting	0.35 (-0.27,	20	6-18 years	85	Good
	_	ASD+ADHD (n=20) and	Planning	0.97)				
		ADHD (n=20)	Response					
			Inhibition					
			Working Memory					
72	Sinzig 2014	ASD (n=26), and ADHD	Response	0.44 (-0.08,	29	4-9 years	70	Good
		(n=30)	Inhibition	0.96)				
			Attention					
			Set Shifting					
73	Stubenrauch,	ADHD (n=21),	Response	0.51 (-0.09,	24	8-12 years	55	Good
	2014	ADHD+RD (n=17) and	Inhibition	1.11)				
		RD (n=22)						
74	Sukhodolsky,	ADHD (n=64), TS	Attention	0.40 (0.05, 0.76)	71	Not reported	74.25	Good
	2010	(n=56) and ADHD+TS $(n=45)$	Response					
		(11-+3)	Inhibition					
		1			1	1	1	

Study No.	Study Name & Year	Diagnostic Group	EF Domains Analysed	Hedges' g, (95% CI)	Control Sample	Age Range	Gender Distribution	JBI Quality Assessment
					size		(% of Males)	
75	Termine, 2016	ADHD (n=39), TS (n=13) and TS+ADHD (n=8)	Planning	0.93 (0.33, 1.54)	66	6-15 years	Not reported	Good
76	Tiffin-Richards, 2008	ADHD (n=20), ADHD+Dyslexia (n=20) and Dyslexia (n=20)	Set Shifting Working Memory	0.90 (0.25, 1.55)	19	10-14 years	79	Good
77	Tsuchiya, 2005	ADHD (n=22) and ASD (n=17)	Set Shifting	1.03 (0.41, 1.66)	25	Not reported	76	Good
78	Turker, 2019	ADHD (n=43), ADHD+RD (n=15) and RD (n=27)	Working Memory	0.68 (0.22, 1.15)	89	8-18 years	62	Good
79	Tye, 2014	ADHD (n=18), ASD+ADHD (n=29) and ASD (n=19)	Response Inhibition	0.53 (-0.13, 1.03)	26	13-18 years	100	Good
80	Unterrainer, 2016	ASD (n=18), ADHD (n=42) and ASD+ADHD (n=19-23)	Planning	0.21 (-0.30, 0.73)	42	6-14 years	Not reported	Good
81	Van De Voorde, 2010	ADHD (n=19), RD (n=17), ADHD+RD (n=21)	Response Inhibition Working Memory	1.02 (0.30, 1.75)	19	8-12 years	69.7	Good
82	Van De Voorde, 2011	ADHD (n=19), RD (n=17), ADHD+RD (n=21)	Response Inhibition	0.70 (0.05, 1.35)	19	8-12 years	69.7	Good
83	Wang, 2018	ADHD (n=30), RD (n=33), ADHD+RD (n=28)	Response Inhibition Working Memory	1.01 (0.47, 1.55)	30	Not reported	58	Good

Study No.	Study Name &	Diagnostic Group	EF Domains	Hedges' g,	Control	Age Range	Gender	JBI Quality
	Year		Analysed	(95% CI)	Sample		Distribution	Assessment
					size		(% of	
							Males)	
84	Ware, 2012	FASD (n=142) and	Set Shifting	0.85 (0.58, 1.12)	133	8-18 years	58	Good
		ADHD (n=82)	Fluency					
			Response					
			Inhibition					
85	Willcutt, 2005	ADHD (n=113),	Set Shifting	0.66 (0.39, 0.93)	151	8-18 years	53	Good
		ADHD+RD (n=64) and	Response					
		RD (n=109)	Inhibition					
			Set switching					
			Working Memory					
86	Xiao, 2012	ADHD (n=16) and ASD	Response	1.30 (0.45, 2.15)	16	8-14 years	100	Good
		(n=19)	Inhibition					
87	Yang, 2009	ADHD (n=26) and ASD	Set Shifting	0.36 (-0.19,	30	3-15 years	88	Good
		(n=20)	Response	0.90)				
			Inhibition					
			Working Memory					
88	Zarchi, 2014	Velocardiofacial	Set Shifting	0.53 (-0.02,	22	Not reported	50	Good
		(22q11.2 deletion)	Response	1.07)				
		(n=39) and Williams	Inhibition					
		(7q11.23 deletion)	Working Memory					
		syndromes (n=24)						

Study Authors	Title	Exclusion reason
Hovik KT,	Distinct Patterns of Everyday Executive Function Problems Distinguish	Data screening deemed it to be an outlier, removed to ensure statistical
Egeland J,	Children with Tourette Syndrome From Children With ADHD or Autism	integrity
Isquith PK, et al	Spectrum Disorders.	
2014		
de Jong CGW,	How Distinctive Are ADHD And RD? Results Of a Double Dissociation	Data screening deemed it to be an outlier, removed to ensure statistical
Van De Voorde	Study.	integrity
S, Roeyers H,		
Raymaekers R,		
Oosterlaan J,		
Sergeant JA.		
2009		
Kibby MY,	Is Executive Dysfunction a Potential Contributor To The Comorbidity	Data screening deemed it to be an outlier, removed to ensure statistical
Newsham G,	Between Basic Reading Disability And Attention-Deficit/Hyperactivity	integrity
Imre Z, Schlak	Disorder?	
JE. 2021		
Holingue C,	Links between Parent-Reported Measures of Poor Sleep and Executive	Data screening deemed it to be an outlier, removed to ensure statistical
Volk H, Crocetti	Function in Childhood Autism and Attention Deficit Hyperactivity Disorder	integrity
D, Gottlieb B,		
Spira AP,		
Mostofsky SH.		
2021		

