Executive function in young preschool children with symptoms of ADHD

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SUMMARY

The overarching goal of research presented in this thesis was to provide new knowledge about basic, self-regulatory skills- or executive function (EF)- in young preschool children with behavioral symptoms characteristic of Attention-Deficit/Hyperactivity Disorder (ADHD). Etiological models of ADHD emphasize an onset during kindergarten and preschool years, and neuropsychological theories have converged on deficits in early developing EF processes as a possible developmental pathway towards ADHD. Despite a growing interest in EF development and the introduction of several developmentally appropriate methods of EF measurement for use with the youngest age groups, studies addressing EF in young children with elevated levels of ADHD symptoms are still scarce. Research hypotheses in this thesis had thus to be based on theoretical models of EF development, together with findings from the preschool group as a whole (pooled data from children aged 3 –6 years), and from older children.

We hypothesized that EF structure in early preschool years would differ from that described in older children (Paper II), but that associations between deficiencies in early emerging EF processes and symptoms of ADHD would be identifiable. This was expected to hold both when EF was assessed through neuropsychological tests (Paper I), and by use of parents' ratings of EF behavior in everyday settings (Paper III). The relationship between clinically administered tests of EF and parents' ratings of EF behavior was specifically addressed in an additional empirical chapter.

Our results indicate that at age three, some differentiation has taken place, which is measurable both by neuropsychological tasks and ratings of EF behavior in everyday settings. Labels used to define EF subcomponents in school-aged children and adolescents may not map directly onto emerging EF skills during early preschool years. Performance on neuropsychological tests of inhibition and working memory were related to symptoms of ADHD in our sample. Effect sizes were small, limiting the measures' clinical utility at this early stage in development. Behavioral ratings of EF in these two domains were more closely related to symptoms of ADHD than the performance-based measures. According to parent ratings of EF, children meeting diagnostic criteria for ADHD presented with higher problem scores across EF domains, and a different EF profile relative to children with internalizing problems and typically developing controls. We found that performance-based measures of EF and ratings of EF behavior were related in our sample. These two methods of

measurement are likely to tap into different aspects of early EF and should not be used interchangeably as parallel measures of EF.

ABBREVIATIONS

ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
BRIEF-P	Behavior Rating Inventory of Executive Function - Preschool Version
CFA	Confirmatory Factor Analysis
DSM	Diagnostic and Statistical Manual for Mental Disorders
EF	Executive function
EdF	Executive dysfunction
EFA	Exploratory Factor Analysis
MANOVA	Multiple Analysis of Variance
MANCOVA	Multiple Analysis of Covariance
ODD	Oppositional Defiant Disorder
PAPA	Preschool Age Psychiatric Assessment interview
PFC	Prefrontal Cortex
PCA	Principal Components Analysis
SPSS	Statistical Package for Social Sciences
StB	Stanford-Binet Intelligence Scales
VWM	Verbal Working Memory
NVWM	Nonverbal Working Memory

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1. INTRODUCTION

Self-regulation is considered one of the major achievements of early childhood. It marks the child's transition from being primarily "other-regulated" (parents) as an infant and a toddler to increasingly "self-regulated" as a preschooler (Willoughby, Kupersmidt, Voegler-Lee, & Bryant, 2011). Regulatory processes thought to be central in the monitoring and control of cognitive activity, emotional response and overt behavior are collectively referred to as executive function (EF) (Carlson, 2005; Welsh, Pennington, & Groisser, 1991). Relative to their same-aged peers, children experiencing difficulties with EF may be more easily distracted and disorganized, and act as 'out of control'. They may get 'stuck' in one way of solving a problem, and have trouble adjusting to new people and situations. On a cognitive level, these difficulties have been linked to weaknesses in specific regulatory sub processes such as inhibition, working memory, mental flexibility and planning (Espy, Sheffield, Wiebe, Clark, & Moehr, 2011).

Executive dysfunction is considered a central characteristic of several early debuting neuropsychiatric disorders (Geurts, Verte, Oosterlaan, Roeyers, & Sergeant, 2004; Nadebaum, Anderson, & Catroppa, 2007; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Among these is the most commonly occurring disorder in the preschool population (age three to five years), Attention Deficit- Hyperactivity Disorder (ADHD). In the research literature, behavioral symptoms defining ADHD have been related to difficulties primarily within the two core EF domains inhibition and working memory (Brocki, Nyberg, Thorell, & Bohlin, 2007; Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005). Although extensively studied in school-aged children, emerging EF and its possible links to symptoms of ADHD is not much studied in preschoolers. In early childhood, when fundamental executive skills first become operational, their organization is likely to be different from what has been described in older children and adolescents (Lee, Bull, & Ho, 2013). Research suggest, however, that links between ADHD symptoms and EF deficiencies are present already during the preschool period (Pauli-Pott & Becker, 2011).

The measurement of the complex, multi-level construct EF also bring with it several methodological challenges, which are subject to lively debate among researchers and practitioners. Children's performance in clinically administered tests of EF tend to correspond poorly with behavioral ratings, and there is growing consensus that ratings of EF behavior should not be treated as a proxy for EF test performance (Toplak, Bucciarelli, Jain, & Tannock, 2009)- or vice versa. It has become common clinical practice to include both neuropsychological tests and behavior ratings when assessing EF in children. Both methods, however, have their limitations with regard to both validity and reliability, which may be particularly important to take into consideration when assessing EF in the youngest age groups (Anderson & Reidy, 2012; Chan, Shum, Toulopoulou, & Chen, 2008; Toplak, West, & Stanovich, 2013).

More knowledge is needed, about early forms of EF, and of how symptoms of ADHD may be related to basic, self-regulatory processes from early on in development. Such information will be valuable for researchers aiming to gain a better understanding of the earliest roots of behavioral problems associated with ADHD- either from a clinical or a theoretical perspective. The main goal of research presented in this thesis was to contribute to this, by exploring the structure of EF and associations between EF and ADHD symptoms in a large sample of non-referred, three-year old children.

1.1. Perspectives and definitions

1.1.1. ADHD

Attention-deficit/Hyperactivity Disorder is a neurodevelopmental disorder, characterized by developmentally inappropriate levels of hyperactivity, impulsivity and/or inattention (American Psychiatric Association, 2000). A Norwegian survey from 2002 reports that approximately 2,5 % of children and adolescents under 18 years are diagnosed with the disorder (SINTEF Helse, 2004). A systematic literature review has estimated the pooled prevalence worldwide to be approximately 5% (Polanzyk et al 2007). ADHD is one of the most common disorders in preadolescent years, with high heritability estimates; 70-80% (Coghill & Banaschewski, 2009; Faraone & Mick, 2010) and an early onset of symptoms- often as early as the preschool years (Palfrey, Levine, Walker, & Sullivan, 1985). ADHD is associated with impaired academic and social skills, leading to low self-esteem and significant emotional distress for the affected individual and his or her family (Biederman et al., 2004; Klassen, Miller, & Fine, 2004; Lee, Lahey, Owens, & Hinshaw, 2008; Rennie, Beebe-Frankenberger, & Swanson, 2014; Spira & Fischel, 2005). Long-term follow-up studies of children, together with retrospective studies of adults with ADHD have shown that the disorder often persist into adulthood (Biederman, Petty, Evans, Small, & Faraone, 2010; Kieling & Rohde, 2012), and that its' adverse effects is exacerbated by the presence of comorbid disorders, such as oppositional- defiant disorder (ODD), conduct disorder (CD), learning disabilities, mood and substance use disorder, and mood and anxiety disorders (Kieling & Rohde, 2010).

1.1.2. ADHD in preschool age

The preschool years are here defined as ages three through five. The term "young children" is used when the age group referred to not necessarily is limited to the preschool period, but also may comprise younger children (toddlers and/or infants).

Knowledge about the presentation and identification of ADHD in preschool children lags behind what we know about ADHD in older children and adolescents (Egger & Angold, 2006; Egger & Emde, 2011). Diagnostic criteria for ADHD are tailored for children six years and older, and the lack of developmentally appropriate diagnostic criteria which also account for developmental variation has been pointed to as a major challenge in this field of research. Diagnostic tools developed for use in the youngest age groups, such as Kiddie-SADS (Kaufman et al., 1997) and the Preschool Age Psychiatric Assessment (Egger & Angold, 2004) are important sources of information about both normal development and early forms of psychiatric disorder, and play a particularly important role in the formulation of diagnostic categories for use with children under the age of six. According to recent prevalence estimates, which are based primarily on such structured diagnostic interviews, 2- 6% of preschool children meet the diagnostic criteria for ADHD (Greenhill, Posner, Vaughan, & Kratochvil, 2008; Kaplan & Adesman, 2011; Wichstrom et al., 2012). Estimates of the ratio boys to girls vary considerably, between 2:1 to 6:1 (Polanczyk & Rohde, 2007).

Elevated levels of restlessness and inattention are common in the preschool population, and many children will have grown out of these difficulties by the time they enter school. Still, a considerable proportion goes on to have significant behavioral problems which cause impairment across several areas of functioning. Early estimates of diagnostic stability in preschool ADHD have generally reported that approximately half of preschool children with clinically significant behavioral problems met diagnostic criteria for ADHD at follow-up assessments ≥ 2 years later (Campbell, Ewing, Breaux, & Szumowski, 1986; Palfrey et al., 1985; Pierce, Ewing, & Campbell, 1999). These were studies based on parent and/ or teacher checklists to ascertain an ADHD diagnosis. More recent estimates, usually based on structured parent interviews alone or in combination with other diagnostic tools, tend to be higher. Results from a three-year follow-up of the Preschool ADHD Treatment Study are representative of this research, indicating that 77% of the children initially diagnosed with ADHD (early preschool years) still met diagnostic criteria for the disorder at time two (early school age) (Riddle et al., 2013; see also Harvey, Youngwirth, Thakar, & Errazuriz, 2009; Law, Sideridis, Prock, & Sheridan, 2014). Taken together, this indicates a relatively high degree of stability in diagnostic classification across the preschool period and into the first school years with regard to ADHD. The stability of symptom *type* (i.e. inattention, hyperactivity, impulsivity) seem, however, to be considerably lower; a large proportion of children with an early ADHD diagnosis fulfill criteria for a different ADHD subtype at time two and three within a three-year period (Lahey, Pelham, Loney, Lee, & Willcutt, 2005). Studies based on a dimensional approach to ADHD, and studies investigating a broader spectrum of early debuting psychiatric disorders, have added important information about developmental trajectories of early emerging behavioral difficulties by showing that high levels of early ADHD symptoms may serve as a precursor of a broad spectrum of problem behaviors later in development (Copeland et al., 2013; Lahey & Willcutt, 2010; Wahlstedt, Thorell, & Bohlin, 2008).

The preschool period involves rapid developmental changes in most functional areas; social, emotional and cognitive. Normal diversity is large, and it is an important clinical challenge to identify children that will develop chronic behavioral problems while avoiding false positive diagnosis of ADHD in normally developing, active children. Unresolved questions with regard to the validity of an early diagnosis, together with the potential adverse effects that such a "label" may have on a child's self-perception and of how he or she is perceived by others, are concerns that have led to an understandable reluctance to diagnose ADHD at this early point in development (Egger & Angold, 2006; Kieling & Rohde, 2010). Possible adverse effects of such a stigma must, however, be weighed against negative response from the child's environment which may be caused by abnormal behavior in the absence of any conceivable explanation (Wichstrom et al., 2012). Another important consideration is that early identification of deviant development also opens opportunities with regard to early intervention. Targeting ADHD-related problems at an early point in development, before negative experiences related to school, social relations and negative attitudes from others become barriers for positive change, early treatment has the potential to alter the trajectory of the disorder (Halperin, Bedard, & Curchack-Lichtin, 2012; Sonuga-Barke & Halperin, 2010).

ADHD frequently co-occur with other childhood psychiatric disorders. Across childhood, comorbidity is associated with more severe difficulties and poorer prognosis (Pliszka, 2000; Waschbusch, 2002; Youngwirth, Harvey, Gates, Hashim, & Friedman-Weieneth, 2007). For the present purposes, the term comorbidity is defined as the presence of at least two disorders or symptom clusters in the same child at the same time. The terms comorbid and co-occurring are used interchangeably hereafter.

Comorbidity have been shown to be equally common in preschool children with ADHD, as in older children; studies of clinically referred preschoolers have reported that more than two thirds of preschool children diagnosed with ADHD meet criteria for at least one other disorder (Posner et al., 2007; Wilens et al., 2002a). Estimates from population-based studies tend to be somewhat lower; a recent Norwegian survey reported that 46 % of preschool children with ADHD had at least one other behavioral or emotional disorder (Wichstrom et al., 2012).

There are clear similarities between preschool and school age ADHD also with regard to patterns of comorbidity. Two of the most frequent, co-occurring disorders in childhood ADHD are addressed in this thesis; oppositional defiant disorder (ODD), and anxiety (Egger & Angold, 2006; Wilens et al., 2002b). ODD is characterized by a persisting pattern of negativistic, defiant, disobedient and hostile behavior towards authority figures (American Psychiatric Association, 2000). Of the disorders categorized under the term anxiety, separation anxiety (i.e. excessive anxiety concerning separation from the home or a parental figure) and specific phobias such as social phobia (i.e. marked and persistent fear of social or performance situations) are the most common internalizing problems in young children (Egger & Angold, 2006). In a recent Norwegian prevalence study, 20.8% of preschool children meeting diagnostic criteria for ADHD also had ODD; while 5.9% had a concurrent anxiety disorder (i.e. separation anxiety, social phobia, and/or general anxiety) (Wichstrom et al., 2012).

1.1.3. Executive function

The research literature contains a wide range of definitions of EF. Although there is a lack of of agreement on a standard definition or a uniform recognition of its component processes, various accounts refer to EF as a set of interrelated processes necessary for goal directed behavior. Executive processes are considered distinct from modular cognitive functions, such as visuo-spatial abilities, language skills, and memory. Investigations of EF structure in school-age children and in adults have identified inhibition, working memory (or updating) and mental flexibility as core component processes (Lehto, Juujaervi, Kooistra, & Pulkkinen, 2003; Miyake & Friedman, 2012). The emergence of executive skills is linked to the maturation of neural networks based in prefrontal cortex (PFC) (Moriguchi & Hiraki, 2013).

In this thesis, EF is referred to as a set of regulatory processes playing a central role in the monitoring and control of cognitive activity, emotional response and overt behavior. In line with current neuropsychological accounts of EF, inhibition, working memory, mental flexibility, planning and emotional control are considered key executive processes (Anderson, 2002; Lezak, 1995). In the following, EF components of particular relevance to the presented research are explained. Early development of these processes are briefly delineated, in order to render a description of EF in the young preschool child.

