The relationship between cognition and ESSENCE in childhood

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To my mother

Γηράσκω ἀεὶ διδασκόμενος

Σόλων

The relationship between cognition and ESSENCE in childhood

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ABSTRACT

Aims: To examine the relationship between cognition and ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations) features in children, ages 7-8 years. To investigate the importance of intellectual functioning for academic achievement in Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). **Methods:** Studies I-III included children from the general population longitudinal SELMA study. The cohort was tested with the Wechsler Intelligence Scale for Children (WISC-IV). The assessment included parental questionnaires and interviews. Data on expressive language at age 2.5 years language screening were collected. Study IV (systematic review and meta-analysis) investigated the relationship between Wechsler intelligence scales' results and academic achievement in 6-16-year-olds with ADHD or ASD. **Results:** Vocabulary of ≤50 words at age 2.5 years was associated with lower general intellectual functioning, verbal comprehension, perceptual reasoning, and working memory at age 7-8 years (study I). Twenty-two percent of the 7–8-year-olds displayed working memory deficits but only 4% of the total study group had additional behavioural regulation and/or hyperactivity/inattention problems (study II). Distribution of autistic traits in the study group was continuous. General intellectual functioning, verbal comprehension, and verbal working memory were negatively associated with autistic traits (study III). Correlations between IQ and academic achievement, and between processing speed and academic achievement were moderate in ADHD, in line

with the narrative analysis (study IV). **Conclusions:** Limited use of spoken words at age 2.5 years increases the risk of cognitive deficits at age 7-8 years. Working memory deficits measured with WISC-IV at age 7-8-years do coexist with ADHD symptoms in a small subgroup, but also exist without additional ADHD symptoms. Prosocial behaviour might play a role in this. Elevated level of autistic traits is accompanied with a risk of difficulties in verbal comprehension and verbal working memory. General intellectual functioning is associated with reading, written language, and mathematics achievement in ADHD. The studies highlight the need for clinical follow-up in children with early ESSENCE features and awareness regarding the ESSENCE dimensionality demanding a broad assessment.

Keywords: intellectual functioning, working memory, Wechsler scales, general population, ESSENCE, neurodevelopmental disorders

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SAMMANFATTNING PÅ SVENSKA

Avhandlingen avser att undersöka sambandet mellan kognition och ESSENCE (Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations) symtom hos 7-8-åriga barn. ESSENCE är ett samlingsnamn för utvecklingsneurologiska svårigheter och tillstånd med tidig debut. Avhandlingen avser också att undersöka sambandet mellan intellektuell funktion och akademisk prestation hos barn med ADHD eller autism. Studierna I-III inkluderar barn från den longitudinella befolkningsbaserade studien SELMA. Barnen undersöktes med begåvningstestet Wechsler Intelligence Scale for Children (WISC-IV). Undersökningen innefattade även föräldraskattningar och föräldraintervju. Data om expressiv språkförmåga vid 2.5-års språkscreening samlades in. Sambandet mellan resultat från Wechslerskalorna och akademisk prestation hos 6-16-åriga barn med ADHD eller autism undersöktes genom en systematisk översikt och metaanalys (Studie IV). Resultaten visade att expressivt ordförråd på 50 ord eller färre vid 2.5 år hade ett samband med lägre allmän intellektuell funktion, verbal funktion, perceptuell funktion och arbetsminne i 7-8 års ålder (Studie I). Tjugotvå procent uppvisade begräsningar i arbetsminnesfunktion, men enbart en mindre andel (4%) uppvisade samtidiga svårigheter med beteendereglering och/eller hyperaktivitet och ouppmärksamhet (Studie II). Autistiska drag i studiegruppen låg längs ett kontinuum. Allmän intellektuell funktion, verbal funktion och verbalt arbetsminne hade ett negativt samband med autistiska drag (Studie III). Korrelationerna var måttliga mellan IQ och akademisk prestation samt mellan mental bearbetningshastighet och akademisk prestation hos barn med ADHD, i linje med den narrativa syntesen (Studie IV). Sammanfattningsvis visar de fyra studierna att begränsningar i expressivt ordförråd i 2.5 års ålder ökar risken för reducerad kognitiv funktion i tidig skolåldern. Begränsningar i arbetsminne hos 7-8-åriga barn kan finnas samtidigt som ADHD symtom, men även utan. Prosocialt beteende kan spela en roll för det sambandet. Att uppvisa en högre andel autistiska drag medför en risk för begränsningar i verbal funktion och verbalt arbetsminne. Allmän intellektuell funktion mätt med WISC har ett måttligt samband med akademisk prestation i läsning, skrivande och matematik hos barn med ADHD. Studierna betonar vikten av klinisk uppföljning av barn med tidiga ESSENCE symtom samt att dimensionaliteten i ESSENCE kräver ett brett perspektiv i kliniska bedömningar.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Marinopoulou, M., Billstedt, E., Lin, P. I., Hallerbäck, M., & Bornehag, C. G. (2021). Number of words at age 2.5 years is associated with intellectual functioning at age 7 years in the SELMA study. *Acta Paediatrica, 110*(7), 2134–2141.

II. Marinopoulou, M., Unenge Hallerbäck, M., Bornehag, C. G., & Billstedt, E. (2023). Is WISC-IV Working Memory Index associated with ADHD symptoms in 7-8-year-olds? *Applied Neuropsychology: Child*, 1–10. Online ahead of print.

III. Marinopoulou, M., Billstedt, E., Wessman, C., Bornehag, C. G., & Hallerbäck, M. U. (2023). Association between intellectual functioning and autistic traits in the general population of children. *Child Psychiatry and Human Development*. Online ahead of print.

IV. Marinopoulou, M., Åsberg Johnels, J., Bornehag, C. G., Unenge Hallerbäck, M., & Billstedt, E. (2023). Do Wechsler intelligence scales predict academic achievement in children with ADHD or autism? A systematic review and meta-analysis. *Manuscript.*

CONTENTS

ABBREVIATIONS

ADHD	Attention – Deficit / Hyperactivity Disorder
ANOVA	Analysis of Variance
ASD	Autism Spectrum Disorder
BRI	Behavioral Regulation Index
BIF	Borderline Intellectual Functioning
BRIEF	Behavior Rating Inventory of Executive Function
CHC	Cattell-Horn-Carroll
DLD	Developmental Language Disorder
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition
EF	Executive Function
ESSENCE	Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations
ESSENCE-Q	ESSENCE - Questionnaire
FDI	Freedom from Distractibility Index
FSIQ	Full Scale IQ
FTF	Five to Fifteen (questionnaire)
GAI	General Ability Index
ID	Intellectual Disability

IQ	Intelligence Quotient
NDD	Neurodevelopmental Disorder
PIQ	Performance IQ
POI	Perceptual Organization Index
PRI	Perceptual Reasoning Index
PSI	Processing Speed Index
SDQ	Strengths and Difficulties Questionnaire
SELMA	Swedish Environmental Longitudinal, Mother and child, Asthma and allergy (study)
SPM	Standard Progressive Matrices
SRS	Social Responsiveness Scale
VCI	Verbal Comprehension Index
VIQ	Verbal IQ
WAIS	Wechsler Adult Intelligence Scale
WISC	Wechsler Intelligence Scale for Children
WISC-III	Wechsler Intelligence Scale for Children, Third Edition
WISC-IV	Wechsler Intelligence Scale for Children, Fourth Edition
WISC-R	Wechsler Intelligence Scale for Children, Revised
WISC-V	Wechsler Intelligence Scale for Children, Fifth Edition
WMI	Working Memory Index

1 INTRODUCTION

The knowledge of Neurodevelopmental Disorders (NDDs) has increased significantly during the last decades. There is an increased awareness of the overlap between NDDs and of the dimensionality of NDD symptoms meaning that the boundary between diagnosis and non-diagnosis is not clear-cut. The Early Symptomatic Syndromes Eliciting Neurodevelopmental Clinical Examinations (ESSENCE) framework emphasises these perspectives and highlights the need to identify the impairing symptoms of NDDs (Gillberg, 2010). Cognition and its impact in daily life has been the focus in several studies of clinical NDD groups, albeit to different extents. There is, for example, robust evidence suggesting that language delay in preschool years is associated with NDDs later in childhood (Miniscalco et al., 2018; Miniscalco et al., 2006). Furthermore, working memory has been identified as an area of impairment in Attention-Deficit / Hyperactivity Disorder (ADHD) and a combination of deficits in attention, hyperactivity, working memory and other Executive Functions (EFs) occur in clinical ADHD groups (Pievsky & McGrath, 2018). Studies have also shown that there is a relationship between Intelligence Quotient (IQ) in childhood and later outcome in individuals with Autism Spectrum Disorder (ASD) (Billstedt et al., 2007; Pickles et al., 2020).

Yet, the associations between outcomes such as early expressive vocabulary, cognitive functions (e.g. working memory, attention and IQ) and NDD symptoms are not as clear in samples from the general population of children. Furthermore, several studies have reported a relationship between IQ (measured with e.g. the Wechsler Intelligence Scale for Children, WISC) and academic achievement in the general population. However, this relationship is less clear in ADHD and ASD.

The overall aim of this thesis is to study the relationship between cognitive functioning, particularly intellectual function and EFs, and ESSENCE features in the general population of children, as well as the importance of intellectual functioning for academic achievement in clinical groups with ADHD and ASD. Studying this relationship in children from the general population broadens the knowledge of the association between these cognitive functions and behavioural traits in NDDs, which, in turn, may have implications for clinical practice relative to identification of NDD and to intervention.

1.1 COGNITIVE EPIDEMIOLOGICAL APPROACH

This thesis has mainly a cognitive epidemiological approach. Cognitive epidemiology focuses on studying the distribution, patterns and factors implicated in cognitive outcomes. Sex, birth factors, parental and social factors, environmental exposures and genetics, have been found to influence cognition at various ages (Guez et al., 2021). Intellectual functioning has received particular attention in cognitive epidemiology due to the high reliability and stability of IQ scores (Guez et al., 2021; Plomin & Deary, 2015), and as a predictor of academic and occupational status (Plomin & Deary, 2015). Through studying large cohorts, cognitive epidemiological research provides knowledge of cognitive development, its variability and its mechanisms, regarding typical and atypical development. Understanding the relationship between cognitive functions, what influences cognitive functions at a certain age, and what promotes development, may contribute to recommendations in public health and education. It also provides implications for clinicians as regards tailoring prevention and intervention programs (Guez et al., 2021).

1.2 COGNITION

Cognition refers to mental processes involved in acquiring and comprehending information (Colman, 2015). Cognitive functions include processes in a range of domains including language, visuospatial, motor, attention, learning and memory, EFs and social cognitive domain. Several of these cognitive functions are included in the construct intelligence, which refers to a general mental ability that integrates cognitive functions (Colom et al., 2010).

Brain development is a complex process that can be affected by several factors leading to milder or more pronounced cognitive deficits. Genetic factors, maternal infections, environmental toxins and maternal alcohol and drug intake during pregnancy are, among others, prenatal risk factors affecting cognitive development, while preterm birth and neonatal strokes are perinatal risk factors. Cerebral infections, acquired brain injuries and malnutrition may affect cognitive development and function postnatally. Cognitive and social cognitive skills advance significantly during childhood. Factors related to the psychosocial environment where the children grow up, e.g. the level of stimulation provided, access to resources, parent education and socioeconomic status, also influence child development, and need to be taken into account (Anderson et al., 2019).

1.3 INTELLECTUAL FUNCTIONING

1.3.1 THEORIES OF INTELLIGENCE

There is a lack of consensus regarding the exact definition of intelligence, but problem solving is included in most definitions. There are several theories of intelligence. Their history and the history of intelligence test interpretation is too extensive to be presented in detail in this thesis. Selected theories and historical events are briefly presented to provide context.