## Supplementary Table 3. List of Excluded Studies at the Stage of Statistical Analysis and Reasons for Exclusion

EF domain	Background Information on EF Domains	Examples of Key Measures Used to Assess
		this Domain
Global EF abilities	• Overall Executive function encompasses a range of processing including but not limited to working memory, response inhibition and flexibility.	<ul> <li>Behavior Rating Inventory of Executive Function (BRIEF; ages 5 to 18 years)<sup>1</sup></li> <li>Behavior Rating Inventory of Executive Function– Preschool Version (BRIEF-P; ages 2 to 5 years)<sup>2</sup></li> <li>Childhood Executive Functioning Inventory (CHEXI;<sup>3</sup> Global measure of EF in children)</li> </ul>
<b>Concept formation/Set</b> <b>shifting</b> <i>The capacity to shift between</i> <i>mental processes to form new</i> <i>concepts and identify the</i> <i>conceptual relationships shared</i> <i>by stimuli</i> <sup>4</sup>	<ul> <li>Emerges in early childhood and matures in adolescence, <sup>5</sup></li> <li>Functional peak observed in mid adolescence (17 years) followed by decline (18-19 years)<sup>6</sup></li> <li>Adult levels of set shifting observed in 8-10 year olds<sup>7</sup> but also in adolescence<sup>8</sup></li> </ul>	<ul> <li>WCST (Wisconsin Card Sorting Test)<sup>9</sup></li> <li>The Children's Cooking Task (CCT)<sup>10</sup></li> <li>Task Switch<sup>11</sup></li> <li>Vienna Test System Trail Making Test-B (VTS TMT-B)</li> <li>Delis-Kaplan Executive Function System (D-KEFS) Number-Letter Switching<sup>12</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Design Fluency Switching<sup>12</sup></li> <li>d2 Selective Attention Test – % errors<sup>13</sup></li> <li>d2 Selective Attention Test – Total Correct<sup>13</sup></li> </ul>
Mental flexibility/Set switching The capacity to switch between mental processes (multiple tasks, operations, or mental sets) in response to changing demands <sup>14,15</sup>	• Emerges in early childhood and matures in adolescence <sup>5,16</sup>	<ul> <li>Trail Making Task B/Trails-P<sup>17</sup></li> <li>Wechsler Intelligence Scale for Children, Fourth Edition (WISC-IV) - Letter-Number Sequencing<sup>18</sup></li> <li>Shift from Digit Span Forward to Digit Span Backward (WISC-IV)<sup>18</sup></li> <li>Word Order Subtest (K-ABC)<sup>19</sup></li> <li>Children's Category Test (CCT)<sup>20</sup></li> </ul>

#### Supplementary Table 4: Key Executive Function Domains and Related Measures

Fluency The capacity to generate novel ideas (ideational fluency) and responses (phonemic and semantic fluency <sup>21</sup> . May be assessed by verbal and non- verbal tasks.	<ul> <li>Emerges in early childhood and matures in early adolescence,<sup>5,16</sup></li> <li>Greatest period of development in early to mid- childhood (5-8) with continued improvement into early adulthood<sup>22</sup></li> </ul>	<ul> <li>Category fluency</li> <li>Letter fluency</li> <li>Verbal fluency test</li> <li>Animals category/Animal Naming Test</li> <li>Controlled Oral Word Association Test (COWA) Phonemic Cue<sup>23</sup></li> <li>Controlled Oral Word Association Test (COWA) Semantic Cue<sup>23</sup></li> <li>Controlled Oral Word Association Test (COWA) FAS<sup>23</sup></li> <li>California Verbal Learning Test-II (CVLT-II) Semantic Clustering<sup>24</sup></li> <li>California Verbal Learning Test-II (CVLT-II) Long Delay Recall<sup>24</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Verbal Category Fluency<sup>12</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Category Switching Fluency<sup>12</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS)</li> </ul>
<b>Planning</b> The capacity to execute a sequence of actions so that a desired goal is achieve <sup>25</sup> .	<ul> <li>Emerges and significantly develops in early childhood, some research suggests brief regression of skills in adolescence, matures in early adulthood<sup>5,16</sup></li> <li>Significant improvement in late adolescence (15-19) with optimal performance in early adulthood (20-29)<sup>7</sup></li> <li>Greatest period of development in early to mid-childhood (5-8) with continued improvement into early adulthood<sup>22</sup></li> </ul>	<ul> <li>Rey-Osterieth Complex Figure<sup>26</sup></li> <li>ToL (Tower of London)<sup>27</sup></li> <li>ToH (Tower of Hanoi)<sup>28</sup></li> <li>Clock Drawing Test<sup>29</sup></li> <li>Block Design Subtest (WPPSI-IV, WISC-IV)<sup>18,30</sup></li> <li>Symbol Search and Symbol Coding (WISC-IV, WPPSI-IV)<sup>18,30</sup></li> </ul>

