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MEN WITH ADHD IN COMPULSORY CARE FOR SUBSTANCE ABUSE

CHARACTERIZATION AND TREATMENT

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Men with ADHD in compulsory care for substance abuse; characterization and treatment

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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To Charlotte and Madeleine

ABSTRACT

Substance use disorder (SUD) is one of the most common comorbid conditions in adults with attention deficit-hyperactivity disorder (ADHD). There are still few studies that address combined ADHD and SUD as compared to studies on ADHD without SUD. The aims of the present thesis were (1); to conduct a clinical characterization of men with ADHD in compulsory care for severe SUD; (2) to investigate whether pharmacological treatment in ADHD/SUD cases was associated with improved long-term psychosocial outcomes; (3) to explore the feasibility of DBT (dialectic behavior therapy)-based skills training in ADHD/SUD patients in compulsory care; and (4) to explore the association between the skills training and the psychosocial outcome after six months. All studies were conducted at a compulsory care institution for men.

In the clinical characterization (Study I), 60 men with ADHD and SUD were compared with (1) 120 men in compulsory care for severe substance abuse without a known ADHD regarding comorbid psychiatric symptoms, psychosocial background, treatment history, and cognition, and with (2) 107 men with ADHD but without severe SUD from an outpatient psychiatric clinic. In Study II, a comparison was made between 30 patients who had received pharmacological treatment for ADHD and 30 non-treated patients. The long-term outcome was measured as the current status regarding abuse, voluntary rehabilitation, accommodation and employment, as well as mortality. In Study III, the feasibility and acceptability of DBT-based skills training were explored; 40 patients were included. The patients were follow-up six months after discharge from compulsory care, (Study IV). The outcome measures were substance abuse status, voluntary treatment status, and accommodation and employment status.

The characteristics of the ADHD/SUD found in Study I were an early onset of antisocial behavior that persisted into adulthood and poor cognitive skills. Study II showed that the overall mortality was high (8.3%) and that the pharmacologically treated group had significantly better outcomes in all measured psychosocial parameters. In Study III, it was found that the DBT-based skills training for ADHD was feasible and acceptable in a context of compulsory care for SUD. Significant symptom reduction, as well as an increased general well-being, was also found. The completers of the DBT-based skills training had fewer relapses and were more often in voluntary treatments, compared to non-completers in the six-month follow-up study (Study IV). However, no causal conclusion regarding the relationship

between the DBT-based skills training and the psychosocial outcome can be drawn due to the base-line differences between completers and non-completers, as well as the lack of a control group.

To sum up, ADHD in combination with SUD is a particularly disabling condition. The combination of severe substance abuse, poor general cognitive ability, severe psycho-social problems, including indications of antisocial behavior, and other co-existing psychiatric conditions should be considered in treatment planning for adults with ADHD and SUD. Pharmacological treatment of ADHD in individuals with ADHD and severe SUD may decrease the risk of relapse and increase the patients' ability to follow a nonpharmacological rehabilitation plan and thereby improve their long-term outcomes. Use of the structured treatment setting in the compulsory care for SUD for the initiation and stabilization of the pharmacological treatment for ADHD may be beneficial for high-risk populations. Furthermore, adapted structured treatments, such as DBT-based skills training, may be feasible in compulsory care and useful for some patients in this group. Discontinuation of voluntary treatment programs during the compulsory care may indicate low motivation or ability to participate in voluntary treatment and therefore predict a negative outcome after discharge.

LIST OF SCIENTIFIC PAPERS INCLUDED IN THE THESIS

- I. **Bihlar Muld, B.**, Jokinen, J., Bölte, S., Hirvikoski, T. (2013). Attention Deficit/Hyperactivity Disorders with co-existing substance use disorder is characterized by early antisocial behaviour and poor cognitive skills, *BMC Psychiatry*, 2013, 13:336.
- II. **Bihlar Muld, B.**, Jokinen, J., Bölte, S., Hirvikoski, T. (2015). Long-term outcomes of pharmacologically treated versus non-treated adults with ADHD and substance use disorder: a naturalistic study, *Journal of Substance Abuse Treatment*, 51(2015) 82-90.
- III. **Bihlar Muld, B.**, Jokinen, J., Bölte, S., Hirvikoski, T. DBT-based skills training for men with ADHD and SUD in compulsory care: a feasibility study, *ADHD Atten Def Hyp Disord* DOI 10.1007/s12402-016-0195-4
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LIST OF ABBREVIATIONS

ADHD	Attention deficit-hyperactivity disorder
ADHD-C	ADHD, combined type
ADHD-HI	ADHD, predominantly hyperactivity/impulsivity subtype
ADHD-I	ADHD, predominantly inattentive subtype
ADHD/Psych	ADHD/Psychiatric group
ASD	Autism spectrum disorder
ASRS	World Health Organization Adult ADHD Self-Report Scale
ASPD	Antisocial personality disorder
BAI	Beck Anxiety Inventory
BDI	Beck's Depression Inventory
CBT	Cognitive behavioral therapy
CD	Conduct disorder
CSTC	Cortico-striato-thalamo-cortical loops
DBT	Dialectical behavior therapy
DIVA	Diagnostic Interview for ADHD in Adults
DMN	Default Mode Network
DR	Dopamine receptor
DSM	Diagnostic and Statistical Manual of Mental Disorders
EF	Executive function
FSIQ	Full-Scale Intelligence Quotient
GAF	Global functioning
GAI	General Ability Index
IASP	International ADHD in Substance Use Disorder Prevalence
ICD	International Classification of Diseases, tenth revision
IQ	Intelligence Quotient
LVM	(Swedish) Lagen om vård av missbrukare i vissa fall = Care of Substance Abusers (Special provision) Act
MPH	Methylphenidate
MRI	Magnetic resonance imaging

MRR	Mortality rate ratio
NICE	National Institute for Clinical Excellence
NSCH	National Survey of Children's Health
ODD	Oppositional defiant disorder
OROS	Osmotic-Controlled Release Oral Delivery System
PD	Personality disorder
SCL-90	Symptom Checklist-90
SiS	(Swedish) Statens Institutionsstyrelse = National Board of Institutional Care
SUD	Substance use disorder
TCS	Treatment Credibility Scale
US	United States
WAIS	Wechsler Adult Intelligence Scale

1 INTRODUCTION

Attention deficit-hyperactivity disorder (ADHD) is a neurodevelopment disorder which, in most cases, persists into adulthood. In adults, ADHD is associated with considerable functional impairments and co-existing psychiatric disorders, including substance use disorder (SUD). The aims of the present thesis were to characterize male patients with ADHD in compulsory care for SUD in order to explore the long-term outcome of pharmacological treatment for ADHD in this patient group, to investigate the feasibility of dialectical behavior therapy (DBT)-based skills training in a compulsory care context, and to explore the association between the skills training program and psychosocial functioning six months after discharge from compulsory care.

1.1 ADHD

1.1.1 The Conceptualization and nomenclature of the ADHD

ADHD-like symptoms were described as mental restlessness and over-activity by physicians as far back as the 18th century (Lange, Reichl, Lange, Tucha, & Tucha, 2010). In the 20th century, the conceptualization and view of the disorder changed. In terms of a defect in moral control, George Still described symptoms similar to today's definition of ADHD in 1902 (R. A. Barkley & Peters, 2012). Later, in the 1930s and 1940s, restlessness and hyperactivity-impulsivity came to be seen as being caused by an acquired brain damage, reflected in the diagnostic term, Minimal Brain Damage. In the 1960s, the diagnosis Minimal Brain Dysfunction was introduced, referring to more extensive neurological causes of the disorder than brain trauma or infections. Further shifts of the conceptualization are reflected in the introduction of the diagnostic term "Hyperkinetic reaction of childhood" in DSM-II in 1967 and replaced by "Attention deficit-hyperactivity disorder" in 1987 when the third edition of DSM was published (American Psychiatric Association, 1980). During recent decades, the view concerning the disorder has been influenced by the current knowledge of the persistent nature of childhood ADHD with increased opportunities for adults with ADHD to be diagnosed and treated (R. A. Barkley, Fischer, Smallish, & Fletcher, 2002). Furthermore, the recent extensive increase in knowledge in genetics and neurobiology has contributed to our understanding of ADHD (Lange et al., 2010).