Using factor analysis, psychologist Charles Spearman developed a two-factor theory of intelligence, which was published in 1904. According to the theory, intelligence consists of a general factor (*g*) reflecting a broad, dominant factor influencing all performance on cognitive tests, and a specific factor (*s*) reflecting ability in specific cognitive domains, thus influencing only tests measuring this specific ability. Though not denying the existence of *g*, Louis Thurstone proposed in 1938 that intelligence consists of multiple mental abilities, named "Primary Mental Abilities", that included verbal comprehension, verbal fluency, numerical ability, spatial visualisation, memory, perceptual speed and reasoning (Goldstein et al., 2015). In 1963, Raymond Cattell expanded Spearman's theory by developing a model based on two second-order general factors, called fluid intelligence (g_f) and crystallised intelligence (g_c). Fluid intelligence refers to reasoning and problem-solving ability in novel situations. Crystallised intelligence reflects knowledge and skills acquired through cultural and educational experiences. This model was refined by Horn and Cattell. In addition to fluid intelligence and crystallised intelligence, their model also included the factors general visualisation, general speediness, facility in the use of concept labels and carefulness (Horn & Cattell, 1966). Horn continued developing the model by adding broad abilities, leading to what nowadays is known as the Horn-Cattell model, also called the extended G_f-G_c theory (Goldstein et al., 2015).

In 1993, psychologist John Carroll proposed the three-stratum theory of intelligence. According to the theory the first stratum consists of more specific traits which combined allow the measurement of stratum two traits, i.e. higher-level traits such as fluid intelligence, general memory and learning and processing speed. These combined result in the measurement of the third stratum, which is unitary and consists of *g*. This latter stratum is the most

evident difference between Carroll's model and the Horn-Cattell model (Goldstein et al., 2015). McGrew integrated the Horn-Cattell theory and Carroll's three-stratum theory in 1997 to what is nowadays referred to as the Cattell-Horn-Carroll (CHC) theory of cognitive abilities. The theory was updated later and is empirically validated. In brief, the theory posits a multidimensional hierarchical model of intelligence where *g* is at the highest level. Several broad abilities are gathered below *g* and several narrow abilities below them. Example of broad abilities are fluid intelligence, crystallised intelligence, quantitative knowledge and short-term memory. The narrow abilities comprising a broad ability correlate more with each other than with other narrow abilities (Flanagan & Dixon, 2013; Schneider & McGrew, 2012).

The existence of a general factor of intelligence influencing performance across cognitive domains has been intensively debated. Nowadays, there is comprehensive factor-analytic evidence supporting this concept. The contemporary view of intelligence acknowledges a hierarchical structure with several cognitive ability domains encompassing specific abilities (Wechsler, 2003b). This is in line with a statement signed by 52 researchers (Gottfredson, 1997) defining intelligence as a general capacity involving several abilities, including reasoning, problem solving, complex understanding and learning from experience.

Though outside the scope of this thesis, it should be mentioned that some theories posit the concept of multiple intelligences. Howard Gardner proposed a theory that describes eight distinct and independent intelligences that interact with each other (Goldstein et al., 2015). These are linguistic intelligence, logical-mathematical intelligence, spatial intelligence, musical intelligence, bodily-kinaesthetic intelligence, interpersonal intelligence, intrapersonal intelligence and naturalist intelligence. However, the theory has been criticised and lacks empirical evidence supporting it (Sternberg, 2015). Another theory involving the concept of multiple intelligences is Robert Sternberg's triarchic theory of successful intelligence. In this theory, intelligence encompasses three aspects: analytical, creative and practical, and is defined as the ability to achieve goals. The theory included even wisdom as an aspect later on (Sternberg, 2015).

1.3.2 PSYCHOMETRIC TESTING OF INTELLIGENCE

In the late 1800s, Sir Frances Galton constructed the first comprehensive intelligence test, which included reliable sensory and motor tasks. It was based on his view that well-developed senses reflect higher intelligence. However, the test's validity was limited. Alfred Binet and his colleagues developed the Binet-Simon scale to measure intelligence in children in schools in Paris in 1905 and to identify those in need of special education. The tasks were cognitive including judgement, comprehension and reasoning. The revised edition contained norms (Flanagan & Kaufman, 2009). The Binet-Simon scale has subsequently been adapted and translated into several languages and revised, the Stanford-Binet fifth edition (Roid, 2003) being the latest one.

William Stern was the first to introduce the concept of a mental quotient in 1914, calculated as the ratio between a child's mental age (in this case performance on the Binet-Simon scale) and chronological age. The concept was revised by Lewis Terman and named "intelligence quotient" (IQ), defined as the aforementioned quotient multiplied by 100 (Greenwood, 2015). David Wechsler, a psychologist renowned for his development of intelligence scales, revised this quotient to reflect standard scores that are "standardized differences from the mean obtained by same age-peers" (Flanagan & Alfonso, 2017).

Wechsler defined intelligence as "the aggregate or global capacity of the individual to act purposefully, to think rationally and to deal effectively with his environment" (Wechsler, 1939). Wechsler was influenced by other contemporary scientists, e.g. Spearman and Thurstone, and combined his clinical skills and advanced statistical training to develop intelligence tests (Flanagan & Kaufman, 2009). He believed that further attributes besides the cognitive factors contribute to "intelligent behaviour" and influence a child's performance and its effectiveness in coping with challenges. For a clinician, assessing a child's intellectual functioning requires considering the child's unique characteristics besides obtaining test scores (Wechsler, 2003b). Owing to their clinical and psychometric characteristics, the Wechsler intelligence scales have been of great importance in the field of test development and research (Flanagan & Kaufman, 2009).

Incorporating well-researched theory in test construction became rapidly very

important in the 1980s producing continuous advances in test development and interpretation. However, this does not imply that Wechsler lacked theory in his test construction, as he was up to date with intelligence theories and psychometric knowledge of that time. Wechsler's definition of intelligence in 1939 includes both global and differentiable abilities and is line with contemporary CHC theory (Kaufman et al., 2016). Being a well-validated theory, the CHC theory is commonly used in the construction and interpretation of contemporary intelligence tests (Flanagan & Kaufman, 2009). Though not explicitly based on CHC theory, the fit of the WISC in CHC models has been tested and aspects of the CHC theory are part of the theoretical framework of the latest edition, WISC-V (Wechsler, 2014). The five indexes included in WISC-V correspond to five of the CHC broad abilities. The theoretical framework of Wechsler Intelligence Scales is broader, incorporating both structural and functional theories of intelligence, and relevant psychological and neuropsychological research (Kaufman et al., 2016).

1.3.2.1 WISC

The WISC is one of the first-choice instruments globally for assessment of general intellectual functioning in children aged 6 to 16 years. It is an individually administered standardised test used in clinical, educational and research settings. Reasons for using WISC are to identify individual cognitive strengths and weaknesses, to support diagnostic decision (Intellectual Disability, ID) and to provide information for interventions and adjustments in school and daily life.

The WISC has its origins in the adult test Wechsler-Bellevue Intelligence Scale (Wechsler, 1939). This test was considered innovative for the time, since it assembled subtests into Verbal and Performance composites, besides the global IQ measure (Flanagan & Kaufman, 2009). The WISC was introduced in 1949 (Wechsler, 1949) and was a downward extension of an alternate form of the Wechsler-Bellevue Intelligence Scale published in 1946, but modified for child assessment (Flanagan & Kaufman, 2009). The WISC has been updated periodically until the most recent version, WISC-V, was published in 2014 (Wechsler, 2014).

There has been an increase in composites/indexes throughout the new WISC versions. The original *WISC* provided three composite scores named Full Scale IQ (FSIQ), Verbal IQ (VIQ) and Performance IQ (PIQ). The revised edition, *WISC-R* (Wechsler, 1974), provided the same three composites but included a larger normative sample with higher representativity (Flanagan & Kaufman, 2009) and was considered the most psychometrically adequate intelligence test for children at this time (Kaufman et al., 2016). Also, *WISC-III* (Wechsler, 1991) included FSIQ, VIQ and PIQ but new factor-analytically derived indexes were introduced that represented domains of cognitive function. These were called Verbal Comprehension Index (VCI), Perceptual Organization Index (POI), Freedom from Distractibility Index (FDI) and Processing Speed Index (PSI). FDI was renamed as Working Memory Index (WMI) in the subsequent edition, *WISC-IV* (Wechsler, 2003a). POI was changed to Perceptual Reasoning Index (PRI) in order to emphasise the fluid reasoning abilities measured in the included subtests. VIQ and PIQ were excluded in the WISC-IV but it continues to have a four-factor structure with the indexes VCI, PRI, WMI and PSI, and to provide a score of FSIQ. In studies I-III the WISC-IV was used. The WISC-IV indexes measure the following cognitive function domains:

- **VCI** provides a measure of verbal concept formation, verbal abstract reasoning and acquired knowledge. It includes the subtests Similarities, Vocabulary and Comprehension.
- **PRI** provides a measure of fluid reasoning and visuospatial processing, and comprises the subtests Block Design, Picture Concepts and Matrix Reasoning.
- **WMI** is designed to measure working memory abilities and includes the subtests Digit Span and Letter-Number Sequencing.
- **PSI** measures the mental speed of information processing and includes the subtests Coding and Symbol Search.
- **FSIQ** is an overall score which reflects general intellectual functioning, or *g* (Wechsler, 2003b).

An additional composite score, the General Ability Index (GAI), was developed for WISC-III and is provided in the subsequent versions. In WISC-IV, GAI is based on a combination of VCI and PRI, and provides a measure of

general cognitive ability with less influence of working memory and processing speed (Raiford et al., 2005).

The structure of the latest edition of the WISC, *WISC-V* (Wechsler, 2014), comprises five factors with the indexes VCI, Visual Spatial Index, Fluid Reasoning Index, WMI and PSI. In this version, WMI comprises Digit Span and Picture Span, which is a subtest measuring visual working memory. The corrected correlation coefficients for FSIQ and indexes between WISC-IV and WISC-V are high (Wechsler, 2014).

Knowledge of the structure of the editions of WISC and how composites correlate between editions is essential when comparing the scores derived from different editions, due to changes in included subtests and indexes over the years. Figure 1 provides an overview of the composite scores included in the editions of WISC.

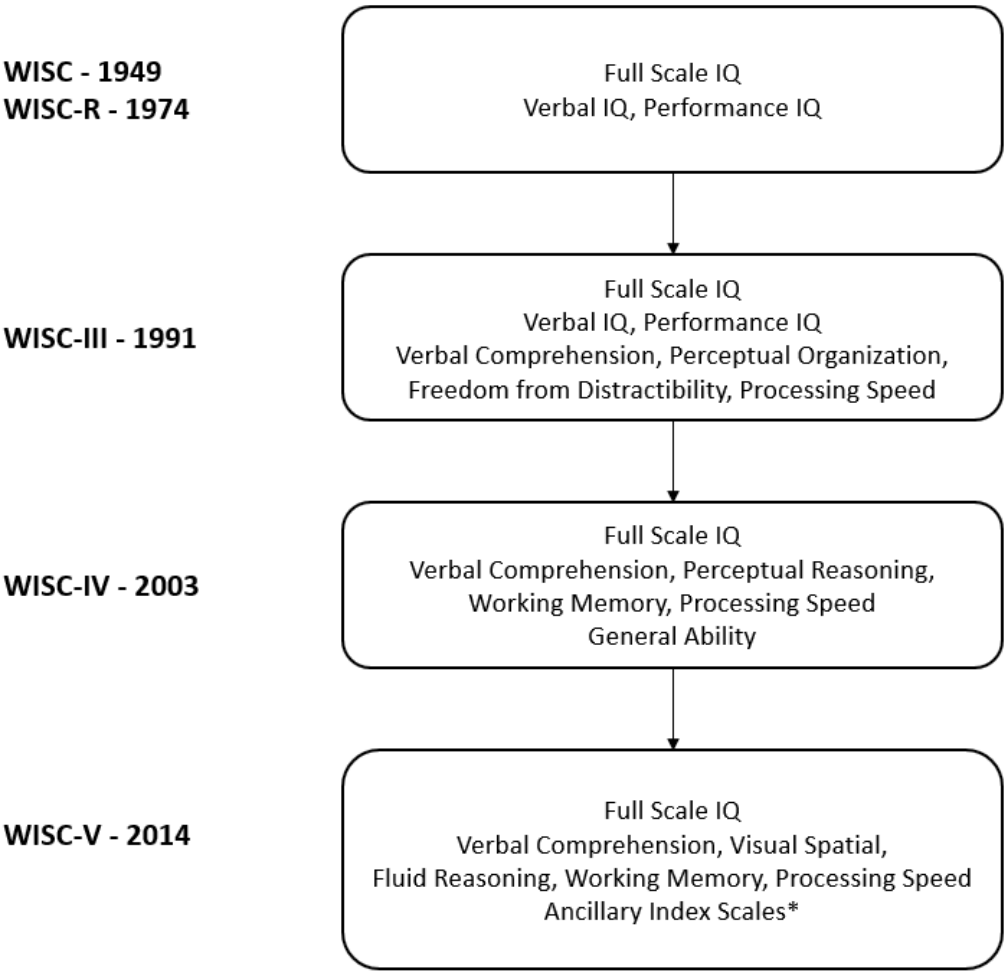

Figure 1. WISC composite scores in the different WISC editions

*Quantitative Reasoning, Auditory Working Memory, Nonverbal, General Ability, Cognitive Proficiency

Pre-schoolers and children up to 7 years and 7 months can be assessed with the Wechsler Preschool and Primary Scale of Intelligence (WPPSI; Wechsler, 2012), and adolescents from 16 years and older and adults with the Wechsler Adult Intelligence Scale (WAIS; Wechsler, 2008).