1.1.3.1. Inhibition

Inhibitory control is, in its simplest form, defined as the ability to suppress or withhold a response originating in the child's own repertoire (an example would be waiting for a signal to squeeze a soft ball placed in your hand). Inhibition tasks may differ in complexity along several dimensions (Nigg, 2001); one of the most salient is working memory load (for instance, keeping in mind the instruction to await a signal or to follow more complex verbal instructions with two or more conditional rules). Another relevant consideration is whether a given task requires the child to inhibit a prepotent response, and/or conflict tasks in which the child must make a response conflicting with the response "at hand" (Carlson & Moses, 2001). The presence or absence of salient motivational cues has also been argued to be an important conceptual aspect with regard to inhibition (Carlson & Tamm, 2000; Nigg, 2001; Zelazo & Müller, 2002). According to studies of normative EF development, basic inhibitory abilities (i.e. suppressing prepotent responses) are established during the first year of life. At age three years, more complex inhibitory skills emerge, but performance on neuropsychological tests purporting to tap into these processes seem closely related to type of task and/or task complexity (Carlson, 2005; Kloo & Perner, 2005).

1.1.3.2.Working memory

Working memory (WM) constitute a limited-capacity, multicomponent cognitive system that allows for the storage and manipulation of information for a few seconds (Baddeley, 1996; Baddeley, 2012). WM is commonly divided into verbal/ nonverbal or phonological/

visuospatial WM. Considered a necessary foundation for several higher-order cognitive processes, WM permits internal representation of information to guide decision making and overt behavior so that behavior is not dominated by the immediate sensory cues in the environment (Martinussen et al., 2005). In research on EF in children, definitions of WM tend to vary; some refer to WM as information retention (simple WM), while others emphasize the distinction between short term (passive) information storage, and more complex cognitive processes, limiting use of the term to more active mechanisms such as updating and manipulation of information held in memory (complex WM). Basic WM processes (i.e. keeping information active in memory) are established during the first year of life. Relative to inhibition, WM have a more protracted development, showing steadily improvement throughout the preschool period (Anderson, 2002; Carlson, 2005; Espy, Kaufmann, & Glisky, 2001)

1.1.3.3.Mental flexibility

Mental flexibility refer to the ability to shift between mental states, or rule sets in response to changing situational demands (Miyake et al., 2000). This ability is to a large extent dependent on inhibition (withholding a prepotent response) and working memory (maintenance and updating of a mental set in response to feedback) (Best & Miller, 2010). A task or everyday situation may require mental flexibility at different levels; an attentional shift or shift of mental set, and/ or change of response set. Mental (or cognitive) flexibility increases greatly during the preschool period. According to the research literature, one-year old infants are able to shift from an old to a new response set after a short delay (Diamond & Goldman-Rakic, 1989), and a two-year old child will typically be able to shift from an old to a new response set based on clear verbal instructions (Diamond, Carlson, & Beck, 2005). The tendency to perseverate (being 'stuck' in the old response set) seem to remain, however, approximately until the age of four or five years (Carlson, 2005; Diamond et al., 2005; Espy, Kaufmann, McDiarmid, & Glisky, 1999; Hongwanishkul, Happaney, Lee, & Zelazo, 2005; Zelazo et al., 2003).

1.1.3.4.Planning

Goal-directed behavior involves the organization of steps or elements (actions, material, persons) needed to carry out an intention (Lezak, 1995); i.e., having decided to do a puzzle, a child will need to locate a box of pieces, choose a suitable workplace, and perhaps find someone to help in order to accomplish his or her goal. Planning requires the child to choose between alternative actions and organize them, both sequentially and hierarchically. This complex capacity involves several, other EF-related processes, such as working memory, the ability to stay on task (i.e. inhibit irrelevant or off-track behavior), to identify and choose between several alternative actions, to evaluate progress, and to adjust behavior according to feedback. Efficient planning and organizing is thus a result of the integration of several EF processes. Representative of the few studies investigating these complex abilities in preschool children samples is the finding that children younger than four years of age usually struggle on neuropsychological tasks requiring the ability to plan (e.g. Welsh et al., 1991). Considerable improvement is usually observed between ages four and five years (Carlson, 2005; Espy et al., 2001), and these abilities then continue to develop throughout childhood (Anderson & Reidy, 2012).

1.1.3.5. Emotional control

Emotional control is typically referred to as the child's ability to modulate an emotional state so as to facilitate adaptive, goal directed behavior (Shaw, Stringaris, Nigg, & Leibenluft, 2014). In line with this definition, no explicit distinction will be drawn here, between the regulation of emotion in itself on the one hand, and of behavior in an emotionally arousing situation on the other. The main focus, though, will be on the latter, observable aspect of emotional control. This is considered closely related to the concept of "hot EF", thought to be tapped in meaningful situations, often involving emotional or motivational cues such as reward or punishment. In contrast, "cool" aspects of EF are thought to be involved in handling abstract, decontextualized problems (Gioia, Isquith, Guy, & Kenworthy, 2000; Metcalfe & Mischel, 1999; Zelazo & Müller, 2002). Investigations of the early development of both cool and hot EF have indicated that these two aspects of EF are differentiable already in early childhood, in terms of their associations with general intellectual ability, temperament, and age (Hongwanishkul et al., 2005; Kerr & Zelazo, 2004). According to the above neuropsychological studies, and literature based on neuroimaging studies of young children, the regulation of emotional responses develop in concert with other EF processes, steadily improving throughout childhood (e.g. Hill, Degnan, Calkins, & Keane, 2006; Lamm & Lewis, 2010; Posner, Rothbart, Sheese, & Voelker, 2012).

1.1.4. Structural organization of early EF

Normative studies of early EF development indicate that basic EF processes reach a functional level at different points in development, shifting between phases of active development and of consolidation (Garon, Bryson, & Smith, 2008; Senn, Espy, & Kaufmann, 2004; Tsujimoto, Kuwajima, & Sawaguchi, 2007). Rapid emotional and cognitive changes during this period are likely to be accompanied by changes in the structural organization of EF (Best & Miller, 2010). Neuroimaging data from typically developing children suggest that prefrontal neural systems implicated in EF show a gradual differentiation into separate functional systems during the preschool period (Durston et al., 2006; Posner et al., 2012; Rubia, 2012; Tsujimoto et al., 2007; Tsujimoto, 2008). This research also describes a progressive functional integration during childhood, which sets the stage for the development of more complex EF skills (Luciana & Nelson, 1998; Rubia, 2012). Accordingly, developmental spurts are demonstrated in performance on several EF tasks measuring different aspects of self-regulation, of increasing complexity (Best & Miller, 2010; Carlson, 2005; Carlson & Moses, 2001).

In an influential, theoretical framework of EF, the construct is depicted as a set of separable, but interrelated processes (Miyake et al., 2000). Although originally developed as a model of EF in adults, Miyake's theoretical model of EF has been suggested a theoretical basis for research on EF in children (Garon et al., 2008). Studies analyzing EF factor structure in school-age samples by use of neuropsychological tests typically reveal three dimensions or factors underlying variance in performance on neuropsychological EF tasks; inhibition, working memory (also referred to as updating), and mental flexibility (Brocki & Bohlin, 2004; Lehto et al., 2003; McAuley & White, 2011; van der Ven, Kroesbergen, Boom, & Leseman, 2013; Welsh et al., 1991). Behavioral ratings of everyday EF have suggested a somewhat different structure, with one component reflecting inhibitory self-control, a second reflecting emotional control, and the third comprising a set of metacognitive or "cool" EF processes (working memory, planning, organizing) (Gioia et al., 2000). The unity, expressed as a single factor underlying common variance in different measures of EF, have been differently emphasized and interpreted; as attentional control (Anderson, 2002; Garon et al., 2008), inhibition (Barkley, 1997), information processing speed (Rose, Feldman, & Jankowski, 2011), or as a mechanism underlying the consolidation of basic stimulus–response connections (Sagvolden, Johansen, Aase, & Russell, 2005; Wiebe, Espy, & Charak, 2008).

Factor analytic studies of EF in preschool children have yielded more inconsistent results, with a wide variety of proposed factorial solutions. The majority of these have rendered support to a unitary model of EF in young children (Hughes, Ensor, Wilson, & Graham, 2010; Wiebe et al., 2008; Wiebe et al., 2011; Willoughby, Blair, Wirth, & Greenberg, 2012). A more fractionated EF structure have also been described, however. Inhibition and working memory were identified as separable EF dimensions in two recent preschool studies (Miller, Giesbrecht, Müller, McInerney, & Kerns, 2012; Schoemaker et al., 2012). In the first of these, the two-factor model proved a better fit to data than a single-factor model and a three-factor model including set shifting in a community-based sample of three- to five year old children. Schoemaker and colleagues identified the same two factors in a sample very similar in age, but with clinically diagnosed ADHD, ODD and/or ODD. Based on behavior ratings of EF, other preschool studies have rendered support to a similar three-partite model as previously described in school-aged samples (Bonillo, Araujo Jimenez, Jane Ballabriga, Capdevila, & Riera, 2012; Ezpeleta, Granero, Penelo, de la Osa, & Domenech, 2013).

The above findings suggest that a unidimensional EF construct may capture the structural organization of EF in early childhood better than multifactorial models. It may, however be premature to rule out more complex models of early EF. Differences with regard to operational definitions of EF, method of measurement, and age range of the participants in the above studies may have contributed to the observed inconsistency in findings. This is likely to have affected the number of extracted factors, and how they were interpreted. With very few exceptions (Ezpeleta et al., 2013; Wiebe et al., 2011) studies of EF in preschool children have based their conclusions on collapsed data from samples with age ranges of two years or more. It is also important to note, that few of the proposed models have integrated, let alone investigated in factor analyses, emotional regulation as part of a general EF construct.

1.2. Neurocognition in ADHD

The term neurocognition refers to cognitive functions with an established relation to the function of particular areas, neural pathways or cortical networks in the brain. Similar in content, the term neuropsychological function is used primarily when referring to neurocognitive processes as measured by neuropsychological tests.

1.2.1. Neuropsychological endophenotypes for ADHD

The term endophenotype is typically defined as "a phenotype more proximal to the biological etiology of a clinical disorder than its signs and symptoms (…)"(Doyle et al., 2005). Neuropsychological models of ADHD have been central in attempts to understand mechanisms underlying the behavioral symptoms defining the disorder. The neuropsychological endophenotype is considered an important tool in research aiming to understand relations between specific neurocognitive processes on the one hand, and the observed inattentive, impulsive and hyperactive behavior associated with ADHD on the other.

In a meta-analytic review of research addressing neuropsychological correlates to school-age ADHD, Willcutt and colleagues concluded that EF- broadly defined- were associated with ADHD, and that the relation was largely independent of comorbid psychiatric disorders or learning disorders, which are prevalent in school-age children with ADHD (Willcutt et al., 2005). The most consistent findings have been reported in measures of inhibition (response inhibition in particular) and working memory (primarily in the nonverbal/visuospatial domain) (for reviews, see Martinussen et al., 2005; Pennington & Ozonoff, 1996; Sergeant, Geurts, & Oosterlaan, 2002; Willcutt et al., 2005). A second, important conclusion from the above meta-analysis was that EF deficits are "neither necessary nor sufficient to cause all cases of ADHD" (Willcutt et al., p 1336; see also Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005). Several alternative pathways leading to ADHD have been described in the literature during the last decade; among the most researched are the cognitive energetic model of ADHD (Sergeant, 2000; Sergeant, 2005), reaction time variability (Castellanos et al., 2005), deficits in reinforcement contingencies (Johansen, Aase, Meyer, & Sagvolden, 2002; Sagvolden et al., 2005) and delay aversion (Sonuga-Barke, 2003). The notion of ADHD as a heterogeneous condition is now widely accepted (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006; Nigg & Casey, 2005; Sjowall, Roth, Lindqvist, & Thorell, 2013), and theoretical models of the disorder have during recent years started to incorporate this heterogeneity, considering other neuropsychological mechanisms as well as more basic processes in conjunction with EF (Castellanos & Tannock, 2002; Nigg & Casey, 2005; Sergeant, Geurts, Huijbregts, Scheres, & Oosterlaan, 2003; Sonuga-Barke, Bitsakou, & Thompson, 2010). In one of the first integrative models of ADHD, the dual pathway model (Sonuga-Barke et al., 2003; Sonuga-Barke, 2003), executive dysfunction (EdF) and motivation-based dysfunction (delay aversion) constitute two independent pathways to ADHD. It has later been revised, postulating timing deficiencies as a third pathway (Sonuga-

Barke et al., 2010). The identification of several, distinct mechanisms that may contribute to the development of ADHD psychopathology has during recent years promoted models of the disorder which incorporate its neuropsychological complexity and the heterogeneity of the ADHD population. Within this framework, executive dysfunction mark an ADHD neuropsychological subtype (Sonuga-Barke & Coghill, 2014).

1.2.2. Executive dysfunction in preschool children with ADHD

Research presented in this thesis focus on EF as one of several possible endophenotypes for ADHD. The literature on EF in preschool children with symptoms of ADHD is still sparse, but has indicated that this age group is reminiscent of school-aged children diagnosed with the disorder, in terms of neuropsychological functioning (Pauli-Pott & Becker, 2011; Wilens et al., 2002a) and everyday executive behavior (Ezpeleta et al., 2013; Mahone & Hoffman, 2007).

1.2.2.1.Evidence from clinically administered tests

Impairment in delay aversion and in the two basic EF processes working memory and inhibition has been demonstrated both in non-referred and clinical preschool samples (Pauli-Pott & Becker, 2011). With regard to EF, the strongest associations between EF deficiencies and early symptoms of ADHD have been found within the inhibition domain (Mahone, Pillion, Hoffman, Hiemenz, & Denckla, 2005; Schoemaker et al., 2012; Sonuga-Barke, Dalen, Daley, & Remington, 2002; Thorell & Wåhlstedt, 2006; Youngwirth et al., 2007). Neuropsychological tasks used to address inhibition in this age group most often tap simple inhibitory processes (e.g. Berlin & Bohlin, 2002), but ADHD-related deficiencies have also been demonstrated in tests purporting to measure more complex inhibitory skills, such as the solving of response conflict (Marks et al., 2005; Thorell & Wåhlstedt, 2006). In a recent longitudinal study, complex inhibition was a particularly strong correlate to ADHD in young children (Brocki, Eninger, Thorell, & Bohlin, 2010). Relations between early symptoms of ADHD and working memory is less studied in this age group, and findings less consistent, with some reporting ADHD-related difficulties (Kalff et al., 2002; Mahone et al., 2002; Mariani & Barkley, 1997; Thorell, 2007), and others not (Hughes, Dunn, & White, 1998; Mahone et al., 2005; Schoemaker et al., 2012; Sonuga-Barke et al., 2002).