1.1.2 Diagnostic criteria

The fifth edition of the diagnostic system DSM (American Psychiatric Association, 2013) was published in 2013. The symptom criteria for ADHD remains unchanged with the 18

symptoms similar to those described in DSM-IV (American Psychiatric Association, 1994) (Table 1), divided into the two domains Inattention and Hyperactivity/impulsivity. The main changes in the diagnostic criteria of ADHD in DSM-V (Table 2), compared to DSM-IV, include the introduction of a dimensional measure, i.e., a rating of the severity (mild, moderate, and severe) of the inattention and hyperactivity symptoms and the accompanying impairments. Furthermore, there is a change in the criterion for the onset of the ADHD symptoms, from “before seven years” to “before 12 years”. The cut-off limits for symptoms required for a diagnosis in adults have been changed from six, which are required for younger persons, to five. This applies to both attention and hyperactivity/ impulsivity. In DSM-V, each listed symptom is followed by examples of how it may show up in different age groups in order to be applicable to both older adolescents and adults. Furthermore, the requirement for functional impairments has been moderated, from requiring ADHD-related impairments in at least two settings to several ADHD symptoms which must be present in two or more settings. An additional change is that a simultaneous presence of ADHD and Autism spectrum disorder (ASD) is allowed. However, ADHD will still be ruled out if the symptoms only occur during the course of schizophrenia or if other psychotic disorders are not better explained by other mental disorder, such as Mood disorder, Anxiety disorder, Dissociative disorder or Personality disorder.

In ICD-10 (World Health Organization, 1992), ADHD is termed Hyperkinetic disorder. In essence, the list of ADHD symptoms overlap in the two systems, even though the ICD criteria are more restricted than the DSM criteria. To meet the criteria of Hyperkinetic disorder, symptoms of both attention (5 symptoms), hyperactivity (3 symptoms) *and* impulsivity (1 symptom) are required, as compared to the requirements in the DSM system: six or more symptoms of inattention *and/or* hyperactivity. Furthermore, the exclusion criteria are stricter. If the criteria are met regarding Mood disorder, Anxiety disorder, some type of Reactive disorder, Manic state, or Neurological disease, these diagnoses take precedence over Hyperkinetic disorder, unless there is evidence of a separate Hyperkinetic disorder. Symptoms of Conduct disorder are neither exclusion nor inclusion criteria for Hyperkinetic disorder, but represent a diagnostic subgroup, designated as Hyperkinetic conduct disorder. Thus, Hyperkinetic disorder is considered to refer to individuals with the most severe ADHD symptoms.

Table 2. The DSM-5 criteria for ADHD

<p>(A) Inattention: Six or more symptoms of inattention for children up to age 16, or five or more for adolescents 17 and older and adults; symptoms of inattention have been present for at least 6 months, and they are inappropriate for the developmental level:</p>
<ol style="list-style-type: none"> 1) Often fails to give close attention to details or makes careless mistakes in schoolwork, at work, or in other activities. 2) Often has trouble holding attention on tasks or play activities. 3) Often does not seem to listen when spoken to directly. 4) Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (e.g., loses focus, side-tracked). 5) Often has trouble organizing tasks and activities. 6) Often avoids, dislikes, or is reluctant to do tasks that require mental effort over a long period of time (such as schoolwork or homework). 7) Often loses things necessary for tasks and activities (e.g., school materials, pencils, books, tools, wallets, keys, paperwork, eyeglasses, mobile telephones). 8) Is often easily distracted. 9) Is often forgetful in daily activities.
<p>(B) Hyperactivity and Impulsivity: Six or more symptoms of hyperactivity-impulsivity for children up to age 16, or five or more for adolescents 17 and older and adults; symptoms of hyperactivity-impulsivity have been present for at least 6 months to an extent that is disruptive and inappropriate for the person's developmental level:</p>
<ol style="list-style-type: none"> 1) Often fidgets with or taps hands or feet, or squirms in seat. 2) Often leaves seat in situations when remaining seated is expected. 3) Often runs about or climbs in situations where it is not appropriate (adolescents or adults may be limited to feeling restless). 4) Often unable to play or take part in leisure activities quietly. 5) Is often "on the go" acting as if "driven by a motor". 6) Often talks excessively. 7) Often blurts out an answer before a question has been completed. 8) Often has trouble waiting his/her turn. 9) Often interrupts or intrudes on others (e.g., butts into conversations or games)
<p>In addition, the following conditions must be met:</p>
<ol style="list-style-type: none"> 1) Several inattentive or hyperactive-impulsive symptoms were present before age 12 years. 2) Several symptoms are present in two or more settings (e.g., at home, school or work; with friends or relatives; in other activities). 3) There is clear evidence that the symptoms interfere with, or reduce the quality of, social, school, or work functioning. 4) The symptoms do not happen only during the course of schizophrenia or another psychotic disorder. The symptoms are not better explained by another mental disorder (e.g. Mood disorder, Anxiety disorder, Dissociative disorder, or a Personality disorder).
<p>Based on the types of symptoms, three kinds (presentations) of ADHD can</p>

occur:

Combined Presentation: if enough symptoms of both criteria inattention and hyperactivity-impulsivity were present for the past six months

Predominantly Inattentive Presentation: if enough symptoms of inattention, but not hyperactivity-impulsivity, were present for the past six months

Predominantly Hyperactive-Impulsive Presentation: if enough symptoms of hyperactivity-impulsivity, but not inattention, were present for the past six months.

Because symptoms can change over time, the presentation may change over time as well.

Table 3. The ICD-10 diagnostic criteria for Hyperkinetic disorder

A.

At least six of the following symptoms of Inattention have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental levels:

Inattention

- 1) Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities.
- 2) Often has difficulty sustaining attention in tasks or play activities.
- 3) Often does not seem to listen when spoken to directly.
- 4) Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions).
- 5) Often has difficulty organizing tasks and activities.
- 6) Often avoids, dislikes, or is reluctant to engage in tasks that require sustained mental effort (such as schoolwork or homework).
- 7) Often loses things necessary for tasks or activities (e.g., toys, school assignments, pencils, books, or tools).
- 8) Is often easily distracted by extraneous stimuli.
- 9) Is often forgetful in daily activities.

Six or more of the following symptoms of Hyperactivity-impulsivity have persisted for at least six months to a degree that is maladaptive and inconsistent with developmental level.

Hyperactivity

- 1) Often fidgets with hands or feet or squirms in seat.
- 2) Often leaves seat in classroom or in other situation in which remaining seated is expected.
- 3) Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness).

Impulsivity

- 1) Often blurts out answers before questions have been completed.
- 2) Often has difficulty awaiting turn.
- 3) Often interrupts or intrudes on others (e.g., at school or work and at home).
- 4) Is often unduly noisy in playing or has difficulty in engaging in leisure activities quietly.
- 5) Is often “on the go” or often acts as if “driven by a motor”.
- 6) Often talks excessively.

B. Some hyperactive-impulsive or inattentive symptoms that caused impairment were present before age 7 years.

C. Some impairment from the symptoms is present in two or more settings (e.g., at school or work and at home).

D. There must be clear evidence of clinically significant impairment in social, academic, or occupational functioning.

E. The symptoms do not occur exclusively during the course of a Pervasive developmental disorder, Schizophrenia, or other Psychotic disorder and are not better accounted for by another Mental disorder (e.g., Mood disorder, Anxiety disorder, Dissociative disorder, or a Personality disorder).

1.1.3 Prevalence

Estimations of the prevalence of the ADHD rates vary considerably. One explanation may be that estimation of the prevalence may be lower in studies using the ICD-criteria for ADHD, which are stricter than the criteria in DSM. The prevalence has also been shown to vary depending on which version of DSM has been used in different studies (Faraone, Sergeant, Gillberg, & Biederman, 2003). Another explanation may be different methodologies in the conducted studies (G. Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007).