1.4 EFS

EFs are described as top-down cognitive functions in charge of goal-oriented behaviour. They are associated with the frontal lobes, particularly the prefrontal cortex. Several cognitive abilities, e.g. planning, verbal fluency, inhibiting automatic responses, have been labelled as such (Friedman & Miyake, 2017). A common, established conceptualisation of EF includes inhibitory control, working memory and cognitive flexibility (set shifting), which are also referred to as the "core EFs" (Diamond, 2013). A difference between "cool EFs" and "hot EFs" has been suggested, where the former often refer to the EFs used in more emotionally neutral situations and correspond to the aforementioned traditional conceptualisation of EFs (Fernández García et al., 2021; Zelazo & Carlson, 2012). Hot EFs on the other hand are active in affective and motivationally significant contexts. Skills such as delay of gratification and decision-making have been studied as such (Fernández García et al., 2021; Zelazo & Carlson, 2012). There is however a lack of consensus on the core components of hot EFs (Fernández García et al., 2021). Despite the distinction between cool and hot EFs, these two sets of EFs are not isolated from each other and there is evidence of overlap and integration in behaviour (Fernández García et al., 2021). The term "behavioural regulation" represents a combination of inhibitory control, flexibility and emotional control (Gioia et al., 2000; Rohr et al., 2023).

EFs emerge already in infancy and continue to develop throughout adolescence and early adulthood (Ferguson et al., 2021). It has been proposed that this development is gradual with periods of more pronounced development (Taylor et al., 2013) and that EFs show variable developmental trajectories (Best & Miller, 2010; Ferguson et al., 2021).

EFs are vital for completing tasks and for adequate daily life functioning and are related to important life outcomes (Diamond, 2013), including academic achievement and school success (Zelazo & Carlson, 2020). EFs are impaired in many psychiatric conditions. Both hot and cool EFs are involved in emotion regulation, which in turn is important for effective social functioning (Zelazo & Carlson, 2020).

The assessment of EFs is often carried out with performance-based tests, which evaluate function under standardised conditions in a structured environment

(Toplak et al., 2013). Another way of assessing EFs is through self or informant reported behavioural rating scales. These were introduced to improve the ecological validity of EF measurement and are designed to capture EF skills in everyday contexts (Isquith et al., 2013), i.e. under unstructured conditions (Toplak et al., 2013). These two types of measures are seen as complementary, providing a more comprehensive perspective when combined (Isquith et al., 2013).

1.4.1 WORKING MEMORY

Working memory is described as the ability to hold information active in mind and perform tasks with it during brief periods (Diamond, 2013). Working memory is central to comprehension, learning and reasoning (Baddeley, 2003), and is linked to academic achievement (Alloway & Alloway, 2010). Working memory function develops during childhood, adolescence and early adulthood (Ferguson et al., 2021).

Different types of span tasks are used to assess working memory, e.g. Digit Span in WISC measuring verbal working memory and the Corsi-block test for visuo-spatial working memory (Diamond, 2013). Performance in Digit span backward tasks, reflecting working memory capacity, has been reported to double between ages 5 and 11.5 years (Reynolds et al., 2022).

1.5 LANGUAGE DEVELOPMENT

Speech, language and communication are complex processes. Speech refers to the utterance of sounds and words. Language is defined as "the form, function and use of a conventional system of symbols" to communicate (American Psychiatric Association, 2013). In linguistics, language is broken down into components; phonology, morphology, syntax, semantics and pragmatics. Communication is broader than speech and language and involves the transmission of information through verbal and non-verbal behaviours to relate to and influence another individual (American Psychological Association, n.d.).

Language and communication development starts very early in childhood as evidenced by infants' phonetic discrimination, preverbal vocalisations and babbling. Infants of 9-10 months begin to comprehend words and say their first words weeks later. Substantial vocabulary growth some months later is followed by the first use of two-word combinations at about 18-20 months. By age 3-4 years children possess large vocabularies and can understand and use complex grammar. Language development during the preschool years is generally expansive but there is a substantial variation in skills between individuals. After the preschool years, school-aged children display ongoing language improvement such as vocabulary growth and progress in syntactic abilities (Dick et al., 2008).

Developmental milestones in early language skills in the preschool years have been suggested to predict intellectual functioning later in childhood (Peyre et al., 2017; Vlasblom et al., 2019) and in adulthood (Flensborg-Madsen & Mortensen, 2018). Furthermore, expressive vocabulary at 16-30 months has been found to correlate with academic achievement in language subjects but also in mathematics and science at school year 9 (Dale et al., 2023). It has been proposed that brief language assessment result at early childhood may predict the need for special education later on (McIntyre et al., 2017).

1.6 SOCIAL COMMUNICATION

Social communication involves the communication of emotional and cognitive information through gestures, facial expressions and speech prosody (Robertson et al., 1999). It is a reciprocal process that includes both receptive and productive aspects, and the multimodal use of information (National Institute of Mental Health, n.d.). Further definitions focus on pragmatics and include both verbal and non-verbal communication aspects, e.g. taking turns, adapting communication to contextual aspects, and understanding figurative language (American Psychiatric Association, 2013).

Social communication development begins very early. Newborns are sensitive to social stimuli and orientate towards faces (Dawson et al., 2004), and have the ability to imitate facial movements (Toth et al., 2006). By 12 months of age, many infants display joint attention skills, i.e. they intentionally coordinate their attentional focus with that of another person around an object or event and share this experience. To use eye gaze and gesture in order to share, follow, and direct attention is defined as joint attention (Dawson et al., 2004). Furthermore, infants display functional play late in the first year, followed by the emergence of symbolic play at around 1 year of age, which further develops successively. Joint attention, imitation, and toy play have been associated with social communication development (Toth et al., 2006). Social communication and social skills continue to develop and become more sophisticated during childhood and adolescence.

Social communication is part of social cognition, which is an umbrella term encompassing functions involved in the perception, processing, interpretation of and response to social information, i.e. the processes that underlie social interaction. Definitions may differ as to which domains social cognition encompasses, but emotion perception and theory of mind are most often included (Wallis et al., 2022).

Social cognitive difficulties are present to varying degrees in a number of conditions, including ASD (Pastorino et al., 2021) and Developmental Language Disorder (DLD) (Nilsson & de López, 2016). Young children with ASD are less oriented towards social stimuli and display impairments in joint attention, imitation and play (Dawson et al., 2004; Toth et al., 2006). The development of theory of mind abilities such as understanding intentions is

delayed in ASD (Coleman & Gillberg, 2012), and social communication difficulties are core impairments in ASD (American Psychiatric Association, 2013).

1.7 ACADEMIC ACHIEVEMENT

Academic achievement refers to the level of competence in specific abilities, e.g. reading, writing, arithmetic, or more generally in schoolwork (American Psychological Association, n.d.).

Several factors are involved in academic achievement, of which intelligence is the best predictor in the general population (Deary et al., 2007; Neisser et al., 1996; Plomin & von Stumm, 2018; Roth et al., 2015). Apart from intelligence, attention and EF, including working memory, contribute to academic achievement (Alloway et al., 2009; Lundervold, Bøe, et al., 2017; Titz & Karbach, 2014). For instance, inattention problems at ages 7-9 years predict lower academic achievement in high school (Lundervold, Bøe, et al., 2017), and low working memory has a negative impact on academic progress (Alloway et al., 2009). Also, other factors, such as motivation (Lavrijsen et al., 2022) and self-control (Duckworth et al., 2019), influence achievement. Several studies report that children with NDD or other conditions affecting cognitive functioning show difficulties in academic achievement (Keen et al., 2016; Lawrence et al., 2021; Reilly et al., 2014; Ziegenfusz et al., 2022).

There is a wide range of tests to assess academic achievement that provide information about individual's academic strengths and weaknesses and detect the presence of learning difficulties. They are also used as outcome measures in research studies. Other outcome measures of school achievement are grades and years of completed education.

1.8 NDDS

NDDs are conditions with an early onset, whose common feature is manifestation during childhood and deficits impacting a person's functioning negatively (American Psychiatric Association, 2013). Though their aetiology is heterogeneous and not fully clear, they are highly heritable, typically multifactorial and hundreds of genes and a number of environmental risk factors are involved in their onset (Bourgeron, 2016; Carlsson et al., 2021; Gidziela et al., 2023). NDDs are often identified and diagnosed in childhood, though some individuals receive their diagnosis in adulthood (Eberhard et al., 2022). Their prevalence is about 10% in children (Gillberg, 2010) and they frequently coexist (Thapar et al., 2017). Generally, more males than females receive a diagnosis of NDD (Yang et al., 2022). Individual outcomes vary, but in many cases NDDs persist into adulthood (Thapar et al., 2017).

The recent version of the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5; American Psychiatric Association, 2013), includes NDDs in a chapter encompassing ID, communication disorders (e.g. language disorder), ASD, ADHD, specific learning disorder and motor disorders (e.g. developmental coordination disorder and tic disorders).

1.8.1 ADHD

ADHD is defined by symptoms of inattention, hyperactivity and impulsivity that interfere with a person's development or functioning. ADHD is categorised in the subtypes "combined presentation", "predominantly inattentive presentation" and "predominantly hyperactive-impulsive presentation". Hyperactivity and impulsivity are often apparent in preschool years, whereas inattention becomes more evident with increasing age, i.e. in the early school years (American Psychiatric Association, 2013). ADHD prevalence in children is about 5% (American Psychiatric Association, 2013). It often coexists with other NDDs, e.g. ASD, and is associated with increased risk of comorbid psychiatric disorders in childhood and adolescence such as oppositional defiant disorder, anxiety and depression (Franke et al., 2018). Individual outcomes vary, but more than 50% of the individuals identified in

childhood continue to present with impairment and to fulfil criteria in adulthood (Di Lorenzo et al., 2021).

ADHD is associated with EF impairment, including working memory, inhibitory control and flexibility, and individuals with ADHD perform lower than controls in EF tasks (Kasper et al., 2012; Martinussen et al., 2005; Pievsky & McGrath, 2018; Ramos et al., 2020; Willcutt et al., 2005). Working memory impairment is evident in both visuospatial and verbal tasks (Kasper et al., 2012). EF test performance is heterogeneous among individuals with ADHD, and task demands and age seem to contribute to the variability in results of different studies (Kasper et al., 2012; Ramos et al., 2020). Furthermore, weaknesses in processing speed have rather consistently been reported in ADHD, albeit not in all individuals (Kramer et al., 2020; Li et al., 2017; Thaler et al., 2013). Slow processing speed has been linked to inattention (Thaler et al., 2013), academic and weaker adaptive skills in ADHD (Cook et al., 2018). ADHD occurs at all levels of intellectual functioning (Katusic et al., 2011; Sawhney et al., 2021). However, the mean IQ at group level has been described as slightly lower in clinical cases with ADHD compared to controls (Frazier et al., 2004; Tallberg et al., 2021). In contrast, a meta-analysis including adults suggested that these differences are minimal and occur in certain groups, e.g. those with psychiatric comorbidity and learning disorders (Bridgett & Walker, 2006). Decreased IQ in childhood has been associated with poorer adolescent and adult functional outcome in ADHD (Roy et al., 2017). As regards WISC, there is no universal profile in ADHD. However, lower WMI and PSI compared to VCI and PRI (Mayes & Calhoun, 2006; Toffalini et al., 2022), and low WMI in all ADHD subtypes, especially in the predominantly inattentive presentation (Molavi et al., 2020), have been reported at group level. Thaler et al. (2013) performed hierarchical cluster analysis, which yielded five profiles in a group of children with ADHD (average index scores but low average PSI, high average index scores, below average WMI and PSI, low average results but with average PSI and superior VCI). The children with below average scores in WMI and PSI displayed lowest adaptive functioning compared to the other clusters.