Poor emotional control has frequently been associated with ADHD in school-aged children (Maedgen & Carlson, 2000; Nigg & Casey, 2005; Walcott & Landau, 2004). This aspect of EF is usually investigated by use of rating scales or interviews (for an overview, see Shaw et al., 2014), but evidence for ADHD-related deficiencies in emotional/motivational aspects of EF has also come from neuropsychological studies investigating "hot" EF in preschool children (Kerr & Zelazo, 2004; Willoughby et al., 2011). A typical finding across childhood is that children with ADHD tend to prefer immediate smaller over delayed larger rewards in simple choice tasks (typically referred to as delay aversion) (Brocki et al., 2007; Luman et al., 2009; Martel, Roberts, & Gremillion, 2013; Sonuga-Barke et al., 2003; Thorell, 2007). Symptoms of ADHD at school entry have also been shown to be predicted by earlier problems with resistance to temptation at age four years (Marakovitz & Campbell, 1998).

Symptoms of ADHD have been associated with poor set-shifting in neuropsychological studies of school-aged children (Roberts, Martel, & Nigg, 2013). The few existing preschool studies addressing these skills in children with symptoms of ADHD have arrived at differing conclusions (Dalen, Sonuga-Barke, Hall, & Remington, 2004; Hughes et al., 1998; Kalff et al., 2002). ADHD symptoms were found to be associated with poor set shifting in a recent study of three- to six year olds (Martel et al., 2013). Interestingly, such difficulties were not found among children with symptoms of ODD, and seemed more closely related to symptoms of inattention relative to hyperactivity/impulsivity in this study.

Although recent research on early EF development indicates that rudimentary forms of planning and organizing skills are established during early childhood, age-appropriate measures targeting them are still scarce (Anderson & Reidy, 2012). An investigation of delay aversion and inhibition as early predictors of ADHD in third grade has, however, indicated that early difficulties on a planning task (The Tower of Hanoi) in 1st grade characterize children with symptoms of ADHD, and predict a diagnosis of ADHD in third grade (Campbell & von Stauffenberg, 2009). Of note, mental flexibility has proved to influence significantly performance on this task in preschool children (Bull, Espy, & Senn, 2004).

1.2.2.2. Evidence from behavior ratings

A few rating scales or inventories have been developed during recent years, to assess everyday EF behavior in school-age and preschool children (Gioia et al., 2000; Gioia, Espy, & Isquith, 2002; Thorell & Nyberg, 2008). A basic assumption underlying the use of these inventories is that they tap into behaviors that are closely related to basic EF processes (e.g. inhibition, working memory, planning) (Toplak et al., 2013). The Childhood Executive Function Inventory (CHEXI) is used to assess EF via parent or teacher ratings of working memory and inhibition (Thorell & Nyberg, 2008). Symptoms of ADHD have been associated with CHEXI ratings within both domains in preschool children (Thorell, Eninger, Brocki, & Bohlin, 2010). The Behavior Rating Inventory of Executive Function (BRIEF) (Gioia, Isquith, Guy, & Kenworthy, 2000) is at present the most commonly used rating scale for assessment of EF in children. The preschool version (BRIEF-P) has in several recent studies been shown to discriminate between different clinical groups and controls (Duku & Vaillancourt, 2013; Isquith et al., 2014; Smithson et al., 2013). Based on teacher BRIEF-P ratings of a large, population-based sample of three-year old children, Ezpeleta and colleagues found that the single subscale with highest predictive value with regard to an ADHD diagnosis was the one reflecting inhibition. Also a broader index reflecting inhibitory self-control, and the global composite EF score proved efficient in differentiating children with ADHD from typically controls (Ezpeleta et al., 2013). In the only study to investigate parent ratings of children (age three-to five) with symptoms of ADHD using the complete BRIEF-P, children with ADHD were rated as more impaired than children without ADHD on all five BRIEF-P subscales. Here, the strongest effect was found for the Working Memory subscale (Mahone & Hoffman, 2007).

1.2.3. EF in preschool children with symptoms of ADHD: A summary

Similar limitations as previously noted with regard to studies of emerging EF apply to the above research in preschool samples with symptoms of ADHD. Adding to this, there is considerable variation in how early psychiatric symptoms are assessed in these studies. As a consequence, children assigned to e.g. an ADHD group in different studies may differ considerably in potentially important aspects, as will children across comparison groups. Further, comorbid symptoms have not always been assessed and controlled for. Bearing these considerations in mind, some preliminary conclusions may be drawn with regard to the relationship between early symptoms of ADHD and EF in young preschool children. Evidence suggests that- on a group level- there are links between symptoms of ADHD and EdF in early preschool years, primarily in two basic, early developing EF processes; working memory and inhibition. Findings with regard to inhibitory difficulties are relatively robust, both across different age groups, different measures (neuropsychological tasks, behavior ratings) and different settings. Regarding working memory, deficits may be ADHD specific, but inconsistent findings have so far made it difficult to conclude whether poor WM characterize early forms of ADHD. Emotional control is not much studied in clinical preschool populations, but there is emerging evidence for an early association between ADHD and "hot" aspects of EF, which seem consistent with findings based on parents' behavior ratings of EF within this domain. Results for more complex, later developing EF components are inconclusive, and further research is needed in order to clarify their potential role in early forms of ADHD.

2. OBJECTIVES

The main objective of this thesis was to investigate early forms of executive function, and how specific executive processes may be related to early symptoms of attention-deficit/hyperactivity disorder in young preschool children. Papers I and III address relations between ADHD symptoms and executive function as measured by either clinically administered tests or behavioral ratings, while paper II is an investigation of the structural organization of executive function as measured by the BRIEF-P.

The research questions were:

1. Do young preschool children with elevated levels of ADHD symptoms, alone or in combination with ODD, differ from children with symptoms of ODD and from typically developing controls in neuropsychological measures of inhibition and working memory? (Paper I)
2. Is performance in tasks measuring either inhibition or working memory specifically related to number of ADHD symptoms in young preschool children?(Paper I)
3. How does the structural organization of EF proposed in the Behavior Rating Inventory of Executive Function map onto EF structure early in the preschool period? (Paper II)
4. To what degree are basic EF processes differentiated at age three years, and how are they related to eachother? (Paper II)

5. Is severity of ADHD related to parent ratings of inhibition and working memory in young preschool children?(Paper III)
6. To what degree do parent ratings of inhibition and working memory discriminate between children meeting diagnostic criteria for ADHD and their symptom-free peers at age three years? (Paper III)
7. Are ADHD and common comorbid disorders (ODD, anxiety) associated with different profiles of executive dysfunction as measured by the BRIEF-P? (Paper III)

3. MATERIALS AND METHODS

3.1. Sample

This thesis was based on data from the Norwegian Longitudinal ADHD Cohort Study (the ADHD Study), which is a sub study of the Norwegian Mother and Child Cohort Study (MoBa) conducted by the Norwegian Institute of Public Health (Magnus, Haug, Nystad, & Skjaerven, 2006). MoBa is a large, population-based birth cohort study designed to study risk factors and health outcomes in pregnancy and adulthood, with a participation rate of 38.7%. About 107'000 pregnancies were included during the recruitment period (1999-2008). Several questionnaires were completed during pregnancy, and at child age 6, 18 and 36 months.

Of all participating mothers, 57.2% returned the 36 month questionnaire, which included 11 questions regarding hyperactivity, impulsivity and attention problems; six from the Child Behavior Checklist (Achenbach & Ruffle, 2000) and five from the DSM-IV diagnostic criteria for ADHD (American Psychiatric Association, 2000). In order to oversample children with relevant symptoms into the ADHD study, about 80% of children invited to the one-day clinical assessment were drawn from those scoring at or above the 90th percentile on these questions, and/or if parents reported hyperactivity as a health problem. These children will later be referred to as "screen positive". A total of 2798 children, born between April 2004 and January 2008 were invited to participate in the ADHD study according to these criteria. Of these, 1048 (37,5%) participated in the clinical assessments. In addition, a comparison group randomly selected from the full MoBa sample were invited. Of the 654 children invited into the comparison group during the same period of time, 147 (22,5%) participated. Children were not invited if they suffered from severe medical conditions compromising the child's ability to take part in the clinical assessments and/or high levels of autistic symptoms. All exclusions (n=149) were due to the latter criterion. Thus, a total of 1195 children were clinically assessed in the ADHD study, at the mean age of 42 months. A flowchart describing the sampling process is presented in Figure 1.

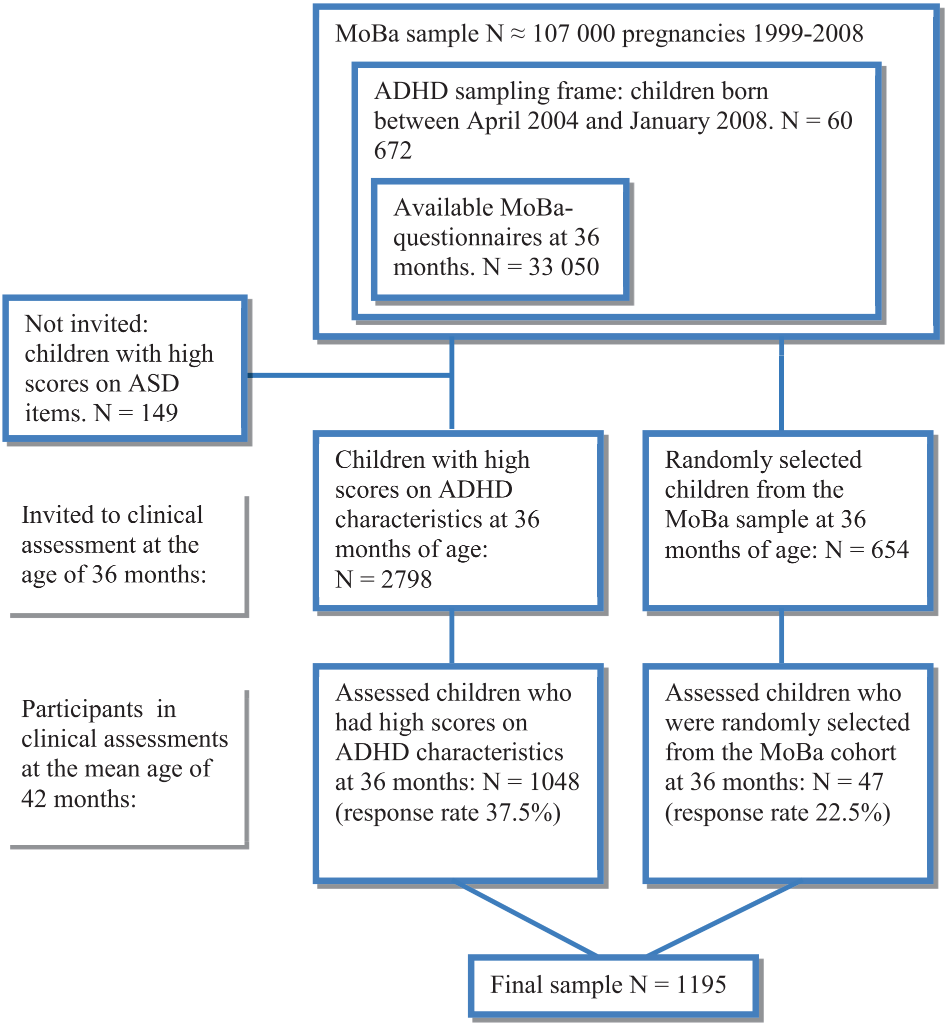

Figure 1. Flowchart of recruitment. MoBa = Norwegian Mother and Child Cohort Study. ASD = autism spectrum disorders. High scores on ADHD characteristics at 36 months = above the 90. percentile on 11 questions: 6 questions from the Child Behavior Checklist and 5 diagnostic criteria for ADHD from the DSM-IV.

3.2. Participants

Each of the three studies presented here were conducted in subsamples of the 1195 children clinically assessed in the ADHD Study. Children participating in the ADHD study were not diagnosed with ADHD, and the term “children with ADHD” or “children with clinical levels of ADHD symptoms” will be used only related to children who meet diagnostic criteria for the disorder. The term “children with elevated levels of ADHD symptoms” also include children who presented with subthreshold levels of ADHD symptoms as defined below (3.2.1).

3.2.1. Paper I

Children with elevated levels of either ADHD or ODD or a combination of these were selected for this study, together with a comparison group consisting of typically developing children. Children in the TD group were defined as “typically developing” as they did not exhibit any symptoms of a psychiatric or developmental disorder at the time of assessment. A total of 1045 children (554 boys, 470 girls) were included in one of four groups (ADHD, n=150; ADHD+ODD, n= 235; ODD, n= 205, and TD, n=455) based on information from a diagnostic parent interview; the Preschool Age Psychiatric Assessment (PAPA) (described below). Inclusion in one of the three clinical groups (ADHD, ADHD/ODD or ODD) required elevated levels of ADHD symptoms and/ or ODD, defined as 1) meeting all the symptom criteria for a DSM-IV diagnosis (i.e., for ADHD at least six of nine criteria of inattentive subtype and/or hyperactive/impulsive subtype; for ODD at least four of eight symptoms of ODD), *including* impairment; 2) meeting all the DSM-IV symptom criteria for a diagnosis, but without report of impairment; or 3) meeting almost all symptom criteria for a diagnosis (lacking 1-3 criteria for ADHD/ 1-2 criteria for ODD) *with* report of impairment. The symptom/impairment criteria under 2) and 3) are considered equivalent to subthreshold ADHD. In order to be judged as “present”, all symptoms had to have lasted for at least three months. Children exhibiting significant symptoms in other functional areas (without ADHD or ODD), such as anxiety or severe language delay, were excluded from this study, as well as children with IQ score below 70 or missing data on this variable.

3.2.2. Paper II

Inclusion in this study required a BRIEF-P parent form with overall number of missing responses less than 12, and less than two missing responses within any single subscale. Among those included, missing scores were replaced with item score 1 (n=110 children) in line with scoring instructions. The sample thus consisted of 1134 children (544 girls, 590 boys).