In individuals up to age 18, the pooled worldwide prevalence has been estimated to be 5.29% (G. Polanczyk et al., 2007). According to a later systematic review and meta-regression analysis, there is no evidence of an increased number of children meeting the criteria for ADHD during the past three decades (G. V. Polanczyk, Willcutt, Salum, Kieling, & Rohde, 2014). However, the extension of the age-of-onset criterion from seven to 12 years in DSM-V has been shown to lead to an increase in the prevalence rate in US children and adolescents from 7.38% to 10.84% (based on parent reports) (Vande Voort, He, Jameson, & Merikangas, 2014). Furthermore, data from the National Survey of Children's Health (NSCH) have shown that ever-diagnosed ADHD increased in children/adolescents (age 4–17 years) from 7.8% in 2003 to 11% in 2011, signifying an increase of 22% from 2003 to 2007, and 16% from 2007 to 2011. Current ADHD increased from 7.2% in 2007 to 8.8% in 2011 (Visser et al., 2014).

In a meta-analysis including studies on children, adolescents, and adults (Willcutt, 2012), the prevalence ranged between 5.0% and 7.1%. In adults, Fayyad found in a cross-national study that the estimated prevalence of adult ADHD ranged between 1.2% and 7.3% (Fayyad et al., 2007).

1.1.4 Genetics

Family, twin, adoption, and other behavior genetic studies have shown a considerable heritability in ADHD (Z. Chang, Lichtenstein, Asherson, & Larsson, 2013; Faraone et al., 2005; Nikolas & Burt, 2010; Thapar, Holmes, Poulton, & Harrington, 1999). The mean rate of heritability has been estimated to be 76% (Faraone et al., 2005), ranging from 60% to 90%. Although the high heritability has been established, trials for identifying specific risk genes involved in ADHD have not led to firm conclusions. Regarding the immense amount of DNA variants, it has not been possible to say so far which of them are truly associated with ADHD (Faraone, 2014). However, genes involved in the dopaminergic pathway, particularly the dopamine D4 (DRD4) and dopamine D5 (DRD5) genes, are thought to be associated with ADHD (Coghill & Banaschewski, 2009; Gizer, Ficks, & Waldman, 2009; Wu, Xiao, Sun, Zou, & Zhu, 2012). The common view is that a plurality of genes are involved (Frodl, 2010), each one contributing with a small, but significant, effect (Neale et al., 2010). Moreover, common genetic variants, as well as neurocognitive traits and behavioral dimensions related to ADHD, have been found in the general population (Faraone, 2014; Martin, Hamshere, Stergiakouli, O'Donovan, & Thapar, 2015). All these findings indicate a complex genetic architecture in ADHD, suggesting a dimensional ADHD model, and also implying that clinically defined ADHD may be seen as an extreme of a continuous trait (Groen-Blokhuys et al., 2014; H. Larsson, Anckarsater, Rastam, Chang, & Lichtenstein, 2012).

An additional research approach is the gene-by-environment interaction, proposing that environmental factors may contribute to the manifestation of genetic effects (Coghill & Banaschewski, 2009; Cortese et al., 2012; J. Nigg, Nikolas, & Burt, 2010; Thapar, Langley, Asherson, & Gill, 2007), explained as a genetic sensitivity to a particular environmental factor (Pennington, 2009).

Among the possible environmental factors contributing to ADHD, it has been found that prenatal exposure to alcohol and drugs, complications during pregnancy, premature birth, and a low birth weight are associated with the condition (Banerjee, Middleton, & Faraone, 2007; Botting, Powls, Cooke, & Marlow, 1997; Langley, Holmans, van den Bree, & Thapar, 2007; Milberger, Biederman, Faraone, Guite, & Tsuang, 1997).

Several studies suggest a possible causality regarding maternal smoking during pregnancy as an environmental factor for ADHD offspring (Banerjee et al., 2007; Langley, Rice, van den Bree, & Thapar, 2005; Rodriguez & Bohlin, 2005), while the conclusion from a later study is that the association between maternal smoking during pregnancy and offspring ADHD may be explained by unmeasured confounding (Skoglund, Chen, D'Onofrio, Lichtenstein, & Larsson, 2014). In a meta-analysis, Wood et al. (2009) have estimated the average contribution of shared environment factor in ADHD to be 24.8% (Wood, Buitelaar, Rijdsdijk, Asherson, & Kuntsi, 2010).

1.1.5 Neurobiology of ADHD

Neuroanatomically, a reduced brain volume has been found in individuals with ADHD, both globally and in specific regions, and both regarding gray and white matter (Castellanos & Acosta, 2004; Nakao, Radua, Rubia, & Mataix-Cols, 2011; Seidman et al., 2011). According to meta-analyses, the most consistent finding is a volume reduction in the basal ganglia (Castellanos & Acosta, 2004; Frodl & Skokauskas, 2012), prefrontal cortex, and cerebellum (Seidman et al., 2006; P. Shaw & Rabin, 2009). A reduction of cortical thickness over large areas has also been found (Luders et al., 2009; Narr et al., 2009; P. Shaw & Rabin, 2009).

The association between ADHD and a dysregulated dopamine activity in the brain reward centers, via the five receptors D1-D5 (Wu et al., 2012), is well established. Dopamine also plays a role in drug abuse and addiction (Volkow, Fowler, Wang, & Swanson, 2004), which may explain the association between ADHD and SUD (Carpentier et al., 2013). An interaction between dopamine and the neurotransmitters, serotonin, GABA, and norepinephrine, in ADHD has also been suggested (Blum et al., 2008; Groenman et al., 2015). Furthermore, ADHD has been suggested to be associated with inadequate activity of

acetylcholine (Wallis et al., 2009), endocannabinoids (van Hell et al., 2012), and glutamate (Dimatelis et al., 2015).

Furthermore, a functional disconnectivity between different brain regions has been found in MRI studies (Cortese & Castellanos, 2012; Dickstein, Bannon, Castellanos, & Milham, 2006; Konrad et al., 2010). Impaired connectivity has been found particularly in the default mode network (DMN), both in the network itself and in its connection to the cognitive control network. The dysfunction refers to failures in deactivating the DMN (activated at wakeful rest) at demands on goal-directed tasks, including sustained attention. The cognitive control network is associated with the functions working memory, inhibitory control, and set shifting, and the dysfunctional connectivity between the DMN and the cognitive control network also contributes to the impairments in sustaining attention (Posner, Park, & Wang, 2014). Furthermore, impaired connectivity is also found in the neural circuits, which are suggested to be associated with the affective and motivational systems [within the cortico-striato-thalamo-cortical (CSTC)] loops (Castellanos, Kelly, & Milham, 2009; Konrad et al., 2010). Thus, impaired functional connectivity is implicated in both the attentional and the affective and motivational system (Posner et al., 2014; Sonuga-Barke, Sergeant, Nigg, & Willcutt, 2008).

1.1.6 ADHD and Cognition

1.1.6.1 General cognitive ability in ADHD

On average, adults with ADHD as a group have been shown to have a slightly lower general intellectual ability than healthy controls (Frazier, Demaree, & Youngstrom, 2004; Schoechlin & Engel, 2005). Bridgett and Walker (2006) found lower average IQ scores of 2.94 in the ADHD group compared to controls (Bridgett & Walker, 2006). Comorbid psychiatric disorders in adult ADHD have been found to entail more cognitive difficulties than adult ADHD without additional psychiatric disorders (Theiling & Petermann, 2014). Furthermore, ADHD, in combination with specific learning disabilities in arithmetic and reading/spelling, has been found to be associated with lower IQ scores than solely ADHD (Frazier et al., 2004; Seidman, Biederman, Monuteaux, Doyle, & Faraone, 2001).

Considerable impairments in multiple cognitive domains are found in ADHD individuals compared to healthy controls (Fuermaier et al., 2015; Hervey, Epstein, & Curry, 2004). However, no psychometric cognitive test or test profile allows individual diagnoses of ADHD since individuals with ADHD display unique profiles of neuropsychological functioning (Lange et al., 2014). Moreover, IQ scores cannot explain the lower academic

performance and functional impairments associated with ADHD. Arnold et al. found that the difference in academic achievements between individuals with untreated ADHD and controls remained after controlling for IQ (Arnold, Hodgkins, Kahle, Madhoo, & Kewley, 2015). Furthermore, a high IQ may be associated with cognitive difficulties and low achievements due to executive dysfunctions (Antshel et al., 2010; Kaplan, Crawford, Dewey, & Fisher, 2000).