Children and adolescents with ADHD have an increased risk of lower academic achievement in several domains (Franke et al., 2018; Lawrence et al., 2021), and childhood inattention problems is one factor identified as having an impact on this (Lundervold, Meza, et al., 2017). Lower scores of prosocial

behaviour, i.e. sharing, comforting and other behaviours that benefit others (Hay, 1994), have also been presented in children and adolescents with ADHD in comparison to their peers (Ragnarsdottir et al., 2018; Velo et al., 2021). However, more research is needed to understand prosocial abilities in children with ADHD and in relation to cognitive abilities.

Pharmacological treatments are associated with improved outcomes in academic achievement compared to non-treatment (Faraone et al., 2015). Patient and parent education in ADHD also plays an important part in managing the disorder. In addition, there is a range of non-pharmacological treatments for children with ADHD such as behavioural interventions including parent training, school-focused interventions and interventions targeting specific areas of daily functioning, that are valuable for co-occurring problems, quality of parenting and academic achievement (Faraone et al., 2015). A comprehensive, holistic approach is recommended in European guidelines, where pharmacological treatment can be a part of it but not the only intervention (National Institute for Health and Care Excellence, 2019; Socialstyrelsen, 2022).

1.8.2 ASD

ASDs core diagnostic features are deficits in social communication and social interaction, and restrictive, repetitive behaviours and interests (American Psychiatric Association, 2013). Coexisting conditions are very common in ASD and include ADHD, ID, language disorder, epilepsy and anxiety disorders to name but a few (Fernell & Gillberg, 2023). ASD or autistic traits also occur in several genetic syndromes, e.g. Fragile X syndrome and Down syndrome (Coleman & Gillberg, 2012), and in neurological disorders (Ryland et al., 2012). ASD has a prevalence of about 1-1.5% (Lyall et al., 2017; Zeidan et al., 2022), and generally persists into adulthood (Billstedt et al., 2005; Helles et al., 2015).

ASD is a highly heterogeneous condition as evident in its clinical presentation, which may differ substantially depending on symptom severity, age, language abilities, level of intellectual functioning and comorbidities (American Psychiatric Association, 2013). Similarly, cognitive characteristics vary, and there is no specific cognitive profile characteristic for all individuals with

ASD. Academic outcomes in ASD are variable (Keen et al., 2016) and academic underachievement is relatively common (Kim et al., 2018; Mayes et al., 2020).

Neuropsychology in ASD has been extensively researched, aiming to describe its characteristics, strengths and difficulties, and increase the understanding of the condition. ASD occurs at all levels of intellectual functioning (Wolff et al., 2022). ID is prevalent in about 23%-30% of the cases (Mutluer et al., 2022; Wolff et al., 2022). Executive dysfunction is common in ASD, as demonstrated in meta-analyses encompassing a range of functions including planning, working memory, inhibition and flexibility (Hemmers et al., 2022; Lai et al., 2017). Furthermore, reduced processing speed scores have been reported in ASD (Hedvall et al., 2013; Mayes & Calhoun, 2008; Oliveras-Rentas et al., 2012), but not in all studies (Wallace et al., 2009). It has been proposed that comorbidity with inattention or ADHD might account for the association between ASD and processing speed (Kramer et al., 2020). Language abilities vary widely in ASD. Language delay is relatively common in ASD and a frequent reason for referral for further assessment early in the preschool years (De Giacomo & Fombonne, 1998). Some children with ASD do not develop spoken language or remain minimally verbal (Tager-Flusberg & Kasari, 2013). This level of expressive language seems to co-occur with ID (Norrelgen et al., 2015). However, most children develop speech, but semantic processing is often affected (Boucher, 2012). Some children may possess superior language skills. Heterogeneity is generally the rule here, but pragmatic deficits, i.e. difficulties in using language appropriately in a social context, are considered universal in ASD (American Psychiatric Association, 2013; Volden et al., 2009). Last but not least, though generally less studied than cognitive deficits in ASD, some individuals with ASD possess particular strengths or talents, such as special memory or visuospatial skills (Meilleur et al., 2015).

Though individual variation is common, the mean cognitive WISC profile has been reported to be uneven in ASD. Several, but not all, studies using earlier versions of WISC or WAIS have reported stronger VIQ than PIQ in children and adolescents with Asperger syndrome (Cederlund & Gillberg, 2004; Gilchrist et al., 2001; Klin et al., 1995; Noterdaeme et al., 2009; Zander & Dahlgren, 2010), which was an earlier diagnostic category of ASD in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; American Psychiatric Association, 1994) for individuals with ASD without

intellectual and language delay. A proportion of individuals were found to continue displaying this discrepancy between VIQ and PIQ as adults (Hagberg et al., 2013). This pattern of higher VIQ compared to PIQ was also present in some cases with "high functioning autism" (Ghaziuddin & Mountain-Kimchi, 2004), i.e. ASD with early language delay but without intellectual disability. Furthermore, higher PIQ than VIQ has been reported in children with autistic disorder (Shah & Frith, 1993), but other studies do not support this pattern at group level (Charman et al., 2011; Ehlers et al., 1997). It has been proposed that VIQ increases during the preschool years, thus making the difference between PIQ and VIQ in preschool more even at school age (Mayes & Calhoun, 2003). An uneven profile with lower FDI/WMI and PSI scores, in comparison to VCI and POI/PRI, is a common finding in later studies of school-aged children with ASD (Mayes & Calhoun, 2008; Oliveras-Rentas et al., 2012). In a recent study including children with ASD without ID (Audras-Torrent et al., 2021), results were heterogeneous, but mean FSIQ was average and WMI was lower than FSIQ and the indexes except for PSI.

Apart from the research on cognitive profiles and functioning, there is a number of cognitive theories focusing on deficits that have been proposed to underlie the clinical presentation of ASD (Coleman & Gillberg, 2012). The theory of mind hypothesis, the weak central coherence theory and the executive dysfunction hypothesis are probably the most known ones. Theory of mind is defined as the ability to ascribe mental states, e.g. beliefs, intentions and desires, to oneself and others, and can be used to predict behaviour (Premack & Woodruff, 1978). The development of these abilities is delayed in ASD and children with ASD irrespective of intellectual functioning level have theory of mind problems (Coleman & Gillberg, 2012). The weak central coherence theory refers to an observed inclination in individuals with ASD to process information locally, more detailed focused, rather than globally/as a whole. Frith (1989, in Frith & Happé, 1994) proposed that typical information processing, "central coherence", which tends to draw together information to create an overall meaning or gist, was weak in ASD, and could explain some of the deficits but also assets in ASD (Frith & Happé, 1994). The executive dysfunction hypothesis proposed that EF deficits underlie many of the social and non-social features in ASD, but the lack of specificity of EF deficits for ASD (Hill, 2004) together with the lack of association between EF and theory

of mind (Hemmers et al., 2022) question this hypothesis. In general, none of the cognitive theories is sufficient on its own to explain ASD.

As regards intervention, individualised, multidisciplinary intervention and support is recommended with the aim of enhancing adaptive functioning and quality of life (Lai et al., 2014). The individual needs may differ at different periods in life and among individuals (Lord et al., 2020). Families, carers and the individual with ASD should receive information on the condition including how it can be managed (Socialstyrelsen, 2022). Interventions to enhance social communication are important (Lord et al., 2020), as well as appropriate accommodations in school (Leifler et al., 2021). Co-existing conditions should also be managed with appropriate interventions (National Institute for Health and Care Excellence, 2021).

1.8.3 DLD

DLD as a term has existed for several years but was proposed in 2017 to be used for language disorder without known biomedical aetiology (Bishop et al., 2017). This term is consistent with the International Classification of Diseases, 11th revision (ICD-11; World Health Organization, 2022) that includes DLD in the chapter "Mental, behavioural or neurodevelopmental disorders". The main features of DLD are persistent deficits in the acquisition, comprehension, production or use of language that are markedly below the age-expected level function and whose onset is during early childhood. These deficits interfere with daily life, for example, limit a person's ability to communicate. DLD coexists frequently with other NDDs, e.g. ASD and ADHD (World Health Organization, 2022).

DLD, which has a prevalence of about 7-7.5% (Norbury et al., 2016; Tomblin et al., 1997), increases the risk of reading difficulties (Botting, 2020; Miniscalco & Dahlgren Sandberg, 2010). Children with DLD may face difficulties in interacting with peers (Lloyd-Esenkaya et al., 2020). Additionally, it is a risk factor for other NDDs (Miniscalco et al., 2018; Miniscalco et al., 2006). About 75% of the individuals with DLD in childhood continue to meet diagnostic criteria in late adolescence and these impairments continue to impact daily functioning into early adulthood (World Health

Organization, 2022). Adults with DLD face an increased risk of psychiatric and social adaptation problems (Clegg et al., 2005).

1.8.4 ID

ID diagnosis requires a combination of deficits in intellectual functioning (IQ score of about 70 or below) and in adaptive functioning, and is classified with four severity levels: mild, moderate, severe and profound. Adaptive functioning refers to the capacity of meeting the socio-cultural and age-appropriate standards of functioning in daily life situations (American Psychiatric Association, 2013). Individuals with ID need support to varying degrees in daily life depending on the severity level. Prevalence of ID varies according to methodology and age of the population studied, but rates of about 1-1.3% are a common estimate (Fernell, 1996; Maulik et al., 2011). Other NDDs, e.g. ASD and ADHD are common in ID (Reilly & Holland, 2011; Tonnsen et al., 2016), while epilepsy, cerebral palsy, visual and hearing problems are common co-existing physical health conditions in ID (Liao et al., 2021). ID is a lifelong condition.

1.8.5 BORDERLINE INTELLECTUAL FUNCTIONING

Borderline intellectual functioning (BIF) is not a diagnosis per se, but rather a category that can be used to describe intellectual functioning in the range between 1 and 2 standard deviations below the normative mean, or as expressed in IQ scores a score between 71-85 (Greenspan, 2017). These ranges include about 13-14% of the population (Greenspan, 2017; Hassiotis, 2015). BIF has been reported to increase the risk of mental health problems (Emerson et al., 2010; King et al., 2019) and academic difficulties (Fernell & Ek, 2010; Peltopuro et al., 2014). While IQ scores in the range corresponding to BIF are not necessarily associated with other conditions, BIF can co-occur with ASD (Hedvall et al., 2014), ADHD (Sätilä et al., 2022), and language problems (Lundervold et al., 2008; Miniscalco et al., 2018). BIF is less researched than ID. It has been argued that BIF has not received sufficient attention and that there is a need for adaptations in school, work, and health care to meet the needs of this group (Fernell & Ek, 2010; Wieland & Zitman, 2016).

1.9 DIMENSIONALITY IN NDDS

NDD diagnoses are concepts based on clusters of symptoms, their frequency and severity. Several symptom-based criteria must be met for diagnosis. The symptoms comprise behaviours that are observable and occur in the general population to varying degrees. Research evidence on overlap and "incomplete" presentations of NDDs has supported a conceptualisation of NDDs as dimensional, meaning that they represent the extreme end of normally distributed cognitive abilities and/or continuous traits (Anckarsäter et al., 2008). The threshold between NDD and non-NDD based on number of symptoms or endpoints of normally distributed abilities is partially consensual (Gillberg, 2010; Thapar et al., 2017). Decisions on where the threshold is set may affect diagnostic conclusions (Gillberg, 2010).