3.2.3. Paper III

Papers II and III used data from the same sample. In paper III, additional analyses were conducted in a subsample, consisting of 308 children (179 boys, 129 girls). In this subsample, information from the diagnostic parent interview (PAPA) was used to assess psychiatric symptoms. Children were assigned to one of three clinical groups; ADHD, ODD and anxiety. Only children meeting diagnostic criteria for a diagnosis were included in this subsample. Inclusion in the ADHD group required at least six of nine DSM-IV-TR criteria of inattentive subtype and/or hyperactive/impulsive subtype ADHD (n=104). The ODD group comprised children with at least four of eight symptoms of ODD according to DSM-IV criteria (n=39). Inclusion in either the ADHD or the ODD group required impairment, and symptom duration of three months or more. Children exhibiting symptoms of one or more of the most frequent DSM-IV anxiety subtypes i.e. specific phobia, social anxiety, separation anxiety and generalized anxiety were assigned to the ANX group if their anxiety symptoms were inappropriate and excessive, and causing impairment (n=48). Children with co-occurring ODD/ADHD were excluded from the ADHD and the ODD groups, respectively. In addition, we included a TD group consisting of 117 children randomly drawn from the MoBa cohort, who did not meet criteria for any psychiatric condition.

3.3. Measures

The clinical assessments in the ADHD study included a neuropsychological examination of the child, a clinical parent interview, and several questionnaires yielding information about the child's development, social and emotional functioning, language skills and behavior regulation. The present thesis is based on data from a clinical parent interview, a behavioral inventory and a selection of neuropsychological tests. These are described below.

3.3.1. Preschool Age Psychiatric Assessment (PAPA) interview

The PAPA interview is a diagnostic interview developed for use with children aged 2-6. It provides information about the scale and frequency of symptoms according to diagnoses in DSM-IV-TR (American Psychiatric Association, 2000), including information on impairment. An adapted, Norwegian version of the PAPA interview was used in the ADHD study. The interview is semi-structured; interviewers probe until there is sufficient information for deciding whether a symptom is present at pre-specified levels of severity. If present, information was also collected about its frequency, situational context and duration. Impairment was considered present if parents reported the child to be moderately impaired in at least one area of functioning, or modest impairment was reported in two or more functional areas (Egger et al., 2006).

3.3.2. General intellectual ability

The Stanford Binet Intelligence scales, 5th edition (SB-5) were used to assess general intellectual ability (Roid, 2003a). It is a widely used test battery, standardized for ages 2-85. An abbreviated IQ measure (ABIQ) was estimated on the basis of scores from the Vocabulary and Object Matrices subtests, estimating verbal and nonverbal IQ, respectively. In the Vocabulary subtest, the first items require the child to point at different body parts, or name objects (small toys). In the last, most difficult items, the child is asked to explain the meaning of selected words. Items in the Object Matrices subtest also increase in complexity, from the detection of shapes that are alike, to fill in a missing shape on the basis of abstract reasoning. The highest possible raw score was 20. Most tests in this battery have a stop rule of discontinuing the test after four consecutive null scores, which was applied according to the test manual.

3.3.3. Working memory

Verbal working memory was assessed by the SB-5 subtest Memory for sentences. In this task, the child is asked to listen to the test administrator read six sentences one by one, and then to repeat it as accurate as possible, without any delay. Sentence length is gradually increased, surpassing the child’s phonological memory span, in order to tap more active working memory processes such as rehearsal and manipulating/updating of information held in memory. Two points were awarded for each correctly repeated sentence, yielding a maximum score of 12. Two other subtests from the SB-5 battery were used to measure nonverbal working memory: In the Delayed Response task, a small toy is hidden under one of three cups while the child is watching. He or she is then asked to indicate where the toy is hidden after a short delay. In the Block Span subtest, the child is to tap blocks in the same order as demonstrated by the administrator. The combined maximum score for the nonverbal working memory tests was 13.

Nonverbal working memory was assessed by an additional, visuospatial search task designed for use with young children; Spin the Pots Task (Hughes & Ensor, 2005). In this task, the child is presented with a tray with eight boxes of different shapes and colors, and attractive stickers are hidden in six of them as the child watches. The child is told to select one box for the administrator to open; if it contains a sticker, the child gets to keep it. The administrator covers the tray with a cloth and spins it around between each trial. The test was terminated after 16 trials if the child had not located all 6 stickers; test score reflected number of trials to locate all the stickers, minus number of empty boxes opened- ranging from 0 to 16. In addition to the load put on the child's visuospatial working memory, this task requires him or her to keep in mind and follow an arbitrary rule across several trials.

3.3.4. Inhibition

The Statue subtest from NEPSY was used to measure simple inhibition (Korkman, Kirk, & Kemp, 2000). In this task, the child is told to stand still, with eyes closed and saying nothing until the administrator says 'stop.' During a 75 second period, the administrator produces distracting stimuli in timed intervals. Performance in this task relies on the child's capacity to sustain a position and inhibit motor responses to distractors throughout a 75 second period. Two points are obtained for each 5 second interval with one or two points withdrawn for any utterance or movement. Total score on this task thus ranged from 0 to 30.
An inhibition score was also obtained from the "Spin the Pots" task; the number of times the child opened a box contrary to the instruction given (the boxes were to be opened by the experimenter). This score is used as a measure of the child's ability to suppress a prepotent response by holding an arbitrary rule in mind. The attractive awards involved (small, colourful stickers) added to the demands put on inhibition in this task.

3.3.5. BRIEF-P

The Behavior Rating Inventory of Executive Function- Preschool version (BRIEF-P) (Gioia, Espy, & Isquith, 2002) was developed to assess executive behavior in children aged 2 through 5 years. The preschool version is an adaptation of the original inventory, BRIEF (Gioia et al., 2000), which is currently the most widely used rating inventory for EF assessment in school aged children (Toplak et al., 2013).
The BRIEF-P has five subscales labeled *Inhibit, Emotional Control*, *Shift*, *Working Memory and Plan/Organize,* which combine into three broader indexes: The Inhibit and Emotional Control scales constitute the *Inhibitory Self-Control* index; combined with the Shift scale, Emotional Control constitute the second index labeled *Flexibility*, and the Working Memory and Plan/Organize scales represent the third index, *Emergent Metacognition,* referring to developing metacognitive aspects of EF. Parents or teachers respond to 63 items, indicating how often a specific behavior has been a problem during the past six months; Never (=1), Sometimes (=2) or Often (3). Thus, higher scores are associated with poorer executive functioning. Recommended threshold for interpretating a score as abnormally elevated is a corresponding T-score of 65 (Gioia et al., 2002).

The data collection in the prospective study commenced in 2007, using the existing Norwegian translation developed for research purposes (Nicholas & Solbakk, 2006). A new BRIEF-P translation, with a closer resemblance to the original version (Gioia et al., 2003) became available for research purposes in 2009, and was implemented in the second half of the data collection (from 2009 to 2011). To ascertain that the different wordings in some of the inventory's items did not lead to differences in factor structure, we compared 4 different factorial solutions that allow same and/or different factor means and factor loadings for the two BRIEF translations (see Appendix). We found the best solution to be the one assuming same loadings and different means. As this analysis suggested a unitary factor structure for the two BRIEF translations, their data were combined in Papers II and III.

3.4. Statistical analyses

Data analyses were conducted using the Statistical Package for the Social Sciences (SPSS versions 18.0 and 21.0; SPSS Inc., Chicago, USA), Mplus version 7.11 (Muthén & Muthén, 2012a), and Watkins' Monte Carlo Parallel analysis program (Watkins, 2000).

In Papers I and III, multivariate analyses of variance (MANOVA)s were used to investigate possible symptom specific deficits in measures of EF. Significant results from MANOVA were further investigated in separate analyses of variance (ANOVA)s and post hoc pairwise comparisons. Bonferroni corrections were used to control for familywise error in the ANOVAs, ensuring that the overall Type 1 error rate remained at .05 across all comparisons. The categorical analyses in Paper I were followed up in univariate and multiple linear regression analyses, investigating how much of the variance in ADHD or ODD symptoms could be explained by variance in the performance-based measures of EF (working memory and inhibition). In Paper III, regression analyses (univariate and multiple) were used in a similar way, to investigate how variance in parents' ratings within the five BRIEF-P subscales contributed to variance in ADHD symptom load. In this paper, discriminant function analyses were performed in a subsample, in order to examine the ability of the two BRIEF-P subscales Inhibit and Working Memory to differentiate between symptom groups and a control group. In addition, possible symptom-specific profiles of EF were investigated by use of a profile analysis (general linear model, repeated measures ANOVA) allowing for the direct comparison of BRIEF-P subscale profiles among the four groups.

In Paper II, the structural organization of EF measured by the BRIEF-P was investigated using both confirmatory (CFA) and exploratory factor analysis (EFA). The two analytical approaches were selected in order to investigate how the three-factor model of EF proposed by the BRIEF-P authors map onto the structural organization of EF at age three years, asking two different questions: i) Does a unidimensional model of EF represent a better fit to data in our sample relative to the three-dimensional model proposed by the BRIEF-P authors? and ii) How are the most salient factors in BRIEF-P ratings of the children participating in our study related to the five proposed first-order factors (i.e. the five clinical subscales) in the BRIEF-P? CFA was chosen because it allows for a direct comparison of competing structural models using goodness-of fit measures and for the statistical testing of differences in fit. The latter was computed using the difftest option in Mplus (Muthén & Muthén, 2012b). EFA is a data-driven procedure, considered appropriate when links between measured (BRIEF-P items) and latent variables (factors) are unknown or uncertain (Byrne, 2005). The EFA output indicates a number of interpretable factors that maximally accounts for covariances among the observed variables. The extraction of factors were guided by the factor eigenvalues and screeplot, together with a Monte Carlo parallel analysis. The rationale for a parallel analysis is that the factor should account for more variance than is expected by chance (Brown, 2006).

Preliminary analyses revealed no significant univariate or multivariate outliers. Basic assumptions were largely met for all the analyses, with some exceptions. Error variance in two of the variables analyzed in Paper I differed significantly across groups; a more stringent significance level ($p <.01$) was therefore set for evaluating the significance of the results. In paper II, the categorical character of the observed variable at item level (score 1-3) in the BRIEF-P, and a large number of positively skewed variables in the data set prohibited the use of maximum likelihood estimation. The CFAs were therefore based on weighted least squares means and variance (WLSMV) (Muthén & Muthén, 2012b). In Paper III, differences in variance-covariance matrices were detected. The Box's *M* test for this difference tend, however to be too strict in large samples. Further analyses were conducted to inspect if any of the ratios exceeded 10:1(Tabachnick & Fidell, 2007). As none of them exceeded 5:1, this was not followed up by any further analyses.

3.5. Ethics

This research was approved by the Regional Committee of Ethics in Medical Research, the Norwegian Institute of Public Health, Oslo University Hospital, and the Norwegian Data Inspectorate. Informed written consent was obtained from the parents of the children in the study. During the clinical assessments, extra care was taken to ensure that the participating children felt comfortable and at ease. At the end of the one-day assessment, the psychologist and/ or the psychiatrist who had examined the child went through the results together with the parents, opening for any questions they might have with regard to the assessments. All participating families were offered a written report, containing information about the study, and a short summary of results from the clinical assessments. Parents who had concerns about their child's development received a written recommendation for further assessment at their local clinic.

4. MAIN FINDINGS

4.1. Paper I

In this paper, we investigated associations between symptoms of ADHD and/or ODD and two core EF component processes, inhibition and working memory. Relations between behavioral symptoms and neuropsychological measures of inhibition and working memory were studied both categorically and dimensionally. We found that children with co-occurring symptoms of ADHD and ODD performed at a significantly lower level than typically developing children in four out of five EF measures. Symptoms of ADHD, both alone and in combination with ODD, were associated with reduced performance on tests of inhibition in the group comparisons. Dimensional analyses showed that performance within both EF domains contributed to variance primarily in ADHD symptom load. The associations between test results and behavioral symptoms remained significant after gender and verbal skills had been controlled for. The young preschoolers investigated in this study showed a pattern of relations between EF and behavioral symptoms of ADHD and/or ODD which resembles patterns of EF difficulties described in older children diagnosed with ADHD and/or ODD. Effect sizes were generally small in this study, indicating that the investigated measures of EF have limited clinical utility at this stage in development.

4.2. Paper II

The aim of this paper was to explore the factor structure of early EF as measured by the Behavior Rating Inventory of Executive Function-Preschool version (BRIEF-P). In the first set of analyses, parent BRIEF-P ratings were subjected to confirmatory factor analyses (CFA). Three theoretically derived models were assessed; the second order three-factor model originally proposed by the BRIEF-P authors, a "true" first order one-factor model and a second order one-factor model. Results yielded support for the three-factor solution proposed by the BRIEF-P authors. However, the difference in fit was marginal between this model and the second order one-factor model. A follow-up exploratory factor analysis (EFA) supported the existence of several factors underlying EF in early preschool years, with a considerable overlap with the five BRIEF-P subscales. Our results thus suggested that some differentiation in EF has taken place at age three years, which is reflected in behavior ratings. The internal consistency of the BRIEF-Ps five clinical subscales was supported, but in early preschool years, subscale interrelations may differ from those observed in the preschool group as a whole.

4.3. Paper III

This study investigated relations between early symptoms of ADHD and EF as measured by the BRIEF-P. Relations between ADHD symptoms and each of the five BRIEF-P subscales were studied dimensionally. The inventory's discriminative ability was examined in a subsample consisting of children with symptoms of either ADHD, ODD or anxiety, and typically developing controls (TD). Patterns of EF difficulties across these four groups were compared in a profile analysis. Of the five BRIEF-P subscales, Inhibit and Working Memory were the two most closely related to ADHD symptoms in our sample, together explaining 38.5% of the variance in PAPA symptom ratings. In the categorical analyses, 86.4% of the children in the ADHD and TD groups were correctly classified by the combined scores of the Inhibit and Working Memory subscales. ADHD symptoms were associated with more severe difficulties across EF domains, and a different EF profile compared to children with internalizing problems and typically developing controls. The findings support the clinical utility of the BRIEF-P as a measure of EF in young preschool children with symptoms of ADHD.

5. GENERAL DISCUSSION

5.1. Methodological considerations

The main findings of this thesis are dependent on several methodological issues related to the measurement of EF and to the generalization of findings. In the following, basic issues will be considered, with regard to the reliability and validity of results presented. The lack of a general agreement about the definition of EF is in itself an important methodological issue; a further discussion of how the term should be defined is however considered to be beyond the scope of this thesis. Issues pertaining to the measurement of EF are, however, seen as particularly relevant to the interpretation of our findings and will be addressed both in relation to the specific EF measures employed, and later on in the discussion of our main results.