The most widely used intelligence measure in adulthood is the Wechsler Adult Intelligence Scale (WAIS). In versions prior to the current WAIS, the WAIS-IV (Wechsler, 2008), the working memory and processing speed subtests were included in the full-scale intelligence quotient (FSIQ), meaning that the specific impairments in ADHD were included in the calculation of the global intellectual capacity. In WAIS IV, the latest version of the test instrument, an alternative index to FSIQ has been introduced (General Ability Index; GAI). GAI aims to reduce the influence of the executive functions working memory and processing speed. A significant difference between FSIQ and GAI has also been found in ADHD adults, but not in matched controls (Theiling & Petermann, 2014).

1.1.6.2 Executive dysfunctions in ADHD

Barkley (1997) has defined Executive functions (EFs) as neurocognitive processes responsible for goal-directed behaviors and deficient self-control. The definition implies deficits in response inhibition as the core characteristic in ADHD, affecting all other EF processes (R. A. Barkley, 1997a, 1997b). This model has later been supplemented by a more multidimensional view of the executive dysfunctions in ADHD. Deficits in impulse inhibition, according to Barkley's model, are, in later models, considered to be just one pathway associated with ADHD.

A more elaborated model is the Dual pathway model (Sonuga-Barke, 2003), which refers to two separate mechanisms within two domains of functioning. The pathway of inhibitory cognitive control (R. A. Barkley, 1997a) refers to an inability to pursue top-down control, i.e., to overcome stimulus triggers and/or affect arousal in favor of pursuing behavior, in order to achieve more long-term goals. The other pathway refers to a neurally based motivational dysfunction, including an aversion of delayed and future rewards (Sonuga-Barke, 2002; Sonuga-Barke et al., 2008). The motivational system is less associated with cognition and academic achievement and more with affective state (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). The terms "hot" and "cold" EF are associated with these different pathways. Inattention in ADHD (Castellanos et al., 2006) and the cognitive

functions, Inhibition, Vigilance, Spatial working memory, and some measures of Planning have been suggested to be related to “cold” EF and a dysfunctional cognitive control system (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). Hyperactivity/ impulsivity is, in this model, suggested to be associated with “hot” EF. However, although being the substantial role of executive dysfunctions in ADHD, not all diagnosed with ADHD have disabling executive dysfunctions (Castellanos et al., 2006; J. T. Nigg et al., 2005; B. A. Roberts, Martel, & Nigg, 2013).

1.1.6.3 Functional impairments

In practically all domains of life, and regardless of age, ADHD is associated with considerable functional impairments. Educational problems and academic underachievement have been shown to be more common in children with ADHD than in peers without ADHD (Biederman, Petty, et al., 2008). The functional impairments in children and adolescents may contribute to an increased risk of an antisocial trajectory and substance abuse (Gordon, Tulak, & Troncale, 2004; Sullivan & Rudnik-Levin, 2001; van Emmerik-van Oortmerssen et al., 2012).

Adults with ADHD have more occupational impairments, including lower levels of professional employment, poorer work performance, and higher rates of quitting or being fired (R. A. Barkley, & Murphy, K. R., 2010; Biederman J, 2006; Fletcher, 2014). Compared to controls, ADHD in adults is also associated with higher rates of divorce and less satisfaction with family, social, and professional lives, compared to controls (Biederman J, 2006).

1.1.7 Coexisting psychiatric disorders

ADHD is associated with a wide range of co-existing psychiatric disorders (Biederman, Newcorn, & Sprich, 1991; Torgersen, Gjervan, & Rasmussen, 2006; Yoshimasu et al., 2012). The rates of estimated comorbidity over the life span vary between 65% and 89% (Sobanski et al., 2007; Sobanski et al., 2008).

In children and adolescents, Oppositional defiant disorder (ODD) and Conduct disorder (CD) are the most common co-existing disorders in ADHD (Biederman et al., 1991). Anxiety and Mood disorders are also frequently reported (Masi, Millepiedi, et al., 2003), often in combination with ODD and CD (Bendiksen et al., 2014; Frick & Nigg, 2012; Ghosh & Sinha, 2012; Kessler et al., 2011).

Mood disorders and SUD are the most common co-existing psychiatric conditions in adult ADHD, followed by Anxiety disorders (Busch et al., 2002; Faraone, Biederman, & Wozniak, 2012; Fayyad et al., 2007; Klassen, Katzman, & Chokka, 2010; Masi, Toni, et al., 2003; T. E. Wilens et al., 2009). The most frequently reported co-existing personality disorders are Borderline personality disorder and Antisocial personality disorder (Anckarsater et al., 2006; Matthies et al., 2011; Moffitt, 1990; Philipsen et al., 2009).

1.1.8 Mortality and related risk behaviors in ADHD

Mortality has been shown to be increased in ADHD. In a large sample of 1.92 million individuals in Denmark, the mortality rate per 10,000 per year was 5.85 (4.25 in adults) in individuals with ADHD, compared to 2.21 in non-ADHD persons. Thus, during the follow-up period of 32 years, the risk of a premature death was more than two times higher in individuals with ADHD than in those without ADHD (Dalsgaard, Ostergaard, Leckman, Mortensen, & Pedersen, 2015). Comorbidity with ODD, CD, and SUD increased the Mortality rate ratios (MRRs), but, also without these comorbid disorders, the MMR was substantially higher in ADHD individuals.

Drug abuse *per se*, especially abuse of illicit drugs, is also related to a high mortality (Stenbacka, Leifman, & Romelsjo, 2010). In deceased drug addicts, death has been found to be caused by the drug abuse in about in 47% according to toxicological analyses (Jönsson, Holmgren, Druid, & Ahlner, 2007).

Dalsgaard et al. found that, in individuals with ADHD, the causes of death were mainly unnatural and mostly associated with accidents (Dalsgaard et al., 2015). In adult ADHD, traffic accidents are more common, as compared to the population as a whole (R. A. Barkley & Cox, 2007; Z. Chang, Lichtenstein, D'Onofrio, Sjolander, & Larsson, 2014). Risk-taking behavior, associated with impulsivity, is an independent predictor of driving offences in ADHD (Kaye et al., 2014).

1.2 ADHD AND SUBSTANCE USE DISORDER

1.2.1 Diagnostic criteria of substance use disorder

For the diagnosis SUD, according to DSM-5 (American Psychiatric Association, 2013), at least two of 11 criteria are required to be met, which are clustered in four groups:

1. Impaired control: (1) taking more or for longer than intended, (2) unsuccessful efforts to stop or cut down use, (3) spending a great deal of time obtaining, using, or recovering from use, (4) craving for substance.
2. Social impairment: (5) failure to fulfill major obligations due to use, (6) continued use despite problems caused or exacerbated by use, (7) important activities given up or reduced because of substance use.
3. Risky use: (8) recurrent use in hazardous situations, (9) continued use despite physical or psychological problems that are caused or exacerbated by substance use.
4. Pharmacologic dependence: (10) tolerance to effects of the substance, (11) withdrawal symptoms when not using or using less. However, persons who are prescribed medications such as opioids may exhibit these two criteria, but would not necessarily be considered to have a Substance use disorder.

DSM-5 suggests using the number of criteria met as a general measure of severity, from *mild* (2–3 criteria) to *moderate* (4–5 criteria) and *severe* (6 or more criteria).

Finally, new to DSM-5 are cannabis and caffeine withdrawal, and the criteria for Tobacco use disorder are now the same as for all other Substance use disorders.