ASD is an illustrative example of the continuity between what is considered typical development and clinical diagnosis. In diagnostic manuals, ASD is conceptualised categorically, however, autistic traits (also called autism-like features) are continuously distributed in the general population of children (Constantino & Todd, 2003; Hoekstra et al., 2007; Kamio et al., 2013; Posserud et al., 2006). This means that a person can have traits of the conditions without meeting all the criteria required for diagnosis. ASD is considered the extreme end of this continuum of traits (Lundström et al., 2012; Robinson et al., 2011). Similarly, based on genetic studies, ADHD has been suggested to be the extreme end of a dimensional trait, i.e. of the continuum of ADHD symptoms in the population (Faraone & Larsson, 2019).

1.10 ESSENCE

The umbrella term ESSENCE was coined by Christopher Gillberg and comprises NDDs, as well as a range of behavioural phenotype syndromes and rare epilepsy syndromes. These conditions have an early onset causing impairment and affecting development. Early manifestations can be unspecific and problems in one or several developmental areas should alert clinicians of the need for further examinations. These manifestations encompass general developmental delay, motor difficulties, speech and language delay, communication and social interaction problems, hyperactivity, impulsivity, attention problems, hypoactivity, behaviour problems, sleep difficulties and feeding problems (Gillberg, 2010). ESSENCE emphasises the changes in clinical symptoms in NDDs through early years (Fernell & Gillberg, 2023), and that overlapping symptoms and co-existence of disorders are highly common, thus highlighting the need for multidisciplinary assessments and intervention (Gillberg, 2010).

1.11 DIAGNOSTICS OF NDDS

Identification and diagnosis of NDDs is crucial in several respects. Diagnosis enables access to services provided by habilitation and/or psychiatry, educational supports, and, depending on the condition, specific rights by law (in Sweden, The Swedish Act concerning Support and Service for Persons with Certain Functional Impairments). Treatments and intervention are more easily accessed. For example, early intervention in ASD might enhance the child's learning opportunities (Lord et al., 2020) and might have a substantial impact on the level of functioning in some cases (Howlin & Moss, 2012). In ADHD, medication has been shown to reduce ADHD symptoms (Faraone et al., 2015). Lastly, diagnosis is a means of communication between involved parties; those affected by the diagnosis, their relatives and professionals. It enables individuals and parents to search for information about a condition on their own, that will make life more "manageable" after diagnosis (Hansson Halleröd et al., 2015).

Children with suspected DLD in Sweden are often identified through the language screening offered in the Child Healthcare Centres. The screening is performed by nurses at Child Healthcare Centres with standardised instruments at ages 2.5 (Mattsson et al., 2001) and 3 years (Westerlund & Sundelin, 2000). Children screening positive are referred to a speech and language therapist for further assessment. Child Healthcare Centres in some counties offer assessment of social interaction skills together with the 2.5-year language screening, using the Modified Checklist for Autism in Toddlers (Robins et al., 2014). A proportion of children with suspected ASD are identified during these procedures. Not all children with ASD are identified at that age, and referral for assessment later in childhood when social demands increase is also common. As regards ADHD, there is no general screening but children with symptoms are referred for assessment due to problems in school or due to parental awareness or clinician awareness when seeking health care for other symptoms.

Diagnostic assessment of ADHD and ASD requires a multidisciplinary team of experienced professionals including a medical doctor and psychologist, and, when necessary other professionals (National Institute for Health and Care Excellence, 2019; Socialstyrelsen, 2022). DLD is diagnosed by a speech and language pathologist after comprehensive assessment. Diagnostics of ID is

conducted by a psychologist in collaboration with a medical doctor that assess potential causal factors and comorbidities (The Swedish Neuropediatric Section of The Society for Swedish Paediatricians, 2020). As highlighted in the ESSENCE framework and other guidelines, coexisting conditions should always be considered in a diagnostic process (Gillberg, 2010; National Institute for Health and Care Excellence, 2019; Socialstyrelsen, 2022), which further emphasises/advocates multidisciplinary assessment. The assessments typically include a parental interview on the child's developmental history and symptoms including those related to specific NDD diagnoses and potential comorbidity, assessment of medical history, (when possible) interview with the child/adolescent, assessment through observation and interaction with the child/adolescent, assessment with psychological and/or, in the case of DLD, language instruments and assessment of functional level (National Institute for Health and Care Excellence, 2019; Socialstyrelsen, 2022). Observational instruments, interviews and rating scales targeting specific domains of symptoms are often used in assessment, and the use of valid, reliable and fair instruments in assessment is fundamental (American Educational Research Association, 2014). However, none of these instruments is sufficient for diagnosis on their own but may be part of a broader assessment.

Assessment of intellectual functioning is central to ID since it is required for diagnosis, and it is among the recommended assessments in diagnostic guidelines of ASD (National Institute for Health and Care Excellence, 2017). Furthermore, a comprehensive neuropsychological evaluation including intellectual, executive, adaptive functioning among other cognitive areas is valuable in characterising strengths and weaknesses, to aid in differential diagnostic and to optimise treatment planning in ASD (Braconnier & Siper, 2021) and other NDDs. WISC is frequently used in neuropsychological assessment in ADHD (Thaler et al., 2013) and ASD (Braconnier & Siper, 2021) to obtain information on a child's or adolescent's intellectual functioning and the functions assessed in WISC, identify strengths and deficits and tailor accommodations in school and daily life. As earlier highlighted, there is no universal cognitive profile in ASD. For that reason, diagnosis of ASD (or any other NDD) or exclusion of such, based on WISC results is neither possible nor advisable. However, assessment with WISC provides important insights on the individual strengths and weaknesses that easily may be overlooked without assessment.

To sum up, the relationship between cognitive functions and NDDs has been the focus in several studies. These have highlighted the association between early language milestones and intellectual functioning later in childhood (Peyre et al., 2017; Vlasblom et al., 2019), between working memory and ADHD (Kasper et al., 2012; Ramos et al., 2020) and between IQ and outcome of ASD (Billstedt et al., 2007; Pickles et al., 2020). However, the relationship between number of words used in early age and later intellectual functioning has not been explored. Furthermore, there is a need of clarification if associations with intellectual functioning, found in NDD groups, also are mirrored in general population samples where ESSENCE symptoms are presented in a continuum. Last, the well-established relationship between IQ and academic achievement in the general population samples needs to be elucidated in ADHD and ASD.

2 AIMS

The overall aim of the thesis is to examine the relationship between cognition and ESSENCE symptoms in a sample of children from a Swedish population at ages 7-8 years, as well as to explore the importance of intellectual functioning for academic achievement in ADHD and ASD.

Specific aims are:

- To study whether limited expressive vocabulary at 2.5 years of age is associated with intellectual functioning at age 7-8 years **(Study I)**.

- To examine whether working memory, measured with the WMI in WISC, is associated with behavioural regulation deficits and hyperactivity/inattention symptoms in a sample of 7-8-year-old drawn from the general population, whether general intellectual functioning is associated with behavioural regulation and hyperactivity/inattention and whether those with low WMI fulfil inattentive ADHD criteria **(Study II)**.

- To describe the distribution of autistic traits in the abovementioned sample, to study if intellectual functioning is associated with autistic traits and to study the association between autistic traits and behavioural difficulties **(Study III)**.

- To investigate if Wechsler Intelligence scales predict academic achievement and/or grades in children with ADHD and/or ASD, by conducting a systematic review and a meta-analysis **(Study IV)**.

3 MATERIALS AND METHODS

3.1 THE SWEDISH ENVIRONMENTAL LONGITUDINAL, MOTHER AND CHILD, ASTHMA AND ALLERGY (SELMA) STUDY

Studies I, II, and III are part of the SELMA study, a longitudinal pregnancy cohort study from the general population in the county of Värmland, Sweden. The primary objective of the SELMA study is to investigate prenatal exposure to environmental factors and how they affect children´s health and development. Prenatal exposure to phthalates has been associated with language delay in preschool-aged children (Bornehag et al., 2018), and prenatal bisphenol F exposure has been associated with cognitive function at age 7 years (Bornehag et al., 2021).

To establish the cohort, pregnant women (median 10th week of pregnancy) were recruited at their first visit in antenatal care centres in the county of Värmland, from September 2007 to March 2010. Not understanding written Swedish (for questionnaire completion), not being resident in the county or moving outside of it or being pregnant beyond week 22 were exclusion criteria to entering the study. During the recruitment period, 8,394 women were reported pregnant, of which 6,658 were invited to participate in SELMA. Of those, 2,582 (39%) agreed to participate (Bornehag et al., 2012). Those declining participation filled in a short questionnaire, whose results showed that the percentage of having completed college or university studies was higher in participating mothers. Furthermore, smoking was less prevalent and allergy symptoms more prevalent in participants. The final study group consisted of 1,954 children after dropout due to miscarriages and other circumstances, and comprised the SELMA cohort. A detailed report of the recruitment process has been published (Bornehag et al., 2012).

Table 1 Participants and methods in thesis

Study	**I Language**	**II Working memory**	**III Autistic traits**	**IV IQ and academic achievement**
Design	Longitudinal (SELMA)	Cross-sectional (SELMA)	Cross-sectional (SELMA)	Systematic review and meta-analysis
Participants n	549	865	874	ADHD n= 1,834 ASD n=176
Sex	271 boys, 278 girls	441 boys, 424 girls	444 boys, 430 girls	*
Age	2.5 years and 7-8 years	7-8 years	7-8 years	6-16 years
Instruments	Language screening WISC-IV ESSENCE-Q Raven's SPM Parental Questionnaire	WISC-IV BRIEF SDQ FTF	WISC-IV SRS SDQ Parental Questionnaire	Scientific databases

*= sex distribution was not reported in all studies included in the review

Note ADHD = Attention-Deficit/Hyperactivity Disorder; ASD = Autism Spectrum Disorder; BRIEF = Behavior Rating Inventory of Executive Function; ESSENCE-Q = ESSENCE-Questionnaire; FTF = Five to Fifteen (questionnaire); Raven's SPM = Raven's Standard Progressive Matrices; SDQ = Strengths and Difficulties Questionnaire; SELMA = Swedish Environmental Longitudinal, Mother and child, Asthma and allergy (study); SRS = Social Responsiveness Scale; WISC-IV= Wechsler Intelligence Scale for Children, Fourth edition

3.2 STUDY I, II, AND III

3.2.1 PROCEDURE

Participating mothers completed questionnaires included in the SELMA study protocol during pregnancy and at different times after the child was born. Information regarding maternal education level and maternal smoking was collected by a questionnaire at cohort recruitment and was used in study I as covariates.

At age 2.5 years, the children participated in the regular language screening program at Child Healthcare Centres, and screening information was then sent to the SELMA study organisation. Data from the language screening are used in study I.

At age 7-8 years, the children were invited to participate in a health and developmental examination including blood sampling, physical examination and neuropsychological assessment. The aim was to examine 1,000 participants. The children participated in assessment with WISC-IV (studies I-III) and their parents filled in questionnaires about the children's development, EF and behaviour (study II and III). The assessments took place between September 2015 and August 2018.

As part of the neuropsychological assessment at age 7-8 years, the parents were interviewed regarding concern about development (study I) and were also asked if their children had externally received an NDD diagnosis (study III). To obtain parental IQ as covariate, one parent (most often the mother) to each participating child was tested with a non-verbal test of general cognitive ability (study I).

3.2.2 PARTICIPANTS

All participants in studies I-III were from the SELMA cohort. Study I included 549 children (271 boys, 278 girls) with data from the language screening at the Child Healthcare Centres at age 2.5 years, WISC-IV and questionnaire in the SELMA study at age 7-8 years, and covariates. In study II, the study group included 865 children (441 boys, 424 girls), and in study III of 874 children

(444 boys, 430 girls), mean age 7.9 years, with data on WISC-IV and the questionnaires used in the respective study.