5.1.1. The measurement of executive function in preschool children

Data obtained from a given test, questionnaire or interview are considered reliable to the extent that they are consistent across different points in time (test-retest reliability), across different raters (inter-rater reliability), and across items purporting to measure the same construct (internal consistency). Validity is determined by the degree to which these assessment tools actually measure what you set out to measure. Construct validity is explored by investigating its relation to other constructs; both related (convergent validity) and unrelated (discriminant validity). The term ecological validity refers to the results' generalizability to an everyday setting.

An accurate understanding of normal cognitive development is critical for obtaining reliable and valid data about EF in young children. A significant period of development is likely to occur before a given cognitive process is fully functional, where a given basic skill goes through a developmental sequence towards a fully functional level; emerging (early acquisition stage, not yet functional), developing (partly aquired) and established (fully established and functional) (Anderson, 2002). Implicit in this perspective is the notion that for a skill to be reliably and validly measured, it must have reached a fully mature, stable level. The current understanding of EF in young preschool children is based on a limited, but growing number of studies. As previously stated, the integration of these findings is challenging with regard to childhood EF in general and preschool EF in particular. The question, whether the indicators (test performance or observable, everyday skills) are likely to reflect the construct we wish to measure (EF) is closely related to the developmental appropriateness of the neuropsychological tasks or behavioral descriptions selected for the studies presented here.

A second, overall methodological consideration is related to “task impurity”. Considered a complex-higher-order capacity, EF builds upon several other, non-executive processes (visuo-spatial abilities, language skills, and memory). Any measure designed to measure EF will necessarily reflect variance in these non-EF capacities in addition to variance stemming from the targeted construct. Depending on what kind of response a given task requires of the child, his or her performance will also be influenced by other fundamental skills such as fine- and gross motor abilities, eye-hand coordination, and processing speed (Rommelse et al., 2007; van der Ven et al., 2013). As the preschool years are characterized by rapid development not only with regard to EF, but also within these functional areas, construct validity is an important methodological consideration in the assessment of emerging EF.

Information about EF may be obtained at different levels, from different sources and for different purposes. Methodological choices need to be based on an understanding of which aspects or levels of EF are reflected by any given measurement tool. This knowledge is particularly valuable in the interpretation of information about EF that has been obtained by a combination of different sources and/ or by different methods.

5.1.1.1.Neuropsychological assessment

The selection of age-appropriate tests for the assessment of EF in preschool children is still limited, and the neuropsychological assessment in the ADHD study were a mix between subtasks taken from standardized, well validated test batteries (SB-5, NEPSY), and experimental tests based on well-known paradigms in the field of pediatric neuropsychology (for an overview, see Isquith, Crawford, Espy, & Gioia, 2005). For the experimental tests, normative data are typically scant, and evidence for reliability and validity limited. The experimental tasks administered to the ADHD study participants were selected on the basis of their face value as measures of EF in young children (i.e. face validity), and on accounts from previous research using them to assess specific EF process components in the age group. Extra care was taken, to include tests that were engaging, not too lengthy, with short and easily comprehensible instructions, and various response modalities. The neuropsychological tests included in the present research were selected from the ADHD study's clinical assessment.

The SB-5 is a well validated estimate of general intellectual ability in the preschool age range. The full scale estimate is highly correlated with one of the most widely used intelligence measures in the age group; the Wechsler Preschool and Primary Scale of Intelligence (WPPSI-R) (Roid, 2003a). In order to keep the neuropsychological assessment as short as possible, thereby reducing possible threats to the scores' reliability (such as fatigue), we chose to use the abbreviated IQ estimate (ABIQ). The correlation between ABIQ and full scale IQ is .81 for the age group 2-5 (Roid, 2003a). As test performance in the youngest children is subject to considerable extraneous variance, usually yielding modest test-retest reliability, this was considered acceptable.

Three SB-5 subtasks were used to assess working memory; Delayed Response, Block span and Memory for sentences. The validity of the two latter tasks as measures of working memory has been questioned. They both represent a relatively low cognitive load in the sense that they primarily demand simple storage and retention of information, and not simultaneous manipulation in WM which is commonly considered central to the working memory construct. However, based on what is known about memory span in typically developing children (Bayliss, Jarrold, Baddeley, Gunn, & Leigh, 2005; Bull, Espy, & Wiebe, 2008, Buss, Fox, Boas & Spencer, 2014), we have argued that the majority of the items in these tasks exceeds the memory span (auditory, visual) of a three-year old child. Overall test performance is thus likely to rely on the child's ability to actively rehearse and update information held in memory.

Spin the Pots task (Hughes & Ensor, 2005) is frequently used as a measure of nonverbal working memory in young children. The task is a self-order pointing task, very similar to "The Boxes Task" (Kerns & McInerney, 2007), and "Multiple Boxes" (Llamas & Diamond, 1991), a type of tasks that has shown good test-retest reliability in both school-aged children (Archibald & Kerns, 1999) and in preschoolers (Beck et al., 2012; Müller et al., 2012). The pattern of correlations observed, between the Boxes task and the backward span tasks included in the above study by Müller et al. also rendered support to the tasks validity as a measure of working memory. It is likely to put a higher load on updating and manipulation of information stored in memory than do the two SB-5 subtasks. The number of times the child opened a box contrary to the instructions given has face validity as a measure of his or her ability to suppress a prepotent response holding an arbitrary rule in mind across several trials (complex inhibition). It should be noted with regard to this last score, that it was dependent on the total number of trials needed to locate all six stickers. This was not corrected for in the subsequent data analyses, and for some of the children who struggled on this test, this may have resulted in an inflated impulsivity score. Preliminary analyses of data in our sample indicated that the task had an appropriate level of difficulty (no floor- or ceiling effects) with normally distributed scores, and sufficient variability. In concordance with this, our impression from administering this task as part of the ADHD study's clinical assessment, was that Spin the Pots is very well suited for use with young preschool children; instructions are easy to understand, the children are easily engaged in it, and relative to some of the other tasks administered, performance seem more robust to temperamental differences, diurnal variations in vigilance, or difficulties in establishing report with the child in the test situation. Frequently used as an inhibition measure in preschool populations, the NEPSY Statue has been reported to differentiate well between preschool children with and without externalizing problems (Mahone et al., 2005; Youngwirth et al., 2007). Test-retest reliability for the Statue subtest was originally reported to be poor (0.50). In the revised NEPSY (NEPSY II; 2007), with updated normative data, the Statue subtest is administered in the exact same manner, but the reliability coefficient is reported to be considerably higher (0.82). These findings indicate that scores on the Statue test may be subject to some extraneous variation. It is uncertain, though, to which degree this may have affected test performance. The task was relatively easy to conduct with the three-year old children in our sample, it was however observed that the task could be a bit more challenging for the most timid and shy children. Instructions are likely to put demands also on verbal working memory. Preliminary analyses indicated an adequate level of difficulty, sufficient variability, and a normal but relatively flat distribution of scores. The latter may in smaller samples (<200) lead to underestimation of variance, but is not likely to represent a problem in the analyses included here, as all relevant analyses were run in subsamples larger than this (Tabachnik & Fidell, 2007).

Performance on each of these performance-based measures was rated by two different clinicians in a randomly drawn subsample of ADHD study participants. Scores from a first and a second rater were strongly correlated, with coefficients ranging from .91 (StB Verbal Working Memory) to.99 (Spin the Pots total score). Inter-rater reliability was on this basis considered adequate for all five measures.

Percentage of correct responses in the TD group from paper I ranged from 51.3 (NEPSY Statue), through 60.5 and 69.2 for the nonverbal and verbal WM scores from StB, to 76.3 for Spin the Pots total score (accuracy level could not be computed for the impulsivity score from Spin the Pots, as it does not have a defined maximum score). According to Miller et al. (1995) the percentage of correct responses of the control group is a good estimate of a measure's discriminating power. A test with an accuracy level of 50% would have maximum discriminative power, but could be difficult to administer in a preschool sample due to difficulties maintaining motivation (Egeland, 2003). In light of this, accuracy level for the included performance-based measures should be in the optimal range.

Despite their young age, the majority of the participating children completed all the tasks in the neuropsychological assessment. Some of the children were, for various reasons, less motivated to finish one or more of the tasks during the assessment. In most cases, this was solved by taking a small break or changing to a new task for a while, before returning to it. If a child still could not be motivated to continue, the test administrator could render small rewards (a few raisins, grapes or small pieces of biscuits) after the completion of a task- independent of task performance- pointing out to the child that "this is a prize for good work". This strategy is likely to have affected test performance through increased motivation, but may also have been the only way to ensure valid test data from some of the children in our sample with the most pronounced difficulties related to task-oriented behavior.

Applying to all clinically administered tests of EF, there is concern that the highly structured test situation (with or without the use of rewards) may serve to camouflage poor regulatory skills. If one sets out to objectively measure a child's maximum capacity with regard to specific EF component processes (e.g. mental flexibility, inhibition) under optimal conditions, this may not be a serious limitation. If, in contrast, the end goal is to gather information about the child's executive capacities in an everyday setting, most would agree that this limitation represents a validity problem. This issue, related both to construct validity and external (ecological) validity will be further addressed in relation to our main findings.

5.1.1.2.Behavior ratings

The Preschool Age Psychiatric Assessment (PAPA) is currently one of very few comprehensive, parent-report psychiatric interviews with demonstrated test-retest reliability and validity for assessing psychiatric symptoms in preschool children (Egger & Emde, 2011).

Convergence with other psychiatric assessments is still little investigated, but the interview has been shown to map onto dimensions of preschool psychopathology defined in DSM-IV fairly well (Sterba, Egger, & Angold, 2007). Diagnoses based on PAPA also seem to share patterns of continuity/discontinuity with those that are based on other, frequently used diagnostic instruments (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012). Estimates of test-retest reliability for the interview have been shown to be adequate, and very similar to those demonstrated in widely used, well established psychiatric assessments developed for older children (Egger et al., 2006). In the ADHD study, inter-rater reliability was checked by a second rater, blind to any information about the child or his/her family. A total of 79 randomly selected audiotapes of the PAPA interview were rated, indicating satisfactory inter-rater reliability; average intra-class correlations were 0.98 for total number of ADHD and ODD symptoms, and 0.86 for anxiety symptoms (any anxiety disorder).

The BRIEF-P items were selected from the original pool of items from BRIEF, which in turn had been selected on the basis of theory, clinical practice and extant research literature. Their convergent and discriminant validity were assessed using a multi-trait-multi-method evaluation (Gioia et al., 2000). For the preschool version, some items were discarded, some were altered, and some new were added in order to reflect preschool-specific settings and behaviors (Isquith, Gioia, & Espy, 2004). The included behavioral descriptors should thus be considered valid indicators of EF in preschool children. A typical finding in studies of the original (school-age) version is that the inventory is strongly related to other parent rating measures of behavioral difficulties. Further, that it is highly sensitive to ADHD-related difficulties (Mahone et al., 2002). This seems to apply also for the preschool version (Ezpeleta et al., 2013; Mahone & Hoffman, 2007). The structure of the inventory (five subscales, three broader indexes) was derived on the same basis as the item selection, and verified by use of factor analysis (Isquith et al., 2004). The proposed structural organization of EF as measured by the inventory has since been verified in two studies of non-referred preschool children (parent and/ or teacher ratings) (Bonillo et al., 2012; Ezpeleta et al., 2013). Two of the subscales have, however, been suggested to measure more than one underlying factor in a third factor analytic study (Duku & Vaillancourt, 2013). The BRIEF-P authors reported modest correlations between parent and teacher ratings ($r=.19$), suggesting relatively low inter-rater agreement. This finding warns against the generalizing of results across raters- at least across different types of raters observing the child in different settings. Appropriate test-retest reliability has been reported for the inventory's five BRIEF-P subscales, as well as satisfactory internal consistency (Isquith et al., 2004). Estimates of internal consistency in our sample proved similar to those reported by the BRIEF-P authors, ranging from .76 to .95.

Our data, both on psychiatric symptoms and EF behavior, were based on information from the parents. In this age group, there is reason to believe that they are a particularly relevant source of information about the child's behavior and abilities across a wide array of situations and settings. The parents' previous experience and expectations with regard to normal behavior in young preschool children will necessarily influence their perception of behavior as within or outside normal variation. The diagnostic cut-off points in PAPA may have reduced the effect of possible unreasonable expectations for the child's behavior, but must be considered arbitrary as long as there is a lack of good descriptions of what should and should not be considered normal levels of inattention, hyperactivity and impulsiveness in this age group. Rater bias may also have affected results based on BRIEF-P inventory, and will be further addressed in the discussion of our main findings. Finally, it should be noted that some of the items in the BRIEF-P overlap with DSM-IV criteria for ADHD. As both are based on information from the parents, this is an important concern that should be kept in mind when evaluating the results presented in paper III, estimating relationships between behavior ratings of EF and early symptoms of ADHD.

Potential sources of both random and systematic error were addressed in order to increase the reliability of results from the clinical assessments. The large sample size protects against the potential effects of random error, but not against possible systematic errors committed during the data collection. The neuropsychological assessment was conducted by clinical psychologists with special competence in child neuropsychology. Junior psychologists were supervised by a senior clinician in order to minimize errors conducted during test administration, and to evaluate the interpretation of the child's responses and scoring of test items in cases of doubt. Test scores were punched twice, by two different persons, in order to detect and rectify punching errors. The PAPA interview was conducted by graduate students in psychology trained in administration and scoring of the interview, or by clinical neuropsychologists or psychiatrists. All neuropsychological examinations were videotaped, interviews were audio taped, and the scoring was supervised by neuropsychologists or child psychiatrist.

5.1.1.3. Relationships between neuropsychological tests and BRIEF-P ratings

The correspondence is typically reported to be poor, between information obtained by use of clinically administered tests and behavior ratings of EF (McAuley & White, 2011; Silver, 2014). In a recent review of studies measuring EF by a combination of neuropsychological tests and behavioral ratings, the mean correlation between scores on performance-based measures and behavioral ratings obtained by use of the BRIEF was reported to be .15 (Toplak et al. 2013). Similar results are described in the few preschool studies that have been published so far, based on the BRIEF-P (Ezpeleta et al., 2013; Ezpeleta & Granero, 2014; Mahone & Hoffman, 2007).