1.2.2 Prevalence of ADHD in SUD

The prevalence of ADHD in the general population is estimated to be 1.2%–7.3% (Fayyad et al., 2007), as compared with 20%–50% in individuals with SUD, thereby entailing a pooled rate of 23.3% (van Emmerik-van Oortmerssen et al., 2012). The extensive variations in the estimations of ADHD in SUD have been suggested to be related to several factors such as different psychoactive substances involved in the studies, different diagnostic instruments, demographic and country-specific factors, treatment/assessment settings, and clinical biases (Perez de Los Cobos et al., 2011; van de Glind et al., 2014). Conversely, the prevalence of SUD in adults with ADHD has been estimated to be about 50% (Sullivan & Rudnik-Levin, 2001). Thus, ADHD is considered to be a strong predictor of SUD (Sullivan & Rudnik-Levin, 2001; T. E. Wilens, 2011; T. E. Wilens, Biederman, Mick, Faraone, & Spencer, 1997).

1.2.3 Associations between ADHD and SUD

As mentioned above, the association between ADHD and all forms of addiction is well established (Biederman et al., 1995; Milberger, Biederman, Faraone, Wilens, & Chu, 1997; T. E. Wilens, 2004a, 2004b; T. E. Wilens & Fusillo, 2007; T. E. Wilens et al., 2011). The ADHD and SUD relationship has been explored from different perspectives, such as

biological vulnerabilities, overlapping neurocognitive underpinnings, personality traits, additional psychiatric comorbidity, and psychosocial impairments.

There is a strong indication of a shared genetic basis for SUD and ADHD (Capusan, Bendtsen, Marteinsdottir, Kuja-Halkola, & Larsson, 2015; Groman, James, & Jentsch, 2009; Skoglund, Chen, Franck, Lichtenstein, & Larsson, 2015; T. E. Wilens, 2004a). The high prevalence of ADHD in families with SUD and vice versa indicates a shared familiarity of the two disorders (Biederman, Petty, Wilens, et al., 2008; T. E. Wilens, 2004a). It has been proposed that specific genotypes increase the risk of ADHD only, while others entail an increased risk for the combination of ADHD and SUD (Carpentier et al., 2013). The dysregulation of primarily dopamine, as well as serotonin, in both ADHD and SUD has been established in several studies (Cardinal, Winstanley, Robbins, & Everitt, 2004; Eagle et al., 2009; Silva et al., 2014; Szobot, Shih, et al., 2008; Volkow et al., 2004; Volkow et al., 2007).

Early occurrence of ADHD symptoms and ADHD-related behavior, such as impulsivity and lack of self-control (Caspi, Moffitt, Newman, & Silva, 1996; Moffitt et al., 2011; Molina & Pelham, 2003), as well as the severity of the ADHD symptoms (Thompson, Riggs, Mikulich, & Crowley, 1996), has been found to be associated with adult substance dependence. The association between ADHD subtypes and the development and severity of SUD has been explored in several studies. One suggestion is that the predominantly inattentive subtype (ADHD-I) predicts multiple substance use outcomes (Molina & Pelham, 2003). The hyperactivity/impulsivity subtype of ADHD (ADHD-HI) has been found to be independently associated with the risk of developing substance abuse (De Alwis, Lynskey, Reiersen, & Agrawal, 2014; Elkins, McGue, & Iacono, 2007; Nogueira et al., 2014; Storebö, 2013; Tamm et al., 2013). Furthermore, ADHD-HI has been shown to be strongly associated with early onset of substance abuse (Z. Chang, Lichtenstein, & Larsson, 2012).

SUD is, independently of ADHD, associated with an increased rate of additional co-existing disorders, including mood, anxiety, psychotic and personality disorders (Fridell, Hesse, & Johnson, 2006; Mariani & Levin, 2007; Regier et al., 1990), but higher rates of comorbid conditions have been found when ADHD and SUD co-exist (van Emmerik-van Oortmerssen et al., 2014; T. E. Wilens, Kwon, et al., 2005). The International ADHD in Substance Use Disorder Prevalence (IASP) Study found that 75% of treatment-seeking SUD patients with comorbid ADHD had at least one additional comorbid disorder, compared to 37% in SUD patients without ADHD. The study also showed different comorbid patterns in the ADHD subtypes. On comparing the subtypes (ADHD-C, ADHD-HI, and ADHD-I), major depression was more common in the inattentive and combined subtype; hypomania and

antisocial personality disorder were more common in the hyperactive/ impulsive and combined subtypes. Borderline personality disorder was increased in all three subgroups, compared to patients with SUD without ADHD (van Emmerik-van Oortmerssen, van de Glind, et al., 2013).

Based on personality traits, Tarter et al. have proposed two pathways linking childhood hyperactivity to SUD in young adulthood. In the so-called internalizing pathway, the personality trait neuroticism is suggested to lead to low self-esteem, in turn leading to social withdrawal, and to an increased risk for SUD. The other suggested pathway, the externalizing one, describes a development from hyperactivity in childhood associated with externalizing behaviour, and later to SUD (Tarter, Kirisci, Feske, & Vanyukov, 2007). Among personality traits, impulsive anger in childhood is found to be strongly associated with ADHD and a predictor of SUD (T. E. Wilens et al., 2011). Additional common intermediate factors involving ADHD and SUD are difficulties and shortcomings in different areas of life, such as academic and vocational problems, heterogeneous social difficulties, and lack of adequate coping skills (Molina & Pelham, 2014). Thus, stress in everyday life, related to the ADHD impairments (Hirvikoski, Lindholm, Nordenstrom, Nordstrom, & Lajic, 2009), may be a pathway to SUD. From in-depth interviews conducted on both ADHD and ASD patients, Kronenberg et al. found that stress was a common reason for starting to use alcohol and drugs (Kronenberg, Slager-Visscher, Goossens, van den Brink, & van Achterberg, 2014). Furthermore, the continued use of alcohol and drugs may be regarded as an expression of the palliative, avoidant, and passive coping styles for coping with stress, which is found to be frequent in patients with ADHD (Kronenberg, Goossens, van Busschbach, van Achterberg, & van den Brink, 2015). Substance abuse for reduction of stress related to ADHD symptoms and to comorbid conditions is related to the self-medication hypothesis (Young & Sedgwick, 2015). A yearning for belongingness has also been identified as an important driving force underlying substance abuse in individuals with ADHD (Nehlin, Nyberg, & Öster, 2015).

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1.2.4 Impulsivity and conduct disorder in ADHD/SUD

Impulsivity and conduct disorder in childhood hold strong positions as explanatory factors in the association between ADHD and SUD.

1.2.4.1 *Impulsivity*

Impulsivity is a core symptom of ADHD and a precursor to SUD (Crunelle, Veltman, van Emmerik-van Oortmerssen, Booij, & van den Brink, 2013; De Alwis et al., 2014; Murphy, Barkley, & Bush, 2002). The construct of impulsivity is multifaceted (W. Roberts, Peters, Adams, Lynam, & Milich, 2014) and ambiguous in terms of the cognitive, emotional, and neural processes that underpin the manifest behaviour. Two paradigms of impulsivity related to the dual pathway model are *impulsive action* and *impulsive choice*. These two manifestations of impulsivity are differently defined, operationalized, and measured. Impulsive action refers to an inability to inhibit an automatic motor control (top-down model) (R. A. Barkley, 1997b) and impulsive choice refers to an aversion to delayed rewards, implying choosing of small immediate rewards instead of delayed greater rewards (bottom-up model). The paradigm of delay aversion also suggests that ADHD-related behavior (such as activity, frustration/stress and inattention) increases when an immediate reward is not available or when expected rewards are absent (Sonuga-Barke et al., 2008). Impulsive action and impulsive choice are measured with different neuropsychological tests (stop-signal tasks and choice- delayed tasks, respectively), and it has been found that the outcomes of these tests are largely uncorrelated (Broos et al., 2012). These findings highlight the heterogeneity of both impulsivity and the ADHD disorder. Both delay aversion and inhibitory failure are implicated in ADHD (M. V. Solanto et al., 2001) and both models of impulsivity are involved in addiction vulnerability (Molina & Pelham, 2014). That is, the impaired higher-order cognitive control system in ADHD does not inhibit automatic impulses to seek the instant gratification/reward that substance use can provide. However, findings also indicate that impulsivity is a specific trait in SUD, not specifically mediated by ADHD (Ivanov, Schulz, London, & Newcorn, 2008; J. T. Nigg et al., 2006)