3.2.3 INSTRUMENTS

3.2.3.1 ESSENCE-QUESTIONNAIRE (ESSENCE-Q)

The ESSENCE-Questionnaire (ESSENCE-Q) is a short screening for recognition of children who might need further assessment. It includes 12 questions covering the following developmental domains: general development, motor development/milestones, sensory reactions, communication/language, activity/impulsivity, attention/concentration, social interaction, behaviour, mood, sleep, feeding and absences. Reply options for each question are "No" (0 points), "Maybe/A little" (1 point), and "Yes" (2 points), rendering a total score with a range of 0-24 points. ESSENCE-Q has good diagnostic validity and high sensitivity (Hatakenaka et al., 2016; Hatakenaka et al., 2017). In study I, parents were interviewed with ESSENCE-Q to evaluate parental developmental worries. Similar to Reilly et al. (2019), the ESSENCE-Q total score was used to compare groups.

3.2.3.2 LANGUAGE SCREENING

The 2.5-year language screening offered at Child Healthcare Centres consists of a nurse examination and a parental questionnaire (Mattsson et al., 2001). One of the questions in the parental questionnaire is "How many words can your child say? Words need not be spoken correctly but you must be able to understand what the child means." Response alternatives are 0-25, 25-50, and more than 50 words. Number of words in two categories (50 words or fewer, more than 50 words) was utilised to measure expressive vocabulary in study I.

3.2.3.3 THE BEHAVIOR RATING INVENTORY OF EXECUTIVE FUNCTION (BRIEF)

BRIEF (Gioia et al., 2000) is a rating scale for assessment of EF in daily contexts. Its 86 items are divided into eight clinical scales and provide two composite measures, Behavioral Regulation Index (BRI) and Metacognition Index, and a Global Executive Composite. The norms are age- and sex-

specific. Composite T-scores of ≥65 correspond to 1 ½ SD above the mean and are clinically significant. BRIEF is reported to differentiate between children with ADHD and controls (Davidson et al., 2016; McCandless & O' Laughlin, 2007; Reddy et al., 2011). BRIEF's internal consistency is high and correlational analysis has supported its convergent and divergent validity (Gioia et al., 2000). BRI was used in study II to measure behavioural regulation (inhibitory control, flexibility and emotional control).

3.2.3.4 THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ)

SDQ (Goodman, 1997) is a behavioural screening instrument with satisfactory to good psychometric properties (Essau et al., 2012; Goodman, 2001). It includes 25 items that comprise five scales with five items each: Emotional problems, Conduct problems, Hyperactivity/Inattention, Peer relationship problems and Prosocial behaviour (score range 0-10 for each scale). Higher scores indicate more difficulties, with the exception of prosocial behaviour where higher scores reflect more prosocial behaviour. A total difficulties score (SDQ Total Difficulties score, range 0-40) is computed by summing the scores of all scales with the exception of Prosocial behaviour. SDQ has been validated in Sweden (Malmberg et al., 2003) and cut-offs have been reported (Smedje et al., 1999). The Swedish parental version of SDQ was used in Study II and III.

3.2.3.5 THE FIVE TO FIFTEEN QUESTIONNAIRE (FTF)

The FTF (Kadesjö et al., 2004) is a parental questionnaire designed to assess child development and behaviour. Its psychometric properties are acceptable to good (Kadesjö et al., 2004; Lambek & Trillingsgaard, 2015). FTF is a valid screening of developmental disorders (Airaksinen et al., 2004; Korkman et al., 2004). The items comprising the subdomain "Attention and concentration" are the same as the DSM-IV (American Psychiatric Association, 1994) ADHD inattention symptoms, and were used in Study II to measure the proportion of children fulfilling these criteria.

3.2.3.6 THE SOCIAL RESPONSIVENESS SCALE (SRS)

Autistic traits were assessed in Study III with the parental version of SRS (Constantino & Gruber, 2005), which is a quantitative questionnaire of 65 items used for ages 4-18 years. The SRS rates the frequency of behaviours in social communication and social interaction, and of restrictive, repetitive behaviours and interests, behaviours related to ASD. The standardised scores used in SRS are T-Scores (mean=50, SD=10). The norms are sex-based. The SRS Total T-Score has a range of 34-127 for boys and 35-142 for girls. According to the SRS manual, T-Scores above 60 indicate clinically significant deficits that affect daily social interactions. T-Scores of 60-75 are in the range described as mild to moderate, and T-Scores of 76 or higher are in the severe range. The parental version of SRS shows high internal consistency (Constantino & Gruber, 2005) and correlates significantly with the Autism Diagnostic Interview-Revised (Constantino et al., 2003).

3.2.3.7 WISC-IV

Intellectual functioning was assessed in studies I-III with the Swedish version of WISC-IV (Wechsler, 2003a). FSIQ, GAI and the indexes have a mean of 100 and SD of 15. The reliability coefficients for FSIQ and the indexes are generally high. The WISC-IV four-factor structure is psychometrically validated by factor-analytic studies (Wechsler, 2003b).

3.2.3.8 THE RAVEN'S STANDARD PROGRESSIVE MATRICES (SPM)

The Raven's SPM (Raven et al., 1998) is a non-verbal test of general cognitive ability. It includes five sets (A to E) with items of progressively increasing difficulty. A shortened version of Raven's SPM (Bouma, 1996; Van der Elst et al., 2013) consisting of sets B, C and D was in Study I administered to one of the parents (most often the mothers) to obtain data on IQ to control for heredity. Normative data are provided by a scoring programme (Van der Elst et al., 2013).

3.3 STUDY IV

3.3.1 PROCEDURE

The systematic review and meta-analysis were pre-registered in the International prospective register of systematic reviews, PROSPERO, with registration number CRD42022338617, and followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

To investigate if Wechsler intelligence scales predict academic achievement and/or grades in children with ADHD and/or ASD, peer-reviewed case-control, cross-sectional and longitudinal studies written in English and published between January 2000 and February 2023 were retrieved through scientific databases. A combination of terms in the following areas was used: intellectual functioning or Wechsler scales, academic achievement, ADHD and ASD. The first search was performed in June 2022 and an updated search was performed in February 2023.

The studies rendered by the searches were screened independently by two reviewers (the PhD student and the principal supervisor) for decision of inclusion or exclusion from the review. In inconclusive cases and for potentially eligible studies, full text was retrieved and screened for eligibility. These procedures were performed independently by the reviewers that were blind to each other's decisions until it was time for discussion and proceeding to the next step. Differences of opinion were resolved by discussion. The two reviewers extracted relevant data for the review and conducted risk of bias assessment independently from each other.

Synthesis methods were tabulation of the included studies, narrative synthesis and meta-analysis.

3.3.2 PARTICIPANTS

The eligible population was children with ADHD and/or ASD diagnosis, assessed with Wechsler Intelligence Scales (WISC or the Wechsler Abbreviated Scale of Intelligence, WASI; Wechsler, 1999, 2011) at ages 6-16 years, and attending school. Academic achievement had to be reported with

quantitative measures for studies to be considered eligible. Comorbidity with ID was exclusion criterion and studies were considered ineligible if they included participants with ID or if the study group included both cases with ID and without ID and where the data could not be separated. Inclusion criteria in the study was that the diagnosis was based on clinical diagnostic decision leaving out studies using only questionnaire to confirm the diagnosis.

3.3.3 INSTRUMENTS

The searches were performed in three databases, the PubMed, PsycINFO and Education Research Complete. The Newcastle-Ottawa Scale (Wells, 2009), was used for risk of bias assessment, since it is suitable for assessing the quality of non-randomised studies.

3.4 ANALYSIS AND STATISTICAL METHODS

All statistical analyses in studies I-III were performed with IBM SPSS, with the exception of the quantile regressions in study III that were performed using R Studio. The statistical significance threshold was set at $p < .05$. The meta-analyses were conducted with Meta-Essentials (Suurmond et al., 2017).

3.4.1 STUDY I

WISC-IV scores for the study group were compared to the norms with one-sample *t*-test. The study group was divided in two groups based on number of words at age 2.5 years: the children that used 50 words or fewer and the children that used more than 50 words. Mean cognitive scores for the groups were calculated. Comparison of cognitive scores between the groups was performed with independent samples *t*-test (two-tailed).

The associations between number of words at age 2.5 years and WISC-IV FSIQ, and index scores at age 7-8 years respectively were analysed with linear regression analyses, adjusted for sex, maternal education level, smoking during pregnancy and parental IQ. The proportion of children with a vocabulary of 50 words or fewer at age 2.5 years was compared with chi-square test of independence in the group of children FSIQ≤85 and the group with higher IQ. Comparison of ESSENCE-Q scores between groups was performed with Mann-Whitney U test.

3.4.2 STUDY II

Comparison between WISC-IV results for the total study group and the norms was performed with one-sample *t*-test. The percentage of children meeting cut-off in BRIEF-BRI and SDQ Hyperactivity/Inattention scale was calculated, and comparison of the proportion of boys and girls meeting the cut-off was compared with chi-square test.

We divided the study group into three subgroups based on results of WMI (WISC-IV) and results of BRIEF-BRI and/or SDQ hyperactivity/inattention symptoms. The subgroups were the following: i) children with adequate

working memory function ("*adequate WMI*"), ii) children with working memory deficits without reaching cut-off for additional behavioural regulation and hyperactivity/inattention problems ("*weak WMI*"), and iii) children with WMI deficits and additional behavioural regulation and hyperactivity/inattention problems ("*weak WMI/BR*"). The proportion of girls and boys between subgroups was compared with chi-square test. The number of children fulfilling DSM-IV inattentive ADHD criteria (measured with FTF) in the subgroups was calculated (completed questionnaire available for 498 children).

One-way between-groups analysis of variance (ANOVA) with the Tukey HSD test for post-hoc comparisons was conducted to analyse differences in WISC-IV index scores (VCI, PRI, PSI and GAI) between the working memory subgroups. Differences in the SDQ scale scores (Emotional problems, Conduct problems, Peer problems and Prosocial behaviour) between the working memory subgroups were explored with ANOVA with Welch's test. Post-hoc comparisons were performed with the Games-Howell test.

The relationship between WMI, BRIEF-BRI and SDQ Hyperactivity/Inattention was explored with Pearson correlation. The relationship between WMI and BRIEF-BRI, and SDQ Hyperactivity/Inattention, respectively, was examined with two separate multiple regression analyses including general intellectual ability (GAI), prosocial behaviour (SDQ), sex, and age as covariates.

3.4.3 STUDY III

Descriptive statistics for WISC-IV indexes, SRS and SDQ were analysed for the total study group and for both sexes. Sex differences in SRS Total Raw score and SRS Total T-Score were analysed with independent samples t-test. The proportion of boys and girls meeting cut-offs was compared with chi-square test of independence.

Pearson correlations were computed to assess the relationships between WISC-IV index scores and the SRS Total T-Score. To study the association between WISC-IV composite scores and SRS Total T-Score, two quantile regressions were performed using the following independent variables in the first

regression: a) FSIQ, age and sex, and in the second regression: b) VCI, PRI, WMI, PSI, sex and age. Both models estimated relations at each quartile of the distribution of the SRS Total T-Score. In addition, quantile regression was performed to study the association between the SRS Total T-Score and the SDQ Total Difficulties score. In this, the impact of SRS Total T-Score, FSIQ, age and sex on the SDQ Total Difficulties score was estimated at each quartile of the SDQ Total Difficulties score distribution. Lastly, the study group was divided in three groups based on the cut-offs of SRS. The mean SDQ scores of the three groups were computed.

3.4.4 STUDY IV

Meta-analyses examining correlations between FSIQ/estimated IQ and domains of achievement, and WISC-III/WISC-IV PSI and domains of achievement were conducted using random effects models. Heterogeneity was measured with the I^2 statistic. Meta-analysis with additional WISC composite scores could not be performed due to limited number of samples examining correlations between these scores and achievement.

3.5 ETHICS

All procedures performed in the studies for this thesis comply with the ethical standards stated in the Helsinki Declaration of 1975, as revised in 2008. All study participants in the SELMA study have provided written informed consent, and two ethics permits are applicable for this thesis; Dnr 2007/062 and Dnr 2015/177, Regional Ethical Review Board, Uppsala.

4 RESULTS

4.1 STUDY I

Of the 549 children (271 boys, 278 girls) in the study group, 36 children (6.6%; 22 boys, 14 girls) were reported to have an expressive vocabulary of 50 or fewer words at age 2.5 years, of which eight children (which constitutes 1.5% of the study group) were reported to have an expressive vocabulary of fewer than 25 words.