Relations between neuropsychological test results and BRIEF-P were not directly investigated in our three papers, as none of them included both measurement methods. In order to facilitate the interpretation of results based on either clinically administered tests or behavior ratings of EF in the above studies (Papers I – III), a set of additional analyses was conducted, examining correspondence between scores on the neuropsychological tests included in Paper I and parents' BRIEF-P ratings. Based on results from our factor analytic study (Paper II), suggesting that item- and subscale interrelations in the BRIEF-P (the Inhibit and Working Memory scale in particular) at age three years may differ from those observed in the preschool group as a whole, additional analyses were run to investigate how the test measures were correlated with scores from the BRIEF-P at both subscale- and item level. Results at scale level are presented in Table 1, while the item level results are included in Table 2. The effects of SES, gender and IQ have been included as possible confounders in previous analyses (Papers 1 and III; see also Rohrer-Baumgartner et al., 2014). As their influence on relations between either tests or ratings of EF and ADHD symptom load consistently was found to be limited, they were not included in these additional analyses. Due to several non-normal distributions in our data, Spearman's correlation coefficients were computed, converting the data into ranked scores (Field, 2009).

The five performance-based measures of EF were related to parents' ratings of EF behavior in our sample. In line with previous research on both school-age and preschool samples, coefficients were small; ranging from .06 to .16.[1] The larger part of variance in test scores and ratings used to assess either inhibition or working memory in our three studies could thus be

[1] In this relatively large sample, several coefficients (below .10) obtained statistical significance signifying associations that are likely to be of little or no practical significance. A probability level of $p<.001$, corresponding to a correlation close to .10, was applied to facilitate the interpretation of the results.

said to stem from other sources than the constructs of interest. This may, however, not be a problem related primarily to the measures' psychometric properties. It is relevant to ask, whether the two types of EF measures actually tap the same underlying construct. A closer inspection of correlational patterns may add to our understanding of which processes are reflected by the two types of measurement methods.

Table 1 Correlations between ADHD symptoms, SES, BRIEF-P scales and indexes, and performance-based measures of inhibition and working memory

	BRIEF-P scales and indexes							
	Inhibit	Shift	Emotional Control	Working Memory	Plan/ Org	ISCI	FI	EMI
ADHD symptoms	**.59**	**.24**	**.34**	**.53**	**.45**	**.55**	**.34**	**.52**
SES	**-.11**	-.09	**.34**	**-.11**	-.10	**-.11**	-.08	**-.12**
EF								
NEPSY Statue	**-.13**	-.03	.01	-.09	-.05	-.08	-.01	-.08
Spin the Pots (Impulsivity)	**.16**	.07	.07	**.13**	.10	**.15**	.08	**.12**
StB Verbal WM	**-.13**	**-.13**	-.09	**-.15**	**-.11**	**-.12**	**-.12**	**-.14**
StB Nonverbal WM	**-.15**	-.05	-.05	**-.14**	**-.11**	**-.13**	-.06	**-.13**
Spin the Pots (Total score)	**-.12**	-.05	-.03	-.08	-.06	-.09	-.04	-.08

Note .N=1134. *StB*= Stanford Binet 5th Edition. WM= Working memory. ISCI= Inhibitory Self Cintrol Index, FI= Flexibility Index, Emergent Metacognition Index. SES= Socio Economic Status as measured by maternal education. Significant coefficients are bolded (p<.001).

In our young preschool sample, the performance-based tests purporting to measure inhibition and working memory processes were related to behavior ratings of EF primarily within these two domains, showing few or no significant correlations with items from the three remaining BRIEF-P scales (Table 2). The relationship between tests and behavior ratings *within* the inhibition and WM domains was less clear-cut.

Performance on the NEPSY Statue was associated almost exclusively with ratings on the Inhibit scale. The impulsivity score from the Spin the Pots was also related to the majority of items in the Inhibit scale, but had a secondary association with the Working Memory scale. Two of the three WM tests were significantly related to items primarily on the Working Memory scale in BRIEF-P, but also to some of the Inhibit scale items (nonverbal WM from StB). Spin the Pots total score showed very few significant correlations with EF behavior ratings in any of the BRIEF-P subdomains.

Table 2 Correlations between BRIEF-P items and performance-based measures of inhibition and working memory

BRIEF-P	Inhibition		Working memory		
	NEPSY Statue	StP Impulsivity	StB VWM	StB NVWM	StP Total
Inhibit					
Item					
3	-.07*	.06*	-.08*	-.05	-.08**
8	-.03	.06	-.05	-.09**	-.07*
13	-.09**	**.15*****	**-.15*****	**-.13*****	-.09**
18	**-.12*****	**.11*****	-.06	-.06	-.05
23	-.10**	**.13*****	-.07*	-.09**	-.08
28	**-.12*****	.10**	-.10**	-.01	-.06*
33	-.08	**.14*****	-.09**	-.08**	-.06*
38	-.09**	.09**	-.08	-.10**	-.07*
43	-.06	**.11*****	-.04	**-.11*****	.00
48	-.05	.08	-.05	**-.13*****	**-.13*****
52	**-.12*****	**.12*****	-.06*	**-.11*****	-.08**
54	-.10**	**.11*****	-.08**	-.10**	-.08**
56	-.11**	.10**	-.07*	**-.15*****	-.06*
58	-.05	**.13*****	-.07*	-.10**	-.07*
60	-.02	.05	-.08**	-.06	-.06
62	-.09**	**.13*****	-.09**	**-.13*****	-.06
Shift					
5	.01	.05	-.10**	.01	-.03
10	.01	-.03	-.07*	-.02	-.01
15	-.04	.07*	-.07*	-.06	-.02
20	.06	-.05	-.06*	.04	.04
25	-.01	.04	-.01	.02	-.02
30	-.10**	.07*	-.06	-.06	-.04
35	-.05	.07*	-.09**	-.06*	-.02
40	-.01	.02	-.08	-.06	-.05
45	-.01	.04	-.04	-.05	-.05
50	-.08*	**.12*****	-.10**	-.09**	-.08**
Emotional Control					
1	.02	.05	-.05	-.04	-.03
6	.00	.02	-.08**	-.03	.01
11	.02	.09**	-.09**	-.05	-.08*
16	.00	.00	-.02	-.01	.04
21	.04	.03	-.04	-.06*	-.01
26	.02	.03	-.06	.00	-.01
31	.00	.10**	-.10	-.05	-.06*
36	-.04	.11**	-.06	-.07	-.05
41	-.06	.05	-.08	-.03	-.06
46	.00	.01	-.06*	-.02	.00
Working Memory					
2	-.03	.06*	-.10**	-.07	-.06*
7	-.07*	**.12*****	**-.13*****	**-.11*****	-.06*
12	-.09**	**.11*****	-.05	**-.12*****	-.06
17	-.06	**.11*****	-.07*	**-.12*****	-.09**
22	-.01	.07*	-.04	-.03	-.04
27	-.01	.09**	**-.15*****	-.10**	-.09**
32	-.06	.05	-.07*	-.09**	-.03
37	-.05	.06	.00	-.04	-.03
42	-.08*	.10**	-.10**	**-.11*****	-.02
47	-.04	.09**	**-.12*****	**-.12*****	-.07*
51	-.04	.04	-.05	-.04	-.04
53	-.03	.05	-.07*	-.08*	-.03
55	-.04	**.11*****	**-.14*****	-.08**	-.05
57	-.03	.07*	-.05	-.07*	-.06
59	-.01	.09	-.09**	-.04	-.05
61	-.10**	.10	-.10**	**-.12*****	.00
63	**-.13*****	.10**	-.10**	**-.15*****	-.06
PlanOrg					
4	-.03	.05	-.07**	**-.10*****	-.03
9	.01	.09**	-.06	-.02	-.02
14	-.06	.04	-.05	-.07	-.03
19	-.01	.05	.00	-.02	-.04
24	-.02	.01	-.10**	-.01	.01
29	-.05	.10**	**-.13*****	-.06	-.04
34	-.05	.03	-.08*	-.05	-.01
39	-.03	.09	-.10**	**-.11*****	-.03
44	.00	.04	-.04	-.05	-.04
49	-.04	.10**	-.05	-.05	**-.11*****

Note: Spearman's correlations, *p<.05, **p<.01, ***p<.001

Children's scores on the NEPSY Statue test correlated almost exclusively with inhibitory problems as rated by parents. This suggests a larger degree of overlap, between simple inhibitory processes thought to be measured in the Statue task (versus Spin the Pots), and inhibitory skills that are directly observable in the child's everyday settings. In light of the literature on early EF development, the finding could reflect a developmental sequence; at age three, simple (but perhaps not more complex) inhibitory skills are likely to have reached a stable developmental level (Carlson, 2005; Garon, 2008) making them more reliably identifiable via ratings of a child's inhibitory skills across time and different situations. Likewise, the observed associations between the three WM measures' and parent-rated EF could reflect differences among the clinically administered tasks with regard to their reliance on emerging EF process components. An additional aspect that should be considered when looking at differential relationships between measures is the previously noted difference between the EF tests with regard to discriminative power. Exemplifying this, the higher accuracy level of the Spin the Pots (total score) in our sample (76.3% versus 60.5% for the StB measure of nonverbal WM) increases the likelihood of obtaining a high score on this test, for children with EF deficits and higher problem ratings on the BRIEF-P.

At this point, it seems clear that the relationship between neuropsychological tasks and ratings of EF behavior may be influenced by several factors related to the specific measures involved, (including measurement error) operationalization of the construct we intend to measure, and to development. The research presented here is of particular relevance to clinical populations, and it is necessary to establish, whether the above findings apply to the clinical group of interest. In our case, this would be children with elevated levels of ADHD symptoms. Together with children exhibiting different kinds of behavior problems, our population-based sample comprised a large proportion of symptom-free children. The possible moderating role of ADHD on the above relationships could therefore be investigated by comparing the previously described correlational patterns in a high- versus a low ADHD symptom load condition. In order to do this, the sample was divided in two at mean number of ADHD symptoms, resulting in two similar-sized groups. Correlations between scores obtained on the performance-based tests and the five BRIEF-P subscales in the two groups ("ADHD high", "ADHD low") are presented in Table 3. Confidence intervals were computed for each coefficient in order to identify possible significant differences between the two groups. Some of the associations reported in Table 1 fell below the level of statistical significance in this second analysis, most likely as a result of restrictions introduced on ADHD symptom range and reduced statistical power.

The coefficients in Table 3 (next page) suggest a trend, towards a slightly higher magnitude in associations between EF test scores and parent ratings of EF in children with high ADHD symptom load as it was defined here. However, only one pair of intervals deviated significantly from each other. Our results thus suggest that estimates of the correspondence between information obtained by the two types of EF measures reported in the first set of analyses (Table 1) are representative across symptom severity.

Regardless of ADHD symptom load, the proportion of variance shared by tests and ratings of EF observed in our data was small- even for tests and behavior ratings targeting the same EF domain. Nevertheless, patterns of interrelations between neuropsychological tests and ratings of inhibition and WM suggest that they tap related constructs. A possible explanation for these seemingly contradictory findings could be that the clinically administered tests and behavior ratings of EF are related to similar constructs, at different levels. This issue will be further addressed in the general discussion's last section.

Table 3 Correlations between EF tests and BRIEF-P parent ratings (scale scores) at high versus low ADHD symptom load

	BRIEF-P scales and indexes							
	Inhibit	Shift	Emotional Control	Working Memory	Plan/ Org	ISCI	FI	EMI
	ADHD symptom load							
EF tests	High/low	High/low	High/low	High/low	High/low	High/low	High/low	High/low
NEPSY Statue (95% confidence interval) (lower *upper*/lower *upper* limit)	-.07/-.05 (-.16 *.02*/-.14 *.03*)	-.08/.06 (-.17 *.01*/-.02 *.14*)*	.06/.04 (-.03 *.15*/-.04 *.12*)	-.05/-.02 (.14 *.04*/-.11 *.06*)	.02/-.02 (-.08 *.11*/-.01 *.07*)	-.02/-.01 (-.11 *.08*/-.09 *.07*)	.00/.05 (-.09. *10*/-.03 *.14*)	-.02/-.02 (-.11 *.07*/.-04 *.06*)
Spin the Pots (Impulsivity)	.15**/.08 (.06 *.24*/.00 *.16*)	06/.03 (-.03 *.15*/-.05 *.11*)	.08/.00 (.00 *.17*/-.08 *.08*)	.09*/.08 (.00 *.18*/.00 .17)	.04/.07 (-.05 *.13*/-.01 *.15*)	.14**/.05 (.05 *.23*/-.03 *.13*)	.09/.01 (.00 *.17*/-.07 *.09*)	.08/.09 (-.01. *.16*/.01 *.17*)
StB Verbal WM	-.10*/-.04 (-.19 *-.01*/-.12 *.04*)	-.11*/.00 (-.20 *-.02*/-.08 *.08*)	.00/.02 (-.09 *.09*/-.06 *.11*)	-.11*/-.05 (-.20 *-.03*/-.13 *.03*)	-.05/-.02 (-.14 *.04*/-.10 *.06*)	-.06/-.02 (-.15 *.03*/.-10 *.07*)	-.05/.02 (-.14*.04*/-.06 *.10*))	-.10*/-.04 (-.19 *.01*/-.12. *04*)
StB Nonverbal WM	-.13**/-.04 (-.22 *-.05*/-.12 *.04*)	-.05/.00 (-.13 *.04*/-.08 *.08*)	-.05/.02 (-.14 *.03*/-.05 *.10*)	-.13**/-.05 (-.21 *-.04*/-.13 *.03*)	-.06/-.02 (-.14 *.03*/-.10 *.06*)	-.12**/-.02 (-.20*-.03*/-.09 *.06*)	-.06/.02 (-.15. *03*/-.06- *01*)	-.11*/-.04 (-.20. *-02*/-.12. *04*)
Spin the Pots (Total score)	-.13**/-.09 (-.22 *-.05*/-.17 *-.01*)	-.06/-.03 (-.15 *.03*/-.11 *.05*)	-.08/.02 (.17 *.00*/-.06 *.09*)	-.06/-.07 (-.15 *.03*/-.15 *.01*)	-.06/-.04 (-.15 *.03*/-.12 *.03*)	-.12**/-.05 (-.21 *-.04*/.-13 *.03*)	-.08/.00 (-.17.*01*/-.08 *.07*)	-.06/-.07 (-.15. *02*/-.15. *01*)

Note: N=1134. StB= Stanford Binet 5th Edition. StP= Spin the Pots. WM= Working memory. VWM= Verbal WM. NVWM= Nonverbal WM.*p<.05; **p<.01.