1.2.4.2 *Conduct disorder*

The substantial role of childhood onset conduct disorder (CD) in the association between ADHD and SUD is well established (August et al., 2006; Elkins et al., 2007; Flory & Lynam, 2003; Harty, Ivanov, Newcorn, & Halperin, 2011; Nogueira et al., 2014; Ohannessian & Hesselbrock, 1995; Torok, Darke, & Kaye, 2012; Tuithof, ten Have, van den Brink, Vollebergh, & de Graaf, 2012). The ADHD-SUD relationship has even been shown to significantly decrease on controlling for the impact of CD. (August et al., 2006; Flory, Milich, Lynam, Leukefeld, & Clayton, 2003), indicating that CD during childhood and/or

antisocial behavior in adulthood are robust predictors of SUD, independently of ADHD (Couwenbergh et al., 2006; Hopfer et al., 2013; King, Iacono, & McGue, 2004; Rodgers et al., 2014; Saban et al., 2014; Westermeyer, Thuras, & Carlson, 2005; Wilson & Levin, 2005). It has been suggested (Anney et al., 2008; Christiansen et al., 2008) that ADHD/CD represents an own etiological entity, only partly overlapping with ADHD as such. This proposed subtype represents a more severe disorder than merely ADHD. The diagnosis hyperkinetic CD in ICD-10 is in line with this suggested distinct subgroup (Faraone, Biederman, Jetton, & Tsuang, 1997; Faraone, Biederman, Mennin, Russell, & Tsuang, 1998).

1.3 TREATMENT OF ADHD

1.3.1 Pharmacological treatment of ADHD

The short-term effect of psychostimulants on symptom reduction in ADHD is well established (Bitter, Angyalosi, & Czobor, 2012; Castells, Cunill, & Capella, 2013; Faraone & Glatt, 2010; Faraone, Spencer, Aleardi, Pagano, & Biederman, 2004; Koesters, Becker, Kilian, Fegert, & Weinmann, 2009; Meszaros et al., 2009). Long-term effects of pharmacological treatment have also been found in several studies (Adler, Spencer, Milton, Moore, & Michelson, 2005; Buitelaar et al., 2012; Fredriksen, Halmoy, Faraone, & Haavik, 2012), although much less prominently.

In current guidelines for the treatment of ADHD (Bolea-Alamanac et al., 2014; CAADRA, 2011; S. J. Kooij et al., 2010; National Board of Health, 2014a; National Institute for Clinical Excellence, 2008), psychostimulants are recommended as the first choice of treatment of ADHD.

1.3.1.1 Unresponsiveness and adverse effects of stimulant medication

About 20%–50% of ADHD individuals continue to have residual symptoms or find the adverse effects of stimulant medication intolerable (Wender, 1998; T. E. Wilens, Spencer, & Biederman, 2002). Reported adverse effects are increases in systolic and diastolic blood pressure and heart rate, insomnia, dysphoria, tics, obsessiveness, headaches, edginess, loss of appetite, and loss of weight (Kolar et al., 2008; T. Wilens, Spencer, TJ., Biederman, J., et al., 2001; T. E. Wilens et al., 2002). Serious adverse effects are, however, uncommon (Graham, 2008)

1.3.1.2 Risks of psycho-stimulant medication

The risks of treatment with stimulants, associated with the abuse potential, are misuse of prescribed stimulants, side-abuse, and diversion (Bukstein, 2008; Faraone & Wilens, 2007; Klassen, Bilkey, Katzman, & Chokka, 2012; Kollins, 2008; Mariani & Levin, 2007; Perez de Los Cobos, Sinol, Perez, & Trujols, 2012; Sepulveda et al., 2011). Comorbid disorders such as CD/ASPD and bipolar disorder and SUD have been regarded as risk factors (Kollins, 2008).

A question has been raised as to whether there is an increased risk of stimulant medication in childhood increasing the risk of developing SUD in adolescents or adults (sensitization hypothesis) (Robinson & Berridge, 1993; Strakowski & Sax, 1998). The current evidence does not, however, support an association between pharmacological treatment of ADHD and a later increased risk of SUD (R. A. Barkley, Fischer, Smallish, & Fletcher, 2003; Biederman, Monuteaux, et al., 2008; Z. Chang, Lichtenstein, P., Halldner, L., D'Onofrio, B. M., Serlachhius, E., Fazel, S., Långström, N., Larsson, H., 2013; Groenman et al., 2013; Mannuzza et al., 2008). On the contrary, stimulant medication may lower the risk of developing SUD and substance abuse (Z. Chang, Lichtenstein, P., Halldner, L., D'Onofrio, B. M., Serlachhius, E., Fazel, S., Långström, N., Larsson, H., 2013; Groenman et al., 2013).

1.3.2 Pharmacological treatment of combined ADHD and SUD

The findings in efficacy studies on pharmacological treatment of ADHD in patients with comorbid SUD are less conclusive compared to the findings in studies on pharmacological treatment of ADHD patients without SUD (Castells et al., 2011; Cunill, Castells, Tobias, & Capella, 2014; T. E. Wilens, Monuteaux, et al., 2005). In several studies, methylphenidate treatment has been shown to reduce ADHD symptoms in patients with comorbid SUD, while the benefits with regard to SUD have been more uncertain (Castaneda, Levy, Hardy, & Trujillo, 2000; Klassen et al., 2012; Schubiner et al., 2002; Somoza et al., 2004). However, in patients with combined ADHD and SUD in a forensic context, short-term efficacy of stimulant medication has been confirmed (Ginsberg & Lindefors, 2012), as well as long-term improvements in cognitive functions, quality of life, and psychosocial functioning (Ginsberg, Hirvikoski, Grann, & Lindefors, 2012; Konstenius et al., 2013). Otherwise, the recommended treatment of first choice in patients with ADHD and SUD is non-stimulants (Bolea-Alamanac et al., 2014; S. J. Kooij et al., 2010; National Institute for Clinical Excellence, 2008).

The question has been raised as to whether the unsure outcome of stimulant treatment for ADHD with comorbid SUD may depend on inadequate dosage (Levin et al., 2015). With reference to imaging studies indicating a greater underlying dysregulation of dopamine transmission and an increased tolerance to stimulants in ADHD/SUD individuals (Volkow, Fowler, & Wang, 1999; Volkow et al., 2004), two RCT studies have been conducted in which more robust doses have been administered using individualized treatment protocols comprising up to 180 mg/day of methylphenidate (Konstenius et al., 2013) and treatment with extended-release mixed amphetamine salts (60 or 80 mg) in combination with cognitive behavior therapy in patients with cocaine use disorder (Levin et al., 2015). Both studies found symptom reduction and a decreased risk of relapses.

1.3.2.1 Recommendations of pharmacological treatment in patients with ADHD and SUD

In current guidelines for the treatment of combined ADHD and SUD (Bolea-Alamanac et al., 2014; S. J. Kooij et al., 2010; National Institute for Clinical Excellence, 2008), non-stimulant medication is recommended as the first-line treatment. There are also recommendations for individualized clinical decisions based on a careful analysis of the advantages and disadvantages of pharmacological treatment (Perez de Los Cobos et al., 2012). If stimulant medication is found to be applicable, a long-acting formulation such as OROS® methylphenidate is recommended since short-acting stimulants provide a more direct stimulant effect (Kollins, 2008; Schubiner, 2005; Szobot, Rohde, et al., 2008).

Additional recommended treatment strategies for patients with combined ADHD and SUD are interventions plans, psycho-education, frequent visits to the treating clinic, keeping track of pills (in outpatients), monitoring by administering the medication under close supervision, urine toxicology screening, treatment response with rating scales, and psychosocial interventions such as cognitive behavioral therapy, relapse prevention, and motivational interviewing (Bukstein, 2008; Kollins, 2008; Mariani & Levin, 2007; Upadhyaya, 2007). The National Board of Health and Welfare in Sweden recommends that ADHD should be treated in parallel with treatment of the substance abuse and, furthermore, that the clinical assessment, as well as prescription of the ADHD medication and the follow-up of the treatment, should be handled by a clinician experienced in SUD. Finally, the recommendation is that the health care providers and social services collaborate in the treatment of this patient group (National Board of Health, 2014a).