WISC-IV results for the total study group at age 7-8 years were in average range, except for WMI that was significantly lower and PRI that was significantly higher than the norm group's mean. Fifty-eight children (10.6%) in the study group had a FSIQ corresponding to the category of BIF, and six children (1.1%) in the study group had FSIQ scores of ≤70 which indicated possible ID. Children that used 50 words or fewer at age 2.5 years had lower WISC-IV scores at age 7-8 years, except for processing speed, than children who used more than 50 words at age 2.5 years. Their mean WMI was approximately 1 ½ SD below the norms, while FSIQ and VCI were about 0.5 SD below the norms.

The relationship between number of words at age 2.5 years and the index scores of WISC-IV at age 7-8 years was examined with linear regression analyses (one index as dependent variable in each analysis), adjusted for sex, maternal education level, smoking during pregnancy and parental IQ. In the analyses, vocabulary of ≤50 words at age 2.5 years, in relation to vocabulary of more than 50 words, was associated with lower FSIQ ($p = 0.001$), VCI ($p < 0.001$), WMI ($p < 0.001$) and PRI ($p = 0.045$) scores, at age 7-8 years.

Vocabulary of 50 words or fewer at age 2.5 years was more common in the group with FSIQ corresponding to ID or BIF compared to children with higher IQ, ($p < 0.002$). The parents of children that used 50 words or fewer at age 2.5 years reported more parental concern at age 7-8 years ($p = 0.011$).

4.2 STUDY II

This study included 865 children. All mean WISC-IV index scores in the study group were average except for mean WMI scores that were 89.9 index points, defined as low average, with 22% (every fourth boy, every fifth girl) scoring 1 ½ SD below the normative mean or lower (WMI score of 77 or below). In the parental questionnaires, 5.3% of the study group displayed behavioural regulation problems (higher BRIEF-BRI), with equal proportion between boys and girls. Higher SDQ Hyperactivity/inattention scores were reported in 7.2% in the study group, more often in boys than girls ($p < .01$).

Most of the children with working memory deficits according to WISC-IV scored average in BRIEF-BRI and SDQ hyperactivity/inattention indicating no additional behavioural regulation or hyperactivity/inattention problems, defined as "*weak WMI"* subgroup. This subgroup also displayed a high level of prosocial behaviour measured with SDQ. A subgroup including 36 children (4% of the total study group) had working memory deficits (WMI score of 77 or below) and additional behavioural regulation (BRIEF-BRI T-Score 65 or above) and hyperactivity/inattention problems (SDQ Hyperactivity/Inattention 7 points or more), which we defined as "*weak WMI/BR*" subgroup. This subgroup scored lower in SDQ Prosocial behaviour scale and had lower GAI, compared to the other subgroups. Eight of the children in this subgroup (data available for 24) fulfilled inattentive ADHD DSM-IV criteria according to the FTF.

As regards sex differences, working memory deficits in the total study group were more frequent in boys than girls. However, the proportion of boys and girls in the two subgroups with working memory deficits was equal.

BRIEF-BRI and SDQ Hyperactivity/Inattention scale correlated positively, while WMI correlated negatively with BRIEF-BRI and SDQ Hyperactivity/Inattention scale. In the regression analyses, WMI and prosocial behaviour were associated with BRIEF-BRI and SDQ Hyperactivity/Inattention. GAI was associated with SDQ Hyperactivity/Inattention, but not with BRIEF-BRI. The regression models explained 15-18% of the variance in BRIEF-BRI and SDQ Hyperactivity/Inattention scores.

4.3 STUDY III

The study consisted of 874 children (444 boys, 430 girls) with a mean age of 7.9 years. Mean FSIQ and WISC index scores in the study group were in the average range, except for WMI which was low average. Boys had slightly higher raw score of SRS (autistic traits), but after conversion to T-Scores, girls had marginally higher scores. SRS Total T-Scores were continuously distributed in the study group. Thirty-six children (4.1% of the study group) had scores within the mild clinical range of SRS (SRS Total T-Score 60-75) and 12 children (1.4% of the study group) had scores corresponding to the severe range (SRS Total T-Score ≥76). An equal proportion of boys and girls scored within these ranges.

SRS Total T-Score correlated negatively with FSIQ, and with the four indexes in WISC-IV (VCI, PRI, WMI, PSI). Results of the first quantile regression showed significant negative associations between FSIQ and SRS Total T-Score throughout all percentiles of the distribution of SRS Total T-Score, and this association was more evident in the upper ends of this distribution. The second quantile regression model showed significant negative associations between VCI/verbal comprehension and SRS Total T-Score, and between WMI/working memory and SRS Total T-Score throughout all the percentiles of the SRS Total T-score distribution. PRI/Perceptual reasoning and PSI/ processing speed were not associated with SRS Total T-Score in the model. Sex was associated with SRS Total T-Score in both models. The quantile regression examining how autistic traits and intellectual functioning influence behavioural difficulties, showed significant positive associations between the SRS Total T-Score and the SDQ Total Difficulties score. The children that displayed more behavioural difficulties showed a greater degree of autistic traits. Female sex was associated with lower SDQ Total Difficulties score. FSIQ was not associated with the SDQ Total Difficulties score.

The group of children scoring in the severe range of SRS, i.e. those that displayed most autistic traits, had elevated SDQ Total Difficulties scores. The mean SDQ Total Difficulties score for this group was above the cut-off.

4.4 STUDY IV

The searches rendered 2,431 results, reduced to 1,849 after de-duplication. Screening of the records identified 12 studies that were included in the systematic review. Nine studies included samples with ADHD and three included samples with ASD. Following the prerequisite in the systematic review protocol, the studies used Wechsler scales to assess intellectual functioning. Academic achievement was assessed with assessment instruments in all but two studies that used grades. Risk of bias was low in three studies and medium in nine studies.

In the narrative synthesis of ADHD studies, we found that FSIQ/estimated IQ, working memory abilities and verbal comprehension abilities predicted academic achievement in reading, written language and mathematics. Slower processing speed affected reading and maths fluency in ADHD. Furthermore, FSIQ, verbal comprehension abilities and processing speed correlated with overall grade at school year 9. Higher verbal comprehension abilities increased the likelihood of receiving passing grades 3-4 years later.

In the ASD studies, we found that FSIQ, working memory and processing speed emerged as significant predictors of academic achievement. Verbal comprehension and perceptual reasoning abilities also influenced academic achievement, but, due to the limited number of studies, their precise contribution is less clear. No studies had evaluated the relationship between Wechsler intelligence scale results and grades in ASD.

Two studies including a total of six samples with ADHD were included in meta-analyses focusing on FSIQ/estimated IQ and processing speed in relation to three sets of outcomes; word reading, written language and mathematics. The overall weighted correlations between FSIQ/estimated IQ and the domains of academic achievement were moderate. Results of the meta-analyses between processing speed and academic achievement also showed moderate overall weighted correlations.

The samples including children with ASD were too few for a meta-analysis to be performed.

5 DISCUSSION

The studies in this thesis have examined the relationship between cognitive functioning and ESSENCE feautures in a group of 7–8-year-old children from a Swedish population sample, as well as the relationship between intellectual functioning and academic achievement in the ESSENCE conditions ADHD and ASD. We found that number of spoken words at 2.5 years of age was related to intellectual functioning at early school age. At age 7-8 years, working memory deficits measured with WISC-IV coexisted with ADHD symptoms in a small subgroup in the sample. Intellectual functioning was negatively associated with autistic traits measured continuously. Finally, general intellectual functioning (FSIQ) was associated with academic achievement in clinical samples with ADHD and ASD.

5.1 LANGUAGE AND INTELLECTUAL FUNCTIONING

Study I investigated whether language problems at 2.5 years of age (measured with number of spoken words) were associated with intellectual functioning (measured with WISC-IV) at age 7-8 years. Thirty-six children (6.6%) in the study group were reported to have an expressive vocabulary of 50 words or fewer, which is consistent with the prevalence rates of DLD (Norbury et al., 2016; Tomblin et al., 1997).

Having used 50 words or fewer at age 2.5 years was associated with lower general intellectual functioning (FSIQ), verbal comprehension, perceptual reasoning, and working memory at age 7-8 years. Parental concern regarding development at that age was reported more often in the group that used 50 words or fewer at age 2.5 years. The findings confirm existing knowledge of the association between early language development and intellectual functioning later in life (Flensborg-Madsen & Mortensen, 2018; Peyre et al., 2017; Vlasblom et al., 2019). Furthermore, working memory results in this group were about 1 ½ SD lower than the norms at age 7-8 years. Working memory contributes to academic achievement (Caemmerer et al., 2018; Titz & Karbach, 2014), and may increase the risk of facing academic difficulties

(Alloway et al., 2009). Deficits in working memory also occur frequently, albeit not in all individuals, in NDDs such as in ADHD (Ramos et al., 2020), and in specific learning disorders (Moll et al., 2016). Therefore, early limitations in expressive vocabulary might be associated with additional difficulties in early school years.

The proportion of children scoring within the range of ID and BIF was in accordance with current prevalence rates (Hassiotis, 2015; Maulik et al., 2011). Significantly more children within these IQ ranges had early expressive vocabulary limitations than the children with higher IQ. However, not all children with ID or BIF scores at age 7-8 years had limited expressive vocabulary at age 2.5 years, suggesting that children in early school years that have IQ scores in the BIF or ID range might not have had obvious language delay at age 2.5 years. Consequently, measuring how many words children are using at age 2.5 years is not sufficient to identify children with later BIF or ID but it is indicative that a child might display further developmental difficulties.

5.2 WORKING MEMORY FUNCTION

The mean working memory function score in the SELMA sample was about 10 index points below the norms. Lower working memory scores have also been reported in a different Swedish sample (Tallberg et al., 2021). In contrast, the mean perceptual reasoning scores in studies I-III were about six index points higher than the norms. The norm group for the Swedish version of WISC-IV is British. Swedish children might have disadvantage in verbal working memory tasks and certain advantage in visual fluid reasoning tasks compared to the British norm group. Since computers, promoting visual skills, are frequently used in Swedish schools, it might be that the educational system has an impact on this uneven profile. However, it is not known if these differences also occur in younger and older children, nor if mean of the visual working memory scores would also be low in Swedish children.

5.3 WORKING MEMORY AND ADHD SYMPTOMS

In a group of 865 children, study II examined whether WISC-IV WMI was associated with behavioural regulation deficits (measured with BRIEF-BRI) and hyperactivity and inattention symptoms (measured with SDQ Hyperactivity/Inattention scale), and whether general intellectual functioning was associated with behavioural regulation deficits, hyperactivity and inattention symptoms. We were also interested to find out if children with low WMI fulfilled inattentive ADHD criteria (reported by parents in the FTF).

A large proportion of children in the study group (18%) displayed working memory deficits but without behavioural regulation and/or hyperactivity/inattention problems, and only to a low degree, if any degree at all, met inattentive DSM-IV criteria. This contrasts with studies showing that children with low working memory are reported to display inattention and EF deficits to a great extent (Alloway et al., 2009; Gathercole et al., 2008; Holmes et al., 2014). This may be due to the use of different instruments to measure working memory, and the use of parental vs teacher ratings. In addition, this subgroup of children displayed a higher level of prosocial behaviour. It might be so that prosocial behaviour has a protective function or that it is facilitated by the lack of ADHD symptoms.

Furthermore, 4% in the study group displayed working memory deficits accompanied with behavioural regulation and/or hyperactivity/inattention problems, most likely corresponding to a clinical ADHD group. Additionally, this subgroup displayed less prosocial behaviour and elevated score in the Conduct problems scale in SDQ, indicating that the combination of deficits in working memory, in behavioural regulation and in attention seems to be accompanied by additional problems. General intellectual ability (GAI), verbal comprehension and processing speed in this subgroup were lower than the norms and in the other subgroups (except for PSI that also was lower in the subgroup with working memory deficits only), which resembles findings in clinical ADHD groups (Kramer et al., 2020; Tallberg et al., 2021).

In the regression analyses, using behavioural regulation and hyperactivity/inattention scores as dependent variables and working memory,

prosocial behaviour, GAI and sex as independent variables, we found that the models explained only 15-18% of the variance in behavioural regulation and hyperactivity/inattention scores. This resembles the findings of Colbert and Bo (2017), where a significant percentage of the variance in inattentive behaviours was not explained by WMI. This suggests that other factors, maybe contextual (e.g. structure at home), explain the rest of the variance.