5.1.2. Representativeness and generalizability of findings

The participants in our three studies were recruited through a two-step process; first into the MoBa, and then from MoBa to the ADHD study. The participation rate in both steps were relatively low (35 and 38%, respectively), and it is necessary to consider whether our sample is representative of the preschool population. Of the 33 050 mothers returning the 36 month questionnaire, 3452 were invited to the ADHD study due to their high scores on the 11 screening questions, and date of birth within the timeframe (April 2004-January 2008). Children with high levels of autism symptoms (n=149) were not invited, due to ongoing recruitment into another MoBa substudy concerning autism based on the same MoBa questionnaire; this clinical group is therefore underrepresented in our sample.
The decision to participate in a scientific study is highly influenced by factors that may or may not affect research findings, such as educational level and health (Drivsholm et al., 2006; Knudsen, Hotopf, Skogen, Overland, & Mykletun, 2010). An investigation of the representativeness of the MoBa sample relative to births registered in the Medical Birth Registry of Norway (MBRN) in the same time window has revealed an underrepresentation of mothers who smoke, young mothers (<25 years), and of single-parent households in MoBa (Nilsen et al., 2009). The same selection mechanisms as described in the MoBa sample are likely to be evident also in the second sampling procedure, from MoBa into the ADHD study. Preliminary analyses show that, compared to mothers who participated in the MoBa and were recruited during the same period of time as our sample, the mothers of the children in our sample reported slightly higher educational levels, had fewer children, and were slightly older at the time of recruitment to the MoBa (G. Biele, personal communication, October 3, 2014). The possibility cannot be ruled out, that the two selection processes have led to the exclusion of some of the children with the most severe behavioral and cognitive problems.

As shown above, the two-step selection into the ADHD study has resulted in differences between our sample and the population with regard to certain factors linked to socioeconomic status, most likely also to the children's socio-emotional environment. Such factors have been shown to affect long term outcomes with regard to children's mental health and neurocognitive functioning. It is however not clear if, and how, these differences may have affected the way the two aspects of functioning (as measured by number of psychiatric symptoms and basic, self-regulatory skills) were related to each other in our studies. The underrepresentation of risk factors in our sample may have attenuated associations between psychiatric symptoms and EF. The oversampling of inattentive and restless children into the ADHD study is however likely to have had and opposite effect on the same associations. Given present knowledge about comorbidity in preschool children with psychiatric symptoms, several other risk factors may or may not follow this pattern, and the possible effects thus become difficult to disentangle. Results from investigations of sample bias in the MoBa and other large cohorts have so far indicated that limitations in representativeness may not compromise the validity of the associations under study. In a study addressing self-selection bias in MoBa, no statistical differences were found, between MoBa participants and data from the national medical birth registry, in associations between pre- and perinatal variables thought to be affected by the risk factors separating the two samples (maternal smoking, single household, young mothers) (Nilsen et al., 2009). Investigations of possible bias in two other large cohorts have later reported similar results (Greene, Greenland, Olsen, & Nohr, 2011; Knudsen et al., 2010). Self-selection bias has also been analyzed in the previously mentioned MoBa study, of children with autism (ASD); here, associations between ASD and peri- and postnatal exposures were found to be close to those reported in the population (Nilsen et al., 2013).

During data collection and the first explorations of the ADHD study's data material, several challenges were discussed related to diagnostic categorization in early preschool age; such as assessment of impairment, boundaries between normal/abnormal development, and the combination of information from different sources (parents, clinicians). In the absence of diagnostic criteria specifically developed for use in this age group, boundaries between diagnostic groups had to be drawn based on a limited empirical literature together with thorough considerations of the above questions. To a certain extent, decisions relating to group definitions were also influenced by previous research in similar samples, as this could facilitate the comparison of results across studies. The above considerations resulted in different selection of cases and controls in Papers I and III. While the clinical groups and the controls in paper I were defined quite widely, focusing on what may be early forms of the disorders under study, the clinical groups in Paper III were defined on the basis of formal research diagnostic criteria in order to compare possible diagnosis-specific profiles of EF difficulties and to facilitate the direct comparison of our results with those from previous (and future) studies of the BRIEF-P. The symptom-free controls in Paper I were selected from the entire ADHD study sample, thus containing a large number of screen-positive children. As a consequence, the reported group differences may have been attenuated relative to what may have been the result using a comparison group drawn from the population. The typically developing control group in Paper III was defined this way, but could be argued to constitute a socalled “supergroup” with equally limited generalizability to the target population.

5.1.3. Strengths and limitations, a summary

Taken together, the neuropsychological tests used to assess EF in our sample are considered developmentally appropriate, valid measures of EF in preschool children. Test performance in young children is, however subject to considerable extraneous variation, both due to situational factors (rapport, test instructions, motivation), and to attributes of the child (temperament, language, motor development). These are factors that to some extent may have affected both reliability and validity of the presented results. Although few, empirical studies of the BRIEF-P have so far rendered support to the inventory as a valid measure of EF in this age group, suggesting that it shares the original versions satisfactory psychometric properties. The generalization of results from the neuropsychological tests of EF and of behavior ratings of EF warrants caution, as they may not apply equally well across settings and across the entire span of symptom severity in the young preschool population.

Limitations in the representativeness of our sample also have consequences for the generalization of findings, and must be taken into consideration. Relative to clinical samples, children from high-risk families are underrepresented, and likewise, children with clinically significant levels of psychiatric symptoms are underrepresented in relation to a non-clinical sample. According to studies of possible bias effects on exposure-outcome variables in the MoBa and other large cohorts, the above limitations related to representativeness are not likely to compromise the external validity of our results. The possibility may, however not be ruled out. Estimates of effect size should be interpreted with the above limitations in mind. Our findings are considered particularly relevant in clinical settings, addressing relations between EF and ADHD-like symptoms in a group of children with behavioral problems sufficient to raise concern in their parents.

5.2. Interpretation of the main results

As our data were obtained at only one time point, they may not serve as a basis for any conclusions with regard to developmental trajectories or causal relationships. Generalization of the present findings to the entire preschool age group must also be made with caution, given the rapid developmental changes taking place during this period. Our results offer, however, a ‘peak’ into EF at a point in development when core self-regulatory processes are thought to reach a first relatively stable, functional level. Investigations of EF in this young sample also offer new information about what may be the earliest signs of deviant EF development likely to contribute to the development of ADHD.

5.2.1. Differentiation and structural organization of early EF

The majority of empirical studies of EF in preschool children have supported a unitary, domain-general EF structure (for an overview, see Lee et al., 2013). The view of EF as a unidimensional construct in young children is consistent with research indicating that the differentiation of core EF components occur from late childhood onward (Shing, Lindenberger, Diamond, Li, & Davidson, 2010; Tsujimoto et al., 2007). At the same time, a growing literature on EF development suggests that early forms of EF process components are differentiated and identifiable at a much earlier point in development (Best & Miller, 2010). How, then, will a unitary model map onto the structural organization of EF at age three- when these skills are thought to emerge?

A substantial proportion of variance, both in performance-based measures and behavioral ratings of EF, was *not* accounted for in our three studies. Effect sizes in both categorical and dimensional analyses were modest (Papers I and III), and the factors extracted in the EFAs (Paper II) explained less than half of the variance in the behavioral ratings. Some systematic relations were evident, though, which may contribute to the understanding of the structure of EF at this early point in development. In the factor analyses (Paper II), separable, but interrelated EF process components were identified. This finding corresponds to results from both the categorical and the dimensional analyses (Papers I and III), showing that core EF components were differently related to symptoms of ADHD and other common psychiatric disorders in our sample. The original three-factor model of EF as measured by the BRIEF-P was supported by our data, providing a slightly better description of early EF structure than two versions of a one-factor solution (Paper II). Consistent with several other studies across the childhood age span, our results thus indicate that basic, self-regulatory processes are differentiable but interrelated in young preschool children (Garon et al., 2008; Hughes, 1998; Senn et al., 2004; Sonuga-Barke et al., 2002). This finding fit into a unity/diversity framework, postulating that different EF components tap into some common, underlying process (unity) and are therefore correlated with one another; they are also separable (diversity) in that correlations between them are substantial, but far from 1.0 (Miyake & Friedman, 2012). Results from the two papers based on the BRIEF-P as a measure of EF (Papers II and III) indicated the presence of several common, underlying factors in behavior ratings of EF in our sample; both in terms of item clustering in the factor analyses, and by the factors' different relations to different psychiatric symptoms assessed in the PAPA interview. Results from the item level EFA must, though, be interpreted in light of the fact that the inventory was developed to asses EF within five clinically and theoretically derived EF domains (Isquith et al., 2004). These pre-specified subdomains would be expected to appear as separable factors in the EFA, and (at least to some degree) to facilitate their combination into the three broader factors or indexes proposed. Although this may have worked in favor of the structural model suggested in BRIEF-P, results from our three papers seem to converge on the finding that some differentiation has taken place at age three, which is measurable by both neuropsychological tasks and ratings of EF behavior in everyday settings. The next question is how these early, common factors may best be described.

Results from the EFA indicate that there is some overlap between the factor structure in our sample and the factors suggested by the BRIEF-P authors. As such, our results render support to the clinically and theoretically derived EF subdomains in BRIEF-P as measurable and meaningful entities/constructs also at age three. Some discrepancies warrant consideration, though. The first factor in the exploratory analysis, explaining by far the largest proportion of variance in EF ratings, was a mix consisting of five items from the Working Memory scale (accompanied by one Plan/Organize item), and two from the Inhibit scale, all closely related to the child's ability to stay on task (Paper II). Two other item clusters related to other aspects of inhibition, and a second cluster of working memory-related items emerged as separate factors, explaining considerably smaller percentages of the observed variation. This pattern may reflect an early stage in the differentiation process, with fluctuating relations between items and smaller item clusters. Extraneous, situation specific variance may dominate in a relatively large proportion of the BRIEF-P items at a developmental stage when underlying, common factors has yet to reach a stable, more integrated functional level.

The "disappearance" of inhibition as a salient, consistent factor in the above results is interesting, as this EF component is considered to be established and differentiable from early on in development. In line with previous findings in preschool samples (Mariani & Barkley, 1997; Brocki et al., 2007; Thorell & Wåhlstedt, 2006), this EF component also show robust connections to symptoms of ADHD in our sample (Papers I and III). A possible interpretation of this finding is that inhibition is the one component most closely related to a common, unitary EF construct. Basic inhibitory processes are not an unlikely candidate for the common factor (unity) underlying variance in EF described in several previous studies of EF structure supporting a single-factor model in preschool age (Hughes et al., 2010; Wiebe et al., 2011; Willoughby, Blair, Wirth, & Greenberg, 2010). In a recent study of EF in toddlers, Friedman and Miyake showed that a common EF factor, very close to response inhibition, predicted individual differences in self-regulation in adolescence (Friedman, Miyake, Robinson, & Hewitt, 2011). On the basis of these and related results in older samples, demonstrating that after accounting for variance in this variable, there was no unique variation left for inhibition, the authors have proposed response inhibition as a candidate for unity in EF (Miyake & Friedman, 2012). The first factor in our EFA, explaining almost half of the total variance in parent ratings of EF could be a candidate for unity in our data. The items included in this factor seem to describe the most basic working memory and inhibition capacities (information retention, resistance to distractions). The common variance is likely to stem from an early-developing capacity that separates the infant or toddler's stimulus-bound behavior from the preschooler's growing ability to self-regulate. It may be argued that this is close to a definition of response inhibition – or, to an even more fundamental process; sustained attention (Anderson, 2002). Investigating EF at a point in development when these capacities are thought to emerge, this makes sense. The transition from a primarily reactive, stimulus-driven attentional selection to more controlled attention is thought to take place during the second year of life, and to support the emergence of simple behavioral regulation skills (Rothbart, Sheese, Rueda, & Posner, 2011; Rueda, Posner, & Rothbart, 2005).

Finally, it should be noted that the unity/diversity framework is based primarily on research investigating the relationship between three EF components; inhibition, updating (close to our definition of complex working memory), and shifting as measured by neuropsychological tests. Clinically administered tests typically assess decontextualized, emotionally neutral aspects of EF, and it could be argued that the proposed framework apply primarily to this type of tasks or settings. There are some indications in our data, suggesting that other dimensions than those measured by these tasks are relevant for EF at age three years. The use of rewards in the experimental task, Spin the Pots, was seen as a possible explanation for contradictory results on the working memory tasks in Paper I. The children's ability to regulate emotionally driven behavior seem likely also to have contributed to the partitioning of the Working Memory and Inhibit subscales into separate process components in the EFA, suggesting that the partition in hot versus cold EF is relevant/evident across the five originally proposed factors. The emergence of emotional control as a second factor, almost identical to the Emotional Control subscale, is also in accordance with the developmental time-table; emotional control is thought to develop in parallel with other EF components, starting in infancy (Posner et al., 2012; Rothbart et al., 2011). The BRIEF authors have previously suggested that the monitoring (and hence, regulation) of one's problem solving, and of one's social behavior constitute distinct subdomains in the school-age version (Gioia & Isquith, 2002). A factor analytic study in a mixed healthy and clinical school-aged sample confirmed this subdivision, noting that behavior regulation in a social context is likely to be more influenced by emotions than is task-oriented behavior (Egeland & Fallmyr, 2010).

5.2.2. EF in young preschool children with symptoms of ADHD

Early symptoms of ADHD were expected to be associated with EF difficulties primarily within the two core EF domains inhibition and working memory in our sample (Papers I and III). Both performance-based measures used to assess inhibition in Paper I differentiated between children with subthreshold- or clinical levels of ADHD symptoms, and typically developing controls in the predicted direction. ODD-related disinhibition proved to be related primarily to co-occurring symptoms of ADHD.

Successful performance on the two neuropsychological tasks measuring inhibition relies heavily on the child's ability to withhold a motor response, or simple response inhibition. This basic inhibitory capacity is also likely to underlie the most clearly defined inhibition factor derived from the behavioral observations (e.g. "Acts too wild or out of control", "Has trouble putting the brakes on his/her actions even after being asked") (Paper II). The finding, that ADHD symptoms in our sample seemed related to response inhibition is consistent with extant studies of EF in preschool samples, where the most robust associations between inhibition and ADHD are found in measures of simpler inhibitory skills (e.g. Berlin & Bohlin, 2002; Sonuga-Barke et al., 2002). In line with this, behavioral observations of EF in the same sample indicated a closer relationship between inhibitory difficulties and ADHD, relative to other diagnostic groups and controls (Paper III). As previously noted, estimates of the relationship between symptoms of ADHD and behavioral ratings of EF are likely to reflect a considerable proportion of shared variance (same informant, overlap between BRIEF-P items and DSM-III diagnostic criteria for ADHD). The finding that data from performance based measures and behavioral ratings of EF converge on response inhibition as the EF component most closely related to symptoms of ADHD is therefore noteworthy.