1.3.3 Psychological treatment of ADHD

As previously mentioned, about 20%–50% of ADHD patients are deemed to be non-responders to pharmacological treatment for ADHD. Insufficient symptom reduction and/or adverse effects are common causes of discontinuation of the medication (Bejerot, Ryden, & Arlinde, 2010; Gualtieri, Ondrusek, & Finley, 1985; Mattes, Boswell, & Oliver, 1984; Wender, 1998; T. E. Wilens et al., 2002). A study has shown that after eight years, only 32.5% had medicated at least 50% of the days of the previous year and, after 16 years, only 10.0% were on medication (Molina et al., 2009). Thus, for patients who choose not to medicate for ADHD and for medicated patients who have residual ADHD symptoms and functional impairments, alternatively and/or complementary psychological treatments may be needed to provide strategies and skills for coping with the accompanying functional impairments in ADHD.

In 1999 Wiggins introduced a brief group treatment for ADHD targeting specific organizational problems (Wiggins, 1999). The results suggested that the psycho-educational model had a beneficial effect on disorganization, inattention, and emotional lability. However, this study demonstrated a negative effect on the participants' self-esteem, which was suggested to be caused by increased awareness of their difficulties in everyday life. Later studies on psychoeducational interventions for adults with ADHD have shown promising results (Hirvikoski, Waaler, Lindstrom, Bolte, & Jokinen, 2014; Montoya, Colom, & Ferrin, 2011; Vidal et al., 2013).

During the last ten years, there has been a growing number of studies on CBT-based treatment programs for ADHD. Promising results have been shown in individual therapies (Safren et al., 2010; C. S. Stevenson, Stevenson, R. J., & Whitmont, S., 2003; C. S. Stevenson, Whitmont, S., Bornholt, L., Livesey, D., Stevenson, R.J., 2002), as well as in group therapies (Emilsson et al., 2011; M. V. Solanto, Marks, D. J., Wasserstein, J., Mitchell, K., Abikoff, H., Alvir, J. M. J., Kofman, M. D., 2010; C. S. Stevenson, Whitmont, S., Bornholt, L., Livesey, D., Stevenson, R.J., 2002; Weiss et al., 2012; Young et al., 2015; Zylowska et al., 2008). Dialectical behavior-based therapy for ADHD (B. Hesslinger, Philipsen, A., Richter, H., 2004; B. Hesslinger et al., 2002; Philipsen et al., 2007) has been developed in Germany and evaluated in psychiatric outpatient contexts. The results have

shown that the DBT-based treatment may be feasible and acceptable and lead to significant symptom reduction in psychiatric outpatient contexts (Hirvikoski et al., 2011; Philipsen et al., 2007).

On comparing the treatment modalities, pharmacological, nonpharmacological, and combined treatment, the latter has been shown in a systematic review to be associated with the greatest long-term functional improvement, both in terms of the proportion of improved outcomes and effect size (Arnold, Hodgkins, Caci, Kahle, & Young, 2015).

Recommendations for multimodal treatment of ADHD have also been included increasingly in different national and/or official guidelines during recent years (Bolea-Alamanac et al., 2014; S. J. Kooij et al., 2010; National Board of Health, 2014a; National Institute for Clinical Excellence, 2008). There is still, however, too great a lack of meta-analyses of psychosocial interventions to draw firm conclusions concerning their efficacy (Moriyama, Polanczyk, Terzi, Faria, & Rohde, 2013). Furthermore, in a large multimodal randomized trial, highly structured psychotherapy for ADHD was compared with individual counseling. Both treatment approaches were combined with methylphenidate and placebo. The outcome measures were obtained after 12, 24, and 52 weeks, respectively. Methylphenidate was found to be superior to placebo and highly structured psychotherapy did not outperform individual counseling. One conclusion drawn was that individual counseling, which is comparable in efficacy with highly structured psychotherapy, may be easier to implement in practical care. (Philipsen et al., 2015).

1.3.4 Psychological treatment of ADHD with comorbid SUD

Whereas the body of literature on cognitive behavioral therapy (CBT) for ADHD is growing, studies on CBT for ADHD in combined ADHD and SUD have not yet been reported. Structured psychological interventions for ADHD in patients with comorbid SUD add some difficulties. Treatment attrition has long been identified as a problem in the treatment of substance dependence in general (Aharonovich et al., 2006). Amotivation (Philips & Wennberg, 2014) and cognitive impairments (Aharonovich et al., 2006) are also found to be risk factors for early discontinuation of treatments. The combination of ADHD and SUD may be assumed to increase the risk of treatment attrition due to impulsive action/choice, since impulsivity characterizes ADHD (Sonuga-Barke et al., 2008), as well as SUD (Ivanov et al., 2008).

The need for alternative and complementary psychological interventions for pharmacological treatment of combined ADHD and SUD has, however, been highlighted more and more. An ongoing treatment trial of integrated cognitive behavioral therapy for patients with SUD along with comorbid ADHD has been presented in a study protocol (van Emmerik-van Oortmerssen, Vedel, et al., 2013; van Emmerik-van Oortmerssen, Vedel, van den Brink, & Schoevers, 2015). Multimodal treatment, including psychoeducation, coaching, and cognitive behavioral therapy in addition to pharmacotherapy, is also recommended in Belgium in practice guidelines for patients with combined ADHD and SUD (Matthys, Joostens, van den Brink, & Sabbe, 2013). The National Board of Health and Welfare in Sweden recommends concurrent interventions for combined ADHD and SUD (National Board of Health, 2014b).

1.3.5 Functional long-term outcomes of ADHD-treatment

Studies on long-term outcomes of treatments for ADHD differ in various respects: age group, design, treatment modalities, follow-up time, and outcome measures (Arnold, Hodgkins, Caci, et al., 2015; Fredriksen et al., 2012).

In a systematic review, the functional outcome measures have been found to be partly age-dependent (Arnold, Hodgkins, Caci, et al., 2015). Measures of academic and social function are most usual in childhood, and drug use and antisocial behavior in adolescence and adulthood. Less improvement involving pharmacological treatment has been found in substance use and antisocial behavior. However, a reduction of the negative impact of ADHD on life functioning has been found, although not to the level of healthy controls (M. Shaw et al., 2012), and a positive correlation between stimulant medication and employment status has been shown (Gjervan, Torgersen, Nordahl, & Rasmussen, 2012; Halmoy, Fasmer, Gillberg, & Haavik, 2009). Furthermore, prison inmates displayed improvements in psychosocial functioning [increased participation in educational programs and evidence-based treatment programs, and better global functioning (GAF)] after 52 weeks of treatment with methylphenidate (Ginsberg et al., 2012). ADHD treatment, especially multimodal treatment, has also been shown to have long-term benefits for academic achievements (Arnold, Hodgkins, Caci, et al., 2015)

1.3.6 Addiction treatment

Addiction treatment, including both pharmacological and psychosocial treatment, is beyond the scope of the present thesis and therefore will be summarized only briefly here. Overall psychosocial interventions are effective in promoting behavior changes in the addictive behavior (Jhanjee, 2014). The frequently used methods CBT (Carroll & Onken, 2005; McRae, Budney, & Brady, 2003; Weisner, Matzger, & Kaskutas, 2003), motivational interviewing (Smedslund et al., 2011; Vasilaki, Hosier, & Cox, 2006), and relapse prevention (Irvin, Bowers, Dunn, & Wang, 1999) have been found to be effective for many drugs of abuse. In individuals with opiate abuse, psychological treatment appears to be more effective when combined with substitution treatment (Jhanjee, 2014).