<b>Response Inhibition</b> The capacity to inhibit a previously learned response <sup>14</sup> .	<ul> <li>Emerges in early childhood, matures in late childhood to early adolescence<sup>16</sup></li> <li>Greatest period of development in early to mid-childhood (5-8) with continued improvement into early adolescence<sup>22</sup></li> <li>Adult levels of response inhibition achieved in late childhood (age 11)<sup>8</sup></li> </ul>	<ul> <li>Stroop Color Word Interference Test_C-W<sup>31</sup></li> <li>Stroop Color Word Interference <sup>31</sup></li> <li>NEPSY-II_Inhibition B<sup>32</sup></li> <li>NEPSY-II_Inhibition C<sup>32</sup></li> <li>5 Digit Test<sup>33</sup></li> <li><i>Go/NoGo Test<sup>34</sup></i></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference – Condition 3 (CWIT 3)<sup>12</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference – Condition 4 (CWIT 4)<sup>12</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Color-Word Interference<sup>12</sup></li> <li>d2 – Accuracy<sup>35</sup></li> <li>d2 – Deviation<sup>35</sup></li> <li>d2 – Percentage of mistakes<sup>35</sup></li> <li>Interference trials</li> </ul>
<b>Working Memory (WM)</b> The capacity to store and manipulate information in temporary short term storage for complex cognitive manipulations <sup>25</sup> .	<ul> <li>Emerges in early childhood and matures in early adolescence.<sup>16,36</sup></li> <li>Peak improvement in late adolescence (15-19) maintained in early adulthood.<sup>7</sup></li> </ul>	<ul> <li>NEPSY-II_Word List Interfernce<sup>32</sup></li> <li>Digit Span (Backward, Sequencing), Arithmetic, Letter-Number Sequencing (WISC-IV, WPPSI- IV)<sup>18,30</sup></li> <li>Working memory scale (K-ABC)<sup>19</sup></li> <li>Delis-Kaplan Executive Function System (D-KEFS) Number Sequencing<sup>12</sup></li> <li>Connors Continuous Performance Test Version 3 (CPT-3) – Commissions subscale<sup>37</sup></li> <li>Degraded Continuous Performance Test (Degraded CPT) – Commissions<sup>37</sup></li> <li>Degraded Continuous Performance Test (Degraded CPT) – Omissions<sup>37</sup></li> <li>Visual-Spatial Working Memory (Visual-Spatial WM)<sup>18,30,38</sup></li> <li>Wechsler Memory Scale-Revised (WMS-R, WMS- IV) Digit Span Backwards<sup>38</sup></li> <li>Wechsler Memory Scale-Revised (WMS-R, WMS- IV) Spatial Span Backwards<sup>38</sup></li> <li>Auditory-Verbal Working Memory (Auditory- Verbal WM)<sup>38</sup></li> </ul>

		<ul> <li>Digit Span Backwards Score<sup>18</sup></li> <li>Letter Number Sequencing Test<sup>18</sup></li> <li>Brief Visuospatial Memory Test-Revised (BVMT- R) Total Recall<sup>39</sup></li> <li>Reading Span – Partial-Credit Unit (PCU) Score<sup>40</sup></li> <li>Reading Span – Sentence Errors<sup>40</sup></li> </ul>
Attention The subjective experience of attending to environmental stimuli by people thought to have introspection and can demonstrate alertness. <sup>41</sup>	<ul> <li>Emerges in newborns and is a mechanism that continues to develop into childhood.<sup>42</sup></li> <li>Attention can be divided into two main forms: sustained and divided attention.</li> <li>Sustained attention refers to attentional focus performed over a sustained time-period.<sup>41</sup></li> <li>Focused attention is where certain environmental stimuli is given a priority over others and the attentional processes serve task demands that engage certain cognitive resources.<sup>41</sup></li> </ul>	<ul> <li>TOVA<sup>43</sup></li> <li>TEA-Ch<sup>44</sup></li> <li>Test of Attentional Performance for Children (KiTAP)<sup>45</sup></li> <li>Letter-Number Sequencing (WISC-IV)<sup>18,30</sup></li> <li>Verbal span tasks (WISC-IV)<sup>18,30</sup></li> <li>Word order subtest (K-ABC)<sup>19</sup></li> <li>Test of Attentional Performance (TAP)<sup>46</sup></li> <li>d2 test of attention<sup>35</sup></li> </ul>

Note: Seven key EF domains in table reproduced with permission from Dr Eleni Demetriou<sup>47</sup>

Supplementary Figure 1. Small Study Effect Outputs. Figure Exploring Any Outliers During Preliminary Analysis





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Supplementary Figure 3. Outputs for Subdomain Cross-Condition analyses. Figures Produced in RStudio.