The notion of inhibition as a primary deficit in ADHD, disrupting other self-regulative processes (e.g. working memory, self-regulation of emotional responses, internal speech) (Barkley, 1997) may not be tested directly by use of our cross-sectional data. Nevertheless, results in Paper I render support to the view of disinhibition as an early emerging difficulty in ADHD at a group level, possibly preceding deviances in other aspects of EF.

Relative to the results for inhibition, findings were less clear with regard to the relationship between symptoms of ADHD and working memory as measured by neuropsychological tests (Paper I). A possible interpretation of the inconsistent results is that the relations between working memory and ADHD observed in school aged samples may not be evident during the first preschool years. ADHD-related difficulties in working memory (as measured by neuropsychological tests) have been demonstrated in later preschool years (Kalff et al., 2002; Mariani & Barkley, 1997; Thorell, 2007; Thorell & Wåhlstedt, 2006). In contrast, none of the previous studies including younger preschoolers found evidence for such an association, despite using measures suitable to obtain valid information about working memory also in the youngest children such as the and Noisy Book (Hughes, 1998; used by Sonuga-Barke et al., 2002) and different versions of the Spin the Pots task (Hughes & Ensor, 2005; used by (Schoemaker et al., 2012). In light of developmental research, describing EF development as a process characterized by shifts between active development and more stable consolidation phases our results may be taken to reflect an emerging relationship between working memory and symptoms of ADHD (Garon et al., 2008). Differences in task complexity may also have contributed to the working memory tests' different relations to ADHD symptoms in our sample; the Spin the Post task is likely to tap more complex working memory skills that may not yet have reached a stable functional level at age three according to the same literature. The comorbid group (ADHD/ODD) was the only one that differed from typically controls in both EF domains in paper I. As the two disorders have been associated with different patterns of EF difficulties, this may indicate an additive effect. Group comparisons in Papers I and III suggest that the two clinical groups may differ with regard to performance on tasks in the verbal domain, and in parent ratings of inhibition and WM. Relatively small symptom-specific deficiencies may thus have contributed to this result. Working memory, as it is operationalized in BRIEF-P, seemed closer related to ADHD; together with inhibitory problems this EF component separated children meeting diagnostic criteria for ADHD from the other two diagnostic groups (Paper III). To the best of my knowledge, only one previous study has addressed EF in young preschool children with ADHD using the complete parent form (all five subscales). The authors found the inventory to be highly sensitive to ADHD related difficulties, with the clearest subscale elevation in the Working Memory scale (Mahone & Hoffman, 2007). In our Paper III, these findings are extended by showing that they are likely to apply across a wide range of symptom severity. A newly published study, based on the BRIEF-P teacher form, investigating EF in preschoolers diagnosed with ADHD and/or ODD, has reported results similar to ours, supporting the specificity of working memory difficulties in children with ADHD (Ezpeleta & Granero, 2014). This finding, published after the completion of our three papers, also renders preliminary support to the pattern of EF difficulties described in the profile analysis of BRIEF-P ratings (Paper III).

Task complexity is likely to be a relevant dimension in this particularly active developmental period, causing differences in performance on tests purporting to measure the same EF component process in Paper I (van der Ven et al., 2013). In relation to ADHD, another source of variance may be equally important to consider. As previously noted, motivational aspects of EF have gained support as one of several possible pathways towards ADHD (Campbell & von Stauffenberg, 2009; Sonuga-Barke et al., 2003; Sonuga-Barke et al., 2010; Thorell, 2007). According to Pauli-Pott and Becker's meta-analysis of preschool studies of EF, age three may represent a "time window" where ADHD-related difficulties in motivationally driven self-regulation are particularly salient (Pauli-Pott & Becker, 2011). After the submission of the three papers presented here, these authors reported further results in support of delay aversion as an ADHD endophentype already during the preschool period in a study of unaffected children with a positive family history of ADHD (Pauli-Pott et al., 2014).

The discriminative ability of the two BRIEF-P scales Inhibit and Working Memory (ADHD versus typically developing controls) investigated in paper III proved similar to estimates reported for the school-age version (parent form, all five subscales combined) (McCandless & O' Laughlin, 2007; Reddy, Hale, & Brodzinsky, 2011). Interestingly, difficulties in inhibition did not contribute to differentiation among the school-aged children, while playing the role as a primary contributor to differentiation in our preschool sample. Taken together, this speaks for the temporal stability of ADHD-related difficulties in EF at the behavioral level. Further, it suggests that difficulties in different aspects of EF behavior are likely to play different roles in ADHD-related EdF across development. The three remaining clinical subscales in BRIEF-P, Shift, Emotional control and Plan/Organize, explained a very small proportion of variance in ADHD symptoms. Nevertheless, our results render support to the inventory's sensitivity to early EF difficulties in three of the most common disorders in the preschool population by demonstrating elevated levels of EF problems in children with symptoms of ADHD, ODD and anxiety relative to typically developing controls.

The above findings with regard to two core, early developing EF component processes fit well into longitudinal studies of EF in children with externalizing problems (ADHD, ODD, CD) (Brocki et al., 2007; Brocki et al., 2010). After the completion of our paper I, Tillman and colleagues have published results from another longitudinal study, providing further support for the hypothesis that EF develop hierarchically, with complex forms of inhibition and working memory building on simpler skills (Tillman, Brocki, Sorensen, & Lundervold, 2013).

A final consideration relates to boundaries between normal and abnormal EF based on the measures used to assess EF in our three papers. The ADHD group in paper I presented with scores that differed less than 1 SD from the control group mean on the neuropsychological tests. Although statistically significant, effect sizes were small. This limits, of course, the neuropsychological measures' predictive validity with regard to an ADHD diagnosis. In contrast, BRIEF-P ratings of inhibition and working memory exceeded the corresponding scores in the control group by 1.5 SD, which is a cut-off typically used in clinical settings. Contrary to expectations, none of the T-scores based on the original norms exceeded the suggested clinical cut-off at T=65 for any of the clinical groups. As our results otherwise support the inventory's validity as a measure of EdF, this may be related to a reluctance among parents to describe certain behaviors as problematic in the lower age range (where behavioral variability is highest), applying to *all* children in our sample. This reluctance may also be more pronounced in the Scandinavian countries relative to other cultures (Hovik et al., 2014; Wakschlag & Hans, 2002; Wichstrom et al., 2012). Adding to this, the under-representation of high-risk families in our sample may have excluded some of the children that would have scored highest on the inventory's problem scales. The applicability of the original norms to the youngest preschool children, and to the Scandinavian countries needs to be further investigated.

5.2.3. Neuropsychological tests and behavioral ratings as measures of emerging EF

Results from neuropsychological tests and behavioral ratings of EF in our sample converge on inhibition and working memory as possible contributors to the early development of ADHD. Our overall findings are thus consistent with a growing literature on EF in preschool children with symptoms of ADHD. Despite some converging results, associations between information obtained by performance-based measures and parent ratings were found to be weak.

Several different explanations have been offered for the lack of consistent relationships between the two types of EF measures, focusing on methodological strengths and weaknesses (reliability, validity) of the different instruments used to assess EF. The observation that the lack of consistency in itself seems consistent (across test paradigm and different ratings/raters) has led a growing number of researchers and clinicians to ask whether the two measurement methods tap the same underlying construct. Translated to the present research project, on EF and early symptoms of ADHD, the question would be whether the included neuropsychological tests of EF and BRIEF-P actually tap the same deficits. A closer look at the two methodological approaches is relevant to this discussion, as it could clarify what kind of information about EF is obtained- and further, which purposes this information may serve.

Neuropsychological tests of EF are administered in a standardized way, in a highly controlled setting. Distractions are kept to a minimum (unless they are part of the test), instructions are clear, and everything is done to ensure that the child may perform at his or her best on any given task. Thus, test performance render objective, reliable information about specific regulatory processes under optimal conditions. On the basis of this information, inferences may be made about brain-behavior relations and the efficiency of specific cognitive processes. Neuropsychological assessment of EF has been referred to as a measure of the child's maximal capacity with regard to EF process components. As such, it taps the *efficiency* of goal-directed behavior (Toplak et al., 2013). A controlled clinical setting allows for the testing of specific hypotheses with regard to EF involvement in different types of tasks, as well as relations between specific aspects of EF and psychiatric symptoms. Illustrating this, investigations of inhibitory and working memory processes in children with ADHD have contributed to the understanding of how specific EF process components may be involved in the development of problem behavior (e.g. Brocki et al., 2007).

Behavior ratings provide information about EF at a more molar level, across different contexts and over a longer period of time. The child's self-regulatory skills are rated, in our case through the eyes of a parent, based on his or her observations of EF as it plays out in the everyday world. Whereas clinically administered tests provide important information about optimal performance, behavior ratings of EF tap *typical* performance in real-world, goal directed behavior. Although vulnerable for possible rater bias, this level of analysis clearly has advantages with regard to external validity (generalization across situations). Of particular relevance to clinical assessments, this facilitates the prediction of both strengths and difficulties related to EF in the child's everyday context.

To sum up, the two measurement methods target core regulatory functions at different levels of specificity, in different situations, by different raters, within different time spans. It follows from this that scores obtained by tests and ratings should not be expected to be strongly correlated. Applying to the research presented here, test scores and parent ratings are not likely to tap the same deficits. They may, however, be argued to reflect deficits in a common, broadly defined construct. In light of the above discussion, it is evident that such a broad definition of EF has some clear limitations when it comes to operationalization and measurement in a research setting. At present, this seems to be the conclusion in the majority of studies assessing EF by a combination of neuropsychological tests and behavior ratings (e.g. Mahone & Hoffman, 2007; Schoemaker et al., 2011).

Clearly, there are strengths and weaknesses associated with both methods that have consequences for how to understand the obtained information, and how to use it. Performance-based measures may be the best level of analysis if the goal is to investigate the classically defined EF subprocesses (inhibition, working memory, shifting, planning) or even more specific abilities, perhaps in a research setting or as part of a comprehensive neuropsychological assessment aiming to describe a child cognitive abilities (optimal performance). Behavioral ratings of EF, such as the BRIEF-P, may better answer questions with regard to the individual's ability to use these skills over time and across different settings (typical performance). Both perspectives are relevant in assessments of EF if one seeks to understand how specific regulatory processes are related to observable behavior in an everyday context.

In a recent review of different sources of data about EF in children, three different approaches to the above described discrepancy were outlined; a first solution is to accept it and to define it more clearly. A second approach would be to develop empirical ways to integrate the two methods, and a third to try to close the gap by developing new assessment tools (Silver, 2014). A growing number of empirical studies combining performance-based measures and ratings of EF have contributed to the understanding of how they are related (Senn et al., 2004; Toplak et al., 2009). During the last few years, studies of neural correlates to core EF process components have contributed to a better understanding of relations between information obtained by different methods; both how they converge (Mahone, Martin, Kates, Hay, & Horska, 2009, Miele et al., 2014), and how they may differ (Faridi et al., 2014). Others have focused on developing measurement tools that narrow the gap between the two methods (Bassett, Denham, Wyatt, & Warren-Khot, 2012; Lawrence et al., 2004; Thorell & Nyberg, 2008). In the years to come, these efforts are likely to provide both researchers and clinicians with assessment tools that facilitate the integration of information from these two sources.

5.3. Implications

5.3.1. Implications for clinical practice

Basic self-regulatory skills in young children are important predictors for academic and social competence. Early forms of EF are identifiable and can be assessed as early as age three. Our results suggest that symptoms of ADHD are associated with difficulties in core executive components already at this early point in development, and clinicians are encouraged to incorporate an examination of EF in assessments of ADHD also in young children. The two core components inhibition and working memory may contribute to the development of ADHD, and should be given particular attention. Neuropsychological tests of inhibition and working memory have limited predictive value with regard to ADHD, while behavioral ratings of these two EF components may differentiate children meeting diagnostic criteria for ADHD, both from other diagnostic groups (ODD, anxiety) and from typically developing children already during early preschool years. As clinically administered tests and behavioral ratings are likely to yield information about different aspects of EF, the one should not be used as a proxy for the other. Information about EF obtained by use of clinically administered tests may be of particular value as descriptions of specific EF skills and their efficiency in the classroom or in task oriented behavior in general. Behavior ratings render information about if and how the child is able to use these skills in less structured settings across a wide variety of everyday settings. Both sources of information are important for the identification and description of EF skills across settings. At present, there is limited support for the efficiency of early intervention strategies among school-aged children with ADHD. Earlier identification and treatment of children presenting with difficulties in self-regulatory processes may, however, provide unique opportunities for lasting change (Halperin et al., 2012).

5.3.2. Implications for future research

By studying executive processes that are likely to play an important role in the development of ADHD, researchers will contribute to a better understanding of the complex interplay among executive processes, development and situational factors leading to the disorder.
In young preschool children, executive processes are in an early phase of differentiation. Labels used to define EF processes in older children and adolescents may not map onto EF structure in this age group, and more knowledge is needed, about early EF development. A better characterization of EF structure at this early point in development is important, as it will guide further research on EF in early ADHD.

Although a growing body of research indicates that core EF processes may be reliably measured also during early preschool years, performance-based measures need to be developed that better target early forms of core EF components as they develop. The small effect sizes in the research presented here is consistent with recent theoretical perspectives on ADHD as a heterogeneous, complex disorder; EF is likely to be one of several factors implicated in ADHD symptomatology and should be studied in relation to other processes. We also need a better understanding of how basic, regulatory capacities may be related to self-regulation in everyday situations.
Research addressing EF in young children with symptoms of ADHD is still scarce, and the boundaries separating normal variation from pathology are unclear- both with regard to EF and to ADHD. Studies that can provide such guidelines should be prioritized in future

research. Associations between working memory and early symptoms of ADHD should be further investigated across raters and samples (clinical, nonclinical), preferably in studies combining different measurement methods. Longitudinal studies, based on follow-up data from children first investigated in early preschool years will add particularly important information about developmental trajectories in EF and in ADHD.

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Appendix

1.1

Summary of Fit indices for four factorial models assuming same and/or different factor means and factor loadings for the two BRIEF translations (n= 488 and n=646)

Model	RMSEA	Chi square Mean value	TLI	CFI
Different loadings different means	.029	5000.830	.959	.964
Different loadings same means	.034	5623.796	.943	.951
Same loadings different means	.027	5130.569	.966	.968
Same loadings same means	.030	5547.117	.956	.959

1.2

Three á priori factor models of BRIEF-P factor structure.