To sum up, WISC-IV WMI and continuous measures of behavioural regulation and hyperactivity/inattention deficits are negatively associated with each other, but working memory deficits are not always accompanied by behavioural regulation and hyperactivity/inattention problems at clinically significant levels.

5.4 INTELLECTUAL FUNCTIONING AND AUTISTIC TRAITS

The distribution of autistic traits in a sample with equal proportions of boys and girls was explored in study III. We also examined the relationship between WISC-IV results and autistic traits (SRS scores), and between autistic traits and behavioural difficulties (SDQ total scores).

Similar to previous studies (Constantino & Todd, 2003; Hoekstra et al., 2007; Kamio et al., 2013; Posserud et al., 2006), autistic traits were continuously distributed in the study group, with no clear line between those who met SRS cut-offs and those who did not (Constantino & Todd, 2003; Kamio et al., 2013), which supports the conceptualisation of ASD as a dimensional disorder (Thapar et al., 2017). In the study group, 1.4% of the children had autistic traits to the extent that a clinical ASD diagnosis was probable, and an additional 4.1% had scores in the mild to moderate range of the SRS that may reflect deficits that occur in children with mild ASD or subthreshold social impairments according to the SRS manual (Constantino & Gruber, 2005).

Interestingly, the proportion of boys and girls within these ranges did not differ. This is not the case in clinical ASD diagnosis in childhood where there is a predominance of boys (male-to-female 4:1) receiving clinical ASD diagnosis (Fombonne, 2009). However, a male-to-female ASD ratio of about 3:1 has been concluded in a meta-analysis (Loomes et al., 2017), and as low as about 2:1 for high scorers in parental ratings of autistic traits (Loomes et al., 2017; Posserud et al., 2006). In addition, several studies of missed ASD diagnosis within adult psychiatric population have reported even sex ratios (Eberhard et al., 2022; Nyrenius et al., 2022), possibly suggesting that the sex ratio in ASD is more even than previous believed, and that screening for ASD in childhood might identify particularly girls with ASD.

The regression analyses showed negative associations between intellectual functioning and autistic traits, which were more pronounced in those displaying a greater degree of traits, and negative associations between verbal comprehension and autistic traits, and working memory and autistic traits. The relationship between autistic traits and behavioural difficulties was positive, and the group with autistic traits in the severe range of the SRS had behavioural difficulties mean score above the cut-off of the SDQ. These findings are in

accordance with other studies that have shown a relationship between intellectual function and autistic traits (Ryland et al., 2014), autistic traits and behavioural difficulties (Saito et al., 2017), and highlighted the connection between ASD and verbal ability (Silleresi et al., 2020). In sum, displaying higher degree of autistic traits is related to decreases in general intellectual functioning scores, verbal comprehension and verbal working memory, as well as increased risk of behavioural difficulties.

5.5 INTELLECTUAL FUNCTIONING AND ACADEMIC ACHIEVEMENT IN ADHD AND/OR ASD

The systematic review study (study IV) investigated if Wechsler scales predict academic achievement and/or grades in children with ADHD and/or ASD, by conducting a systematic review and meta-analysis.

In the included studies, general intellectual functioning was the strongest predictor of academic achievement (reading, writing and mathematics) relative to the other WISC cognitive domains in ADHD (Mayes & Calhoun, 2007; Zendarski et al., 2017) and ASD (Mayes & Calhoun, 2008). The influence of verbal reasoning and conceptualisation, perceptual reasoning, working memory and processing speed (all measured with WISC) was assessed to different extents in the studies and the degree of their influence varies among studies. In general, the findings on WISC and academic achievement in ADHD and ASD are in line with what is known on intellectual functioning in the general population (Neisser et al., 1996; Titz & Karbach, 2014; Wechsler, 2003b), and the findings of recent systematic reviews on the role of working memory in reading (McDougal et al., 2022), and mathematics (Kanevski et al., 2022) in ADHD.

Furthermore, in the meta-analyses with ADHD samples, general intellectual functioning correlated moderately with academic achievement. Processing speed correlated moderately with written language and mathematics, and almost moderate with reading. Slower processing speed has been reported in ADHD (Kramer et al., 2020; Thaler et al., 2013), and been associated with weaker academic skills in ADHD (Cook et al., 2018). Some of the correlations differed in magnitude between studies, probably due to differences in sample characteristics, which, in turn, also reflects the heterogeneous nature of ADHD.

The correlations between intellectual functioning and academic achievement were moderate, indicating that other factors also influence achievement. EFs (Zelazo & Carlson, 2020) and motivation (Lavrijsen et al., 2022) play an important role in academic achievement and influence academic outcomes in ADHD (Biederman et al., 2004; Smith et al., 2020) and ASD (St. John et al.,

2018). Furthermore, the impact of learning environment needs to be considered. Sensory stimuli and distractions in classroom, as well as executive demands often pose challenges for children with ADHD and/or ASD (Ashburner et al., 2010; Kos et al., 2006), which, in turn, may affect learning and academic achievement. Increased understanding of the factors related to achievement in both conditions is vital for creating environments and practices that promote academic success in children with ASD and ADHD (Keen et al., 2016; Zendarski et al., 2017). Accommodations have been suggested to improve school performance in ASD (Leifler et al., 2021), and visual supports and self-monitoring strategies have been found effective (Watkins et al., 2019). For ADHD, educational accommodations and interventions, including close family-school partnership, behavioral classroom interventions, individualised instructional supports (Wolraich et al., 2019) and modifications in classroom environment (National Institute for Health and Care Excellence, 2019) are recommended.

Lastly, only two studies (Ek et al., 2011; Tallberg et al., 2021) have assessed the relationship between WISC and grades, which limits the conclusions that the studies can generate, but the importance of verbal comprehension for academic achievement in ADHD is highlighted in both studies.

None of the studies included in this thesis focused on early expressive vocabulary and later academic achievement in ADHD or ASD. Considering the results of study I and IV, that there is an association between early expressive vocabulary and VCI (study I), and that there seems to be a relationship between VCI and academic achievement (study IV), the need for alertness for delayed language development should be emphasised. This is supported by a recent study showing that expressive language abilities as early as at age 16-30 months contribute to academic achievement at school year 9 (Dale et al., 2023).

5.6 STRENGTHS AND LIMITATIONS

The main strength of studies I-III is the large sample size with children from the general population, thus covering a broad range of intellectual functioning scores, and an equal proportion of boys and girls. Additional strengths are the inclusion of well-validated instruments that are used in several clinical, educational and research contexts, that experienced psychologists conducted the assessment and the standardised format for data collection including collection of significant covariates such as parental IQ. Additional strengths, in study I, the prospective longitudinal design, and in study IV, the review process in which the reviewers were blinded and performed independent full-text assessment and risk of bias assessment.

The main limitation of study I is that a proportion of children with expressive vocabulary limitations at 2.5 years of age did not take part in the 7-8 year assessment, thus limiting the number of participants in this group. Furthermore, teacher questionnaires were not administered in studies II and III and no clinical evaluation of ADHD or autistic traits was conducted in study II and in study III, which are limitations in these studies. Limitations in study IV are the limited number of samples included in the meta-analyses and the modest number of ASD studies that affects the conclusions that can be drawn as regards WISC and academic achievement in ASD.

6 CONCLUSIONS AND CLINICAL IMPLICATIONS

The studies included in the thesis have shown that:

- Limited use of words at age 2.5 years was associated with lower cognitive scores at age 7-8 years. Number of spoken words at 2.5 years might be a useful marker for intellectual functioning at early school age (Study I).
- Working memory deficits measured with WISC WMI do not always signal additional behavioural regulation and/or hyperactivity/inattention problems in 7-8-year-olds, and prosocial behaviour might play a role in this. A subgroup of about 4% displayed a combination of working memory deficits and the additional aforementioned problems (Study II).
- Autistic traits were continuously distributed in the general population of children. A proportion of children displayed an elevated level of autistic traits. Intellectual functioning, verbal comprehension and verbal working memory were negatively associated with autistic traits. Autistic traits, but not intellectual functioning, were associated with behavioural difficulties. Elevated levels of autistic traits in the general population might be accompanied with a risk of additional difficulties (Study III).
- General intellectual functioning (FSIQ) and processing speed were associated with achievement in reading, written language and mathematics in ADHD (Study IV).

As regards clinical implications, when considering the associations found between early expressive vocabulary and intellectual functioning at early school years, the importance of language intervention, stimulating vocabulary and cognitive skills, and monitoring cognitive development in children with early vocabulary limitations cannot be stressed enough. Children with limited expressive vocabulary should be neuropsychologically screened at school start.

As evidenced in working memory results in the SELMA sample, not all children with low scores have coexisting difficulties with behavioural

regulation and/or inattentive and hyperactive behaviours at 7-8 years. This is somehow expected, particularly when considering the continuous nature of functions and traits in the general population. However, it also underlines the importance of keeping a broad perspective and conducting assessments combining cognitive tests and questionnaires (always together with developmental interviews), as well as the importance of clinical experience, when assessing children referred for neuropsychological assessment. In addition, despite a large proportion of children displaying working memory deficits only, low working memory scores or high behavioural difficulties scores should alert clinicians to collect more information on a child's functioning.

Furthermore, the significance of prosocial behaviour for social relationships is intuitive. The results highlight the need for promoting prosocial behaviour in children with NDD symptoms, but also in general.

As regards autistic traits, the main implication of the results is that an elevated level of autistic traits may be accompanied by additional difficulties in verbal function and working memory. Children showing higher levels of autistic features may need additional support in school and daily life.

Lastly, study IV illustrates the importance of assessing intellectual functioning in children with ADHD or ASD in order to predict academic achievement, and at the same time being aware that there are other factors that influence academic achievement.

7 FUTURE PERSPECTIVES

Suggestions for future research arise from the studies included in the thesis, some of which are directly related to the SELMA study, and some are more general.

A follow-up of the SELMA participants during adolescence could contribute with information about the stability of intellectual functioning, and if associations found in early school years continue in adolescence. Following up working memory capacity in the SELMA cohort could clarify if the relative disadvantage found in the current studies continues in adolescence. A follow-up, including NDD diagnostics, of the children with language difficulties at age 2.5 years (Study I), and of the children with scores corresponding to or just below cut-off to clinical ADHD and ASD groups (Study II and III), could provide longitudinal information that might be valuable for earlier identification of NDDs. Furthermore, behavioural problems measured with a more comprehensive instrument than the SDQ could enable exploring associations between cognition and behavioural difficulties in specific domains. Besides parental ratings, including teacher ratings and, depending on participants' age, self-report instruments could provide additional information and strengthen conclusions. Furthermore, including measures of adaptive behaviour could further clarify some of the associations between cognitive functioning and ESSENCE and coexisting behavioural difficulties. Clinician rated autistic traits could enhance our understanding of the connections between autistic traits, intellectual and adaptive functioning. Finally, as not all social interaction difficulties are autistic traits, examining social interaction with other measures or through observation protocols may provide knowledge on how social interaction skills are related to intellectual functioning.

As regards the more general perspectives, future studies could examine the importance of further language milestones or screening items for intellectual function. Examining associations in a larger sample of children with DLD at preschool years could strengthen the associations found in study I. Furthermore, future studies could explore the impact of factors such as structure at home and in educational environments on behavioural regulation, hyperactivity, and inattention, and whether prosocial behaviour has a protective role. In addition, further studies with children and adolescents displaying symptoms or performance near cut-off, i.e. presentations often

labelled as subclinical variants of NDDs, could expand the information on the characteristics of these variants and, particularly, on differences between those and children with clinical NDD diagnosis. Lack of clinical impairment despite symptoms is also of interest. What factors contribute to it? Such studies may highlight potential areas of intervention or malleable contextual factors that might enhance daily life functioning in children from clinical populations. Lastly, as regards academic achievement in ADHD and/or ASD, there is a need for further studies exploring the role of motivation and accommodations in academic achievement in these groups. Developing effective interventions and accommodations to improve academic achievement is central to these groups and further studies may contribute to it.

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