## Appendix B. Chapter 3: Supplementary Tables

Combined	IBRIEF	ASD <sup>a</sup>	ASD and ADHD <sup>®</sup>	ADHD and SLD <sup>c</sup>	ASD, SLD and ADHD <sup>a</sup>
T-sco	ores	$M_{diff}(SE)$	$M_{diff}(SE)$	$M_{diff}(SE)$	$M_{diff}(SE)$
	ASD	-	ns	ns	ns
Inhibit (Inhibitory	ASD and ADHD	ns	-	7.51(2.36) ** b>c	-
Control)	ADHD and SLD	ns	7.51(2.36) ** <sup>b&gt;c</sup>	-	7.45(2.62) * <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	7.45(2.62) * <sup>d&gt;c</sup>	-
	ASD	-	ns	10.12(2.38) *** a>c	-
Shift (Flevihility)	ASD and ADHD	ns	-	9.95(2.46) *** b>c	ns
Shift (Flexibility)	ADHD and SLD	10.12(2.38) *** a>c	9.95(2.46) *** b>c	-	12.32(2.72) *** <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	12.32(2.72) *** <sup>d&gt;c</sup>	-
	ASD	-	ns	9.46(2.40) *** a>c	ns
<b>Emotional Control</b>	ASD and ADHD	ns	-	8.81(2.46) *** b>c	ns
(self- regulation)	ADHD and SLD	9.46(2.40) *** a>c	8.81(2.46) *** b>c	-	11.85(2.48) ** <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	11.85(2.48) ** <sup>d&gt;c</sup>	-
	ASD	-	ns	ns	ns
Initiato	ASD and ADHD	ns	-	ns	ns
minate	ADHD and SLD	ns	ns	-	6.07(2.10) * <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	6.07(2.10) * <sup>d&gt;c</sup>	-
	ASD	-	6.55(2.24) ** b>c	ns	ns
Working Momory	ASD and ADHD	6.55(2.24) ** <sup>b&gt;c</sup>	-	7.41(1.97) ** <sup>b&gt;c</sup>	-
working wemory	ADHD and SLD	ns	7.41(1.97) ** <sup>b&gt;c</sup>	-	7.02(2.19) ** <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	7.02(2.19) ** d>c	-
	ASD	-	ns	ns	ns
Plan/Organica	ASD and ADHD	ns	-	ns	ns
I lan/OI gamse	ADHD and SLD	ns	ns	-	5.72(2.12) * <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	5.72(2.12) * <sup>d&gt;c</sup>	-
	ASD	_	ns	ns	ns
Organisation of	ASD and ADHD	ns	-	ns	ns
Materials	ADHD and SLD	ns	ns	-	ns
	ASD, SLD and ADHD	ns	ns	ns	-
<b>Behaviour Regulation</b>	ASD	-	ns	6.07(2.22) * <sup>a&gt;c</sup>	ns
Index (BRI)	ASD and ADHD	ns	-	7.63(2.29) ** b>c	ns

Supplementary Table 1 for Chapter 3: Mean difference and Standard Error for Significant Post Hoc results across NDCs

	ADHD and SLD	6.07(2.22) * <sup>a&gt;c</sup>	7.63(2.29) ** <sup>b&gt;c</sup>	-	7.70(2.53) * <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	7.70(2.53) * <sup>d&gt;c</sup>	-
GEC (Total Composite)	ASD	-	ns	ns	ns
	ASD and ADHD	ns	-	8.27(2.09) *** b>c	ns
	ADHD and SLD	ns	8.27(2.09) *** b>c	-	9.70(2.24) *** <sup>d&gt;c</sup>
	ASD, SLD and ADHD	ns	ns	9.70(2.24) *** d>c	_

Note: \*Denotes significance at p<0.05, \*\*Denotes significance at p<0.01, \*\*\*Denotes significance at p<0.001

#### **Appendix C. Chapter 4: Supplementary Tables**

#### Supplementary Figure 1. Parent/Carer Questionnaire utilised within CDU Service.

**Parentcarer Questionnaire** 

## Please complete the survey below. Thank you! Please complete this questionnaire to the best of your ability. This will provide us with important information regarding your child's development and family history. If you would like to finish completing this questionnaire at another time, please click the 'Save & Return Later' button at the bottom of this page. You will be able to access the questionnaire again using the same link in the email you were sent previously. Please enter the date: What is the child's date of birth? Childs Age What is the child's country of birth? O Male Female O Other What is the child's gender? If other, please explain: Please answer the following demographic questions regarding the biological mother of the child: Date of birth: Country of birth: Current occupation: Highest level of education: O Primary/Elementary School O High School O Certificate, Diploma or Vocational Training O Bachelors Degree O Postgraduate Degree (Masters, PhD, Graduate Diploma)

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# Please answer the following demographic questions regarding the biological father of the child:

Date of birth:

Country of birth:	
Current occupation:	
Highest level of education:	<ul> <li>Primary/Elementary School</li> <li>High School</li> <li>Certificate, Diploma or Vocational Training</li> <li>Bachelors Degree</li> <li>Postgraduate Degree (Masters, PhD, Graduate Diploma)</li> </ul>
Who is the full time carer of the child?	<ul> <li>Biological mother and biological father are both full time carers (together)</li> <li>Biological mother and biological father are co-parents (separated)</li> <li>Biological mother alone</li> <li>Biological mother with another partner</li> <li>Biological father alone</li> <li>Biological father with another partner</li> <li>Other</li> </ul>
If other, please answer the following questions r	egarding the full time carer:
Relationship to child:	
Date of birth:	
Country of birth:	
Current occupation:	
Highest level of education:	<ul> <li>Primary/Elementary School</li> <li>High School</li> <li>Certificate, Diploma or Vocational Training</li> <li>Bachelors Degree</li> <li>Postgraduate Degree (Masters, PhD, Graduate Diploma)</li> </ul>

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Page 3

Please answer the following questions regarding your family:			
Which languages do you speak at home?			
Which language does your child use the most?			
Would you like an interpreter present at the assessment?	O Yes O No		
Which language interpreter would you like?			
ls your child of Aboriginal or Torres Strait Islander origin?	O Yes O No		
How many siblings does the child have (including half-siblings)?	O 0 O 1 O 2 O 3 O 4 O 5		
Sibling 1 age:		,	
Sibling 1 gender:	O Male O Female		
Any other information regarding the relationship between the child and sibling 1 (half siblings, closeness, conflict)			
Sibling 4 gender:	O Male O Female		
Sibling 2 age:			
Any other information regarding the relationship between the child and sibling 4 (half siblings, closeness, conflict)			
Sibling 5 age:			5
Sibling 2 gender:	O Male O Female		
Any other information regarding the relationship between the child and sibling 2 (half siblings, closeness, conflict)			
Sibling 5 gender:	O Male O Female		
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#### Sibling 3 age:

	<u> 1997 - Andrew Marken and Andrew Andrew</u> a
Any other information regarding the relationship between the child and sibling 5 (half siblings, closeness, conflict)	
Sibling 3 gender:	O Male O Female
Are there any other people important to your child's care (cousin, grandparents)?	O Yes O No
Any other information regarding the relationship between the child and sibling 3 (half siblings, closeness, conflict)	
Please provide information regarding these people and their relationship to your child:	
Sibling 4 age:	·
Please list the concerns you have about your child:	
What was your child's age when you became concerned?	
Who raised these concerns and why?	·
What do you think are your child's strongest points (what does he or she do best)?	
Is your child's development different in any way to other children's development?	O Yes O No
If yes, please explain the differences:	·
Have any of your child's abilities deteriorated or gone backwards (not only slowed)?	O Yes O No
If yes, please describe:	
What questions do you want answered at this assessment?	

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Please answer the following questions regarding the child's past history:		
Conception and Pregnancy (please tick all that apply):	Planned Unplanned Natural Conception IVF/Donor Other	
If other, please provide details:		
Labour Details (please tick all that apply):	<ul> <li>Vaginal (Normal)</li> <li>Planned Caesarean</li> <li>Emergency Caesarean</li> <li>Breech (feet first)</li> <li>Fast Labour</li> <li>Forceps/Vacuum</li> <li>Other</li> </ul>	
If other, please provide details:		
Birth details:	O On time Early Late	
If early or late, by how many weeks?		
Where was your child born (which hospital)?		
Birth weight (kg):		
Birth length/height (cm):		
Birth head circumference (cm):		
Apgar score:		
Baby at birth (please tick all that apply):	<ul> <li>Cried/breathed immediately</li> <li>Needed help to breathe</li> <li>Needed oxygen</li> <li>Went to special care nursery</li> <li>Neonatal intensive care</li> </ul>	
Did you experience any difficulties during this time (e.g. illness, maternal depression)?	O Yes O No	
If yes, please describe:		

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Was your baby tube fed?	O Yes O No
If yes, please provide details regarding the reason for tube feeding and age at which it was stopped:	
To what age was your baby breast fed (in months)?	
To what age was your baby bottle fed (in months)?	
What age did your baby start solids (in months):	
Did your child have any problems with feeding or eating?	O Yes O No
If yes, please describe:	
Is your child's general health good?	O Yes O No
If no, please describe significant illnesses, operations, accidents (e.g., fits or funny turns, fractured skull, breathing problems, growth problems):	
How many (if any) medications is your child currently taking?	O 0 O 1 O 2 O 3 O 4 O 5
Medication 1 name:	
Medication 1 reason for taking (indication):	
Medication 1 dose (how much is taken, how many times a day):	
Medication 2 name:	
Medication 2 reason for taking (indication):	
Medication 2 dose (how much is taken, how many times a day):	

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Medication 3 name:	
Medication 3 reason for taking (indication):	
Medication 3 dose (how much is taken, how many times a day):	
Medication 4 name:	
Medication 4 reason for taking (indication):	
Medication 4 dose (how much is taken, how many times a day):	
Medication 5 name:	
Medication 5 reason for taking (indication):	
Medication 5 dose (how much is taken, how many times a day):	
Did your child have a newborn hearing test?	O Yes O No
If yes, what were the results?	O Pass O Referred for further testing
Has your child ever had any other hearing tests?	O Yes O No
If yes, please state where, when and the result:	
Has your child's vision ever been tested?	O Yes O No
If yes, please state where, when and the result:	
Does your child wear glasses?	O Yes O No
Does your child wear contact lenses?	O Yes O No

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#### If yes, who prescribed them?

How many specialists or therapists have been involved in your child's care in the past or now?	O 0 O 1 O 2 O 3 O 4 O 5
Specialist 1 name:	
Specialist 1 speciality:	
Specialist 1 telephone:	
Specialist 1 address:	
Is Specialist 1 still involved in your child's care?	O Yes O No
Specialist 2 name:	
Specialist 2 speciality:	
Specialist 2 telephone:	
Specialist 2 address:	
Is Specialist 2 still involved in your child's care?	O Yes O No
Specialist 3 name:	
Specialist 3 speciality:	
Specialist 3 telephone:	
Specialist 3 address:	
Is Specialist 3 still involved in your child's care?	O Yes O No

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Specialist 4 name:		
Specialist 4 speciality:		
Createlist 4 telephone:		
Specialist 4 telephone:		
Specialist 4 address:		
Is Specialist 4 still involved in your child's care?	O Yes O No	
Specialist 5 name:		
Specialist 5 speciality:		
Specialist 5 telephone:		
Specialist 5 address:		
	······	
Is Specialist 5 still involved in your child's care?	O Yes	
· · · · · · · · · · · · · · · · · · ·	Ŏ No	
Are any of these doctors aware of your referral to us?	O Yes	2
	0.10	
If yes, who?		
How many times has your child been admitted to	00	
hospital? (If more than three, please provide details regarding the most significant and recent admissions)	$O_2^1$	
n - Janam Janas Anderse - Jana seminer kennes seminer seminer seminer	Ŏ3	
Year of admission:		9
Hospital.		
hospitali		
Condition treated (include any important information):		
Year of admission:		
	·	
Hospital:		

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Year of admission: Hospital: Condition treated (include any important information): Family History: We are interested to know whether anyone in the family had problems with their health, development, learning (especially anything similar to the concerns about your child). This includes you, your children and extended family, cousins, uncles, aunts, grandparents etc. Please list the person's relationship to your child regarding any of the problems you tick. (e.g. Trouble with reading - 1 maternal aunt and 2 brothers). ☐ Reading
 ☐ Spelling
 ☐ Writing Has anyone in your family had trouble with: Maths Talking and Understanding Behaviour Reading - relationship to child: Spelling - relationship to child: Writing - relationship to child: Maths - relationship to child: Talking and Understanding - relationship to child:

Behaviour - relationship to child:

Condition treated (include any important information):

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Does anyone in your family have a history of:	<ul> <li>Hearing loss</li> <li>Eyesight difficulties</li> <li>Disability</li> <li>Autism</li> <li>Epilepsy</li> <li>Social problems</li> <li>ADHD</li> <li>Cerebral Palsy</li> <li>Inherited disorders</li> <li>Repetitive behaviours</li> <li>Other (e.g. emotional problems, mental health concerns)</li> </ul>
Hearing loss - relationship to child:	
Eyesight difficulties - relationship to child:	
Disability - relationship to child:	
Autism - relationship to child:	
Epilepsy - relationship to child:	
Social problems - relationship to child:	
ADHD - relationship to child:	
Cerebral Palsy - relationship to child:	
Inherited disorders - relationship to child:	
Repetitive behaviours - relationship to child:	
Other - relationship to child:	
Family history notes:	

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Milestones	
At what age did your child?	
Sit:	
Crawl:	
Walk:	
Jump:	
Pedal a tricycle:	
Develop a hand preference:	
What is your child's hand preference?	O right O left O none
Hold a pencil to scribble:	
Toilet trained by day:	
Toilet trained by night:	
Language Development At what age did your child?	
Babble (e.g. ma-ma-ma or da-da-da):	
Say first word other than mum or dad:	
Combine two words together (e.g. Mum up):	
Understand single words:	
Follow one-step verbal instructions:	
Understand more complex sentences:	

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How many words can your child now use in a sentence?	
Did your child previously, or does your child?	
Point to show:	O Yes O No
Wave (bye-bye or hello):	O Yes O No
Point to objects of interest:	O Yes O No
If your child doesn't talk, how does how do they let you know what they want?	
Any additional comments on your child's language?	
Play and Behaviour	
What does your child play with?	
Describe how your child plays with toys/games:	
Does your child play alongside another?	
Does your child take turns in a game?	
Behaviour and Temperament - please tick any which you feel describes your child:	<ul> <li>Sleep problems</li> <li>Mixes poorly</li> <li>Withdrawn</li> <li>Distractible</li> <li>Shy</li> <li>Aggressive</li> <li>Sad</li> <li>Calm</li> <li>In a world of their own</li> <li>Temper tantrums</li> <li>Unusually active/restless</li> <li>Sensitive to the feelings of others</li> <li>Dreamy</li> <li>Poor attention</li> <li>Obsessive</li> <li>Moves from one place to another easily</li> </ul>

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School/Preschool/Family Day Care		
Has your child attended (tick all that apply):	☐ Day care ☐ Family day care ☐ Preschool ☐ School	
What year did your child start attending day care?		-
Name of day care:		÷
Telephone of day care:		-
Contact/Teacher/Carer name:		_
What year did your child start attending family day care?		
Name of family day care:		-
Telephone of family day care:		-
Contact/Teacher/Carer name:		
What year did your child start attending preschool?		7 7
Name of preschool:		
Telephone of preschool:		-
Contact/Teacher/Carer name:		-
What year did your child start attending school?		
Name of school:		-
Telephone of school:		-
Contact/Teacher/Carer name:		

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Has the school counsellor, psychologist, or learning support team been involved?	O Yes O No		
Final Information			
Who completed this questionnaire?	☐ Biological mother ☐ Biological father ☐ Both biological parents together ☐ Other		
If Other, please describe their relationship with the child (do not provide any names, only relationship):			
Did anyone assist with completing this questionnaire?	O Yes O No		
If yes, please describe who (do not provide any names):			
Have you used or received any other following (tick all that apply):	Carer Allowance FACHSIA NDIS Better Start ATAPS Better Access to Mental Health Chronic disease management		
Would you have preferred to receive a paper copy of this form in the mail instead of completing it online? Please keep in mind that you would have been required to mail the form back to the hospital after completing on paper.	O No - I preferred to complete it online Yes - I would have preferred a paper copy in the mail		

Thank you for taking the time to complete this questionnaire.

11-05-2022 4:15pm

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Categories of Concerns	Example concerns
Attention and focus	<ul> <li>Difficulties concentrating or focusing.</li> <li>Difficulties following through on tasks at home/school</li> </ul>
General behavioural Issues	<ul> <li>Sensory seeking behaviours</li> <li>Self-stimulatory behaviours</li> <li>Sensitivity to stimuli</li> <li>Repetitive, restricted or rigid behaviours</li> <li>Stimming with objects</li> <li>Disruptive behaviour</li> <li>Problem behaviour</li> <li>Aggressive behaviour</li> <li>Emotional meltdowns</li> <li>Behaviours involving shutting down not explained by anxiety</li> <li>Concerns surrounding behaviour that was not addressed in sensory restricted/repetitive or externalising behaviour categories.</li> <li>Eating non-edible items</li> <li>Bed wetting/toilet issues</li> </ul>
Development	<ul> <li>Concerns about development or developmental delay</li> <li>Developmental assessment</li> </ul>
Learning/Academic skills	<ul><li>Learning at school</li><li>Reading, writing, mathematics</li></ul>
Medical	- Background of medical conditions. For example, fragile X syndrome, a genetic condition that is associated with learning difficulties.
School readiness	<ul> <li>To aid transition/ placement to kindergarten, primary school or high school</li> <li>Appropriate school placement</li> <li>Preparation for school</li> </ul>
Play and Social Skills	<ul> <li>Social skills</li> <li>Developing friendships</li> <li>Playing with others</li> <li>Social communication</li> </ul>
Speech and language	<ul> <li>Speech/ language delays or difficulties, for example:</li> <li>Stutter</li> <li>Delayed receptive/ expressive language</li> <li>Expressive/ receptive communication difficulties</li> </ul>
Query NDC concerns (ASD, ID/GDD, ADHD, SLD)	<ul> <li>Suspected ASD or concerns surrounding ASD.</li> <li>Suspected GDD/IDD or concerns surrounding GDD or intellectual developmental disabilities.</li> <li>Suspected ADHD or concerns surrounding ADHD.</li> <li>Suspected SLD or concerns surrounding Specific Learning Disorders (e.g., Dyslexia).</li> </ul>

# Supplementary Table 1: Concerns Reported by Parents in the PCQ.

*Note.* ADHD = Attention-Deficit/Hyperactivity Disorder, ASD = Autism Spectrum Disorder, GDD = Global Developmental Delay, SLD = Specific Learning Disorder, ID = Intellectual Developmental Disability. *Note:* Majority of categories of concern reproduced and incorporated with permission from Martha Munro<sup>48</sup>.

# Supplementary Table 2: Description of Strengths-based Themes Identified within

### the PCQ

Strengths Based Themes	Description of Themes		
Cognitive and intellectual	Cognitive and intellectual strengths include discrete mental abilities such		
	as thinking, remembering, and learning.		
Social and interpersonal	Social and interpersonal strengths included strengths that required a		
	relationship or connection with others.		
Hobbies and passions	Hobbies and passions were categorised when parents identified that a		
	child enjoyed the activity, regardless of whether it was noted they were		
	good at it.		
Character and personality	Personality strengths that can be said to describe their children's		
	characters in circumstances outside of direct interaction with others,		
	including being outgoing, independent, honest, and having a great sense		
	of humour.		
Physical	Parents frequently listed areas where they felt their children excelled at		
	or enjoyed physical activities, including gross and fine motor skills, as		
	well as sport and more general outdoor activities.		
Behavioural	Behavioural strengths were categorised as those pertaining to concrete		
	patterns of behaviour, generally outside of interpersonal interactions.		
	Examples included perseverance, resilience, and being well-behaved.		
3.7 . 4.11 .1			

*Note:* All themes were reproduced and incorporated with permission from Lorna Hankin's<sup>49</sup> qualitative research (CAN Research).

# Supplementary Tables 3-8: Statistical Analyses Tables for MANOVA Significant Results (Concerns and Strengths in PCQ)

	'Yes' to Learning		'No' to Learning and	
	and Cognition Concerns		Cognition Concerns Raised	
	Raised		(n=54)	
	(	(n=73)		
<b>BRIEF Domains</b>	М	SD	М	SD
Inhibit T scores	60.24	13.01	64.03	10.84
Shift T scores	64.71	14.432	64.51	13.31
Emotional Control T	58.93	2.77	62.79	1.255
scores				
Working Memory T	67.16	11.91	69.94	11.93
scores				
Plan/Organise T	62.46	10.51	64.94	11.27
scores				
GEC T scores	65.53	12.23	70.35	11.46

Table 3a. Dependant Variable Descriptive Statistics for Learning and Cognition Concerns

Table 3b. A two-way MANOVA was conducted on BRIEF domains and parental reported

learning/cognition concerns.

BRIEF	<i>F</i> -	<i>p</i> -value	$\eta_{\rm p}^2$
<b>Combined Domains</b>	statistic		
Inhibit T scores	3.03	.084	.024
Shift T scores	.006	.939	.000
Emotional	3.14	0.79	.025
Control T scores			
Working Memory	1.68	.196	.013
T scores			

Plan/Organise T	1.62	.205	.013		
scores					
GEC T scores	5.07	.026*	.039		
*Note: These values denote a significant effect of aforementioned T-scores with reported					

#### parental concerns

•	-	Ũ	-		
	'Yes' to Play and		'No' to l	Play and	
	Social Concern	s Raised	Social Concerns	Social Concerns Raised	
	(n=	(n=91)		36)	
<b>BRIEF</b> Domains	М	SD	М	SD	
Inhibit T scores	66.77	11.07	59.91	12.18	
Shift T scores	68.91	12.19	62.93	14.24	
Emotional Control T	63.05	11.99	59.59	12.28	
scores					
Working Memory T	71.36	13.84	67.15	10.97	
scores					
Plan/Organise T	65.38	9.92	62.78	11.18	
scores					
GEC T scores	71.66	11.36	65.96	12.06	

Table 4a. Dependant Variable Descriptive Statistics for Social and Play Concerns

Table 4b. A two-way MANOVA was conducted on BRIEF domains and parental reported play

and social concerns.

BRIEF	<i>F</i> -	<i>p</i> -value	$\eta_p^2$
<b>Combined Domains</b>	statistic		
Inhibit T scores	8.611	.004*	.064
Shift T scores	4.917	.028*	.038
Emotional	2.076	.152	.016
Control T scores			
Working Memory	3.251	.074	.025
T scores			
Plan/Organise T	1.492	.224	.012
scores			

GEC T scores	5.941	.016*	.045

\*Note: These values denote a significant effect of aforementioned T-scores with reported parental concerns

	'Yes' to Behavioural		'No' to Be	havioural
	Concerns R	aised	Concerns Raised	
	(n=	=45)	(n=	82)
<b>BRIEF</b> Domains	М	SD	М	SD
Inhibit T scores	66.20	10.77	59.47	12.39
Shift T scores	68.66	12.39	62.41	14.17
Emotional Control T	68	10.23	56.50	11.37
scores				
Working Memory T	70.11	12.27	67.37	11.73
scores				
Plan/Organise T	65.64	10.38	62.35	11.01
scores				
GEC T scores	72.33	10.54	64.97	12.17

Table 5a. Dependant Variable Descriptive Statistics for Behavioural Concerns

Table 5b. A two-way MANOVA was conducted on BRIEF domains and parental reported

Externalising Behavioural concerns.

BRIEF	<i>F</i> -	<i>p</i> -value	$\eta_p^2$
<b>Combined Domains</b>	statistic		
Inhibit T scores	9.35	.003*	.070
Shift T scores	6.10	.015*	.047
Emotional	31.85	<.001*	.203
Control T scores			
Working Memory	1.52	.219	.012
T scores			
Plan/Organise T	2.70	.103	.021
scores			

GEC T scores	11.63	<0.001*	.085

\*Note: These values denote a significant effect of aforementioned T-scores with reported

parental concerns

<i>Table 6a. Dependant</i>	Variable Descriptive	Statistics for Behaviou	rs Pertaining to NDC	Concerns
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	'Yes' to Behaviours		'No' to Be	ehaviours
	Pertaining to Diagnostic		Pertaining to Diagnostic	
	Concern	IS	Concern	8
	(n=	=34)	(n=	93)
<b>BRIEF Domains</b>	M	SD	М	SD
Inhibit T scores	67.64	13.07	59.74	11.26
Shift T scores	67.88	12.11	63.44	14.39
Emotional Control T	67.88	12.11	58.54	11.30
scores				
Working Memory T	72.05	13.44	66.98	11.13
scores				
Plan/Organise T	67.08	11.22	62.21	10.49
scores				
GEC T scores	73.17	12.60	65.53	11.31

Table 6b. A two-way MANOVA was conducted on BRIEF domains and parental reported

Behaviours Pertaining to Diagnostic Concerns.

BRIEF	<i>F</i> -	<i>p</i> -value	$\eta_p^2$
<b>Combined Domains</b>	statistic		
Inhibit T scores	11.23	.001*	.082
Shift T scores	2.56	.122	.020
Emotional	10.19	.002*	.075
Control T scores			
Working Memory	4.60	.034*	.036
T scores			
Plan/Organise T	5.17	.025*	.040
scores			

GEC T	scores	1	0.67	.001*	.079

\*Note: These values denote a significant effect of aforementioned T-scores with reported parental concerns

Table 7a. Dependant Variable Descriptive Statistics for Cognitive and Intellectual Strengths

		'Yes' t	to Cognitive	'No' to Cognitive			
	а	and Intellectu	al Strengths	and Intellectual Strengths			
		Rais	Raised		ed		
		(	(n=67)	(	(n=43)		
BRIEF Don	nains	М	SD	М	SD		
Inhibit T score	S	65.06	12.84	61.10	11.29		
Shift T scores		65.16	14.18	63.71	13.93		
Emotional Con	ntrol T	63.81	13.910	58.92	10.81		
scores							
Working Mem	ory T	69.88	15.50	67.92	9.87		
scores							
Plan/Organise	Т	64.67	11.72	63.00	10.10		
scores							
GEC T scores		69.79	14.09	66.73	0.80		

Table 7b. A two-way MANOVA was conducted on BRIEF domains and parental reported

strengths in cognition/intellect.

BRIEF	<i>F</i> -	<i>p</i> -value	$\eta_{p}^{2}$	
<b>Combined Domains</b>	statistic			
Inhibit T scores	2.89	.092	.026	
Shift T scores	.278	.599	.003	
Emotional	4.266	.041*	.038	
Control T scores				
Working Memory	.656	.420	.006	
T scores				

Plan/Organise T	.633	.428	.006		
scores					
GEC T scores	1.65	.202	.015		
*Note: These values denote a significant effect of aforementioned T-scores with reported					

parental strengths.

Table &	8a.	Dependant	Variable	Descrip	otive	Statistics.	for	Social	and	Inter	personal	Streng	gths
		1					/						_

	Yes' to S	Social and	'No' to Social and		
	Interpersonal Strengths Raised		Interpersonal Strengths Raised		
	(n=	=34)	(n=76)		
<b>BRIEF</b> Domains	M	SD	M	SD	
Inhibit T scores	57.00	11.20	65.18	11.57	
Shift T scores	59.52	13.45	66.40	13.78	
Emotional Control T	57.14	11.02	62.48	12.53	
scores					
Working Memory T	67.05	12.24	69.42	12.41	
scores					
Plan/Organise T	61.61	10.87	64.56	10.63	
scores					
GEC T scores	63.35	11.89	69.97	11.88	

Table 8b. A two-way MANOVA was conducted on BRIEF domains and parental reported

strengths in social and interpersonal skills.

BRIEF	<i>F</i> -	<i>p</i> -value	$\eta_p^2$
<b>Combined Domains</b>	statistic		
Inhibit T scores	11.976	<.001*	.100
Shift T scores	5.937	.016*	.052
Emotional	4.577	.035*	.041
Control T scores			
Working Memory	.858	.356	.008
T scores			

Plan/Organise T	1.780	.185	.016
scores			
GEC T scores	7.282	.008*	.063

\*Note: These values denote a significant effect of aforementioned T-scores with reported

parental strengths.

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