1.3.7 The Act of compulsory care of substance abusers

In Sweden, there is legislation within the Social Service Act pertaining to compulsory care for individuals with severe substance abuse, i.e. the Care of Substance Abusers (Special Provision) Act (Proposition 1987/88:147). The National Board of Institutional Care (Swedish abbreviation, SiS) is the authority responsible for all compulsory care governed by the Social Service Act. For application of the Compulsory Care for Substance Abuse Act, the following criteria must be met:

1. There is an ongoing abuse of alcohol, drugs, or volatile solvents and the person is in need of care in order to break free from his substance abuse.
2. The need for care cannot be met by voluntary measures or any other way, and
3. Due to the substance abuse the person is:
 - a. Exposing his/her psychic or mental health to severe danger
 - b. Running an evident risk of ruining his/her life, or
 - c. It may be feared that the person can severely harm him-/herself or a next of kin.

Criteria 1 and 2 must be met and at least one of the points under criteria 3.

It is the Municipal Social Ward that assesses the need for compulsory care and submits an application to an administrative court. According to the Act, the social services are obliged to apply for compulsory care if the criteria are met.

From the Annual Report from the National Board of Compulsory Care for 2014, it appears that 81% of those who have been required to undergo compulsory care after referral under the emergency care order did so, which means that substance abuse constituted a serious threat to the individuals' mental health and/or may have even been life-threatening (National Board of Institutional Care, 2014).

The stipulated treatment period of compulsory care is six months, and includes detoxification, stabilization of the physical and mental state, motivational interventions, assessments, treatment planning, and transfer to voluntary treatment when the purpose of the inpatient care has been achieved (Reitan & Isaksson, 2014). However, during this period of six months, the SiS has the treatment responsibility, even if the treatment takes place outside the institution.

1.3.7.1 Treatment planning, treatment goals, and adequate outcome measures

The guidelines for treatment planning in the compulsory care context describe a multi-step process (National Board of Institutional Care, 2011). The treatment planning should *inter alia* include a mapping of the patient's entire life situation, including assessments of the patient's problems, care needs, treatment motivation, and resources. Formulations of concrete and realistic goals, including stepwise goals and planned efforts/activities, must be included

2 AIMS

The aims of the thesis were:

1. To conduct a clinical characterization study of men with ADHD and SUD in compulsory care.
2. To investigate the association between pharmacological treatment and outcome in men with ADHD and SUD after discharge from compulsory care.
3. To evaluate the feasibility of DBT-based skills training as a voluntary intervention for men with ADHD and SUD in compulsory care.
4. To conduct a six-month post-discharge follow-up of groups after structured skills training administered as a voluntary intervention in compulsory care due to SUD.

3 METHODS

3.1 COMMON ELEMENTS IN THE STUDIES

All four studies refer to individuals with ADHD and comorbid SUD in compulsory care. The National Board of Institutional Care (SiS) is the authority responsible for compulsory treatment of adults with severe substance abuse according to the Care of Substance Abusers (Special Provision) Act (Proposition 1987/88:147)

3.1.1 Study setting

In all studies, the included patients with ADHD and SUD were treated at the SiS Institution Hornö, Enköping, Sweden. The patient target group of the institution, which is one of 11 SiS institutions for SUD, is adult males who, in addition to substance abuse, are violent and/or may have other severe psychiatric comorbidity

3.1.2 Diagnostic assessment

The data in Study I-II stems from 2004–2008 and in study III-IV from 2011–2014. The assessment procedure was the same, including an extensive multiple data source and consensus-based diagnostic assessments. The diagnostic assessments were made by clinical psychologists and, in patients with an extensive comorbidity, the diagnosis was also discussed with a consulting psychiatrist. The assessment included (1) clinical interviews, (2) when possible, collateral information (questionnaires and clinical interviews) gathered from the participants' *significant others* and, when available (3), additional information was obtained from case files from child/adolescent and/or adult psychiatry, as well as from institutions for involuntary care during childhood and/or adolescence, (4) standardized self-rating questionnaires assessing childhood ADHD symptoms (WURS, Wender Utah Rating Scale) (Ward, Wender, & Reimherr, 1993). Neuropsychological testing was included in all assessments. Some assessment instruments used during 2004–2008 were replaced at the assessments during 2011–2014. Between 2004 and 2008, the clinical interviews were based on the DSM-IV (American Psychiatric Association, 1994). Between 2011 and 2014 they were based on a *structured diagnostic interview* DIVA (J. Kooij, Franken, M., 2010). The Brown Attention-Deficit Disorder Scales (Brown, 1996), regularly used during 2004–2008, were replaced by the World Health Organization Adult ADHD Self-Report Scale, ASRS (Kessler et al., 2005) during 2011–2014.

For the assessment of comorbid disorders, standardized and validated rating scales and interviews were used during both periods: the Structured Clinical Interview for DSM Disorders (SCID-I and II) (First & Herlofson, 1998a, 1998b), the Beck Depression Inventory (BDI) (A. T. Beck, Steer, R. A., & Brown, G. K., 2005), the Beck Anxiety Inventory (BAI) (A. T. Beck, Steer, R. A., 2005), and the long version of the Symptoms Checklist (SCL-90-R) (Degoratis, 1983).

3.1.3 Statistical analyses

The group comparisons were made using the Chi-square test for categorical variables and Student’s t-test for continuous variables. In study IV, the Fisher exact test was used due to small sample sizes. The degrees of freedom were corrected for unequal variance if indicated by Levene’s test for equality of variance. Effect sizes for t-tests were expressed as Cohen’s *d* (Cohen, 1988). Effect sizes were expressed as a ‘small’ effect from 0.2 to 0.3, a ‘medium’ effect around 0.5 (half a SD), and a ‘large effect’ ≥ 0.8 . Effect sizes for Chi-square tests were expressed as Φ (Phi) and interpreted as a weak association (.10–.20), a moderate association (.20–.40), a relatively strong association (.40–.60), a strong association (.60–.80), or a very strong association (>.80).

In study I, we investigated whether the observed differences in WAIS indexes loading on EF were explained by the general intellectual ability (FSIQ) using analyses of co-variance (ANCOVA). The EF index was entered as a dependent variable, group [ADHD/SUD *versus* ADHD/Psych (ADHD/Psychiatric outpatient group)] as a fixed factor and FSIQ as a co-variate.

In Study II, a multiple regression analysis was performed to adjust for the potential effect of follow-up time on outcome measures. Individuals for which data were missing and deceased individuals were excluded using pairwise exclusion from the analyses of long-term outcomes. The statistical analysis was performed using the SPSS statistical software package (IBM, SPSS™, version 20).

3.1.4 Time line for data collection

2008-2009	2011-2014	2012-2015
Data collection study I, II	Data collection study III	Data collection study IV

3.2 STUDY I

3.2.1 Participants

The 60 males with ADHD and SUD in compulsory care (ADHD/SUD group) were compared with two other groups: 120 patients in compulsory care due to severe SUD, without a known ADHD diagnosis, matched for age and years of assessment (the general SUD group) and 107 patients with ADHD without severe SUD from a psychiatric outpatient clinic (ADHD/Psych group). The inclusion/matching criteria in the latter comparison were sex (males), age range (19 to 46 years), and year of diagnostic assessment (2004–2008).

3.2.2 Procedure

Comparison data on the general SUD group and the ADHD/SUD group were obtained from an unidentified dataset from the SiS internal database (DOK, a SiS follow-up and documentation system). Data on the ADHD/Psych population, assessed at the Neuropsychiatric Unit Karolinska, Psychiatry Northwest, Stockholm, Sweden, were extracted from a database based on the patient's medical records. Corresponding data in the ADHD/SUD group were obtained from the assessments documented in the patients' case files.

3.2.3 Measures

In the comparison of background data between the ADHD/SUD group and the general SUD group, the measures were: (1) Family background (psychiatric disorder and/or substance abuse in one or both parents), as well as educational and vocational history; (2) Previous interventions and psychiatric care (educational support in primary school, possible compulsory care during childhood and/or adolescence, previous adult psychiatric care, previous imprisonment); and (3) Current clinical data (preferred abuse substance and self-reported psychiatric symptoms).

For the comparison between the ADHD/SUD group and the ADHD/Psych group regarding ADHD symptoms during childhood, the measure was the number of self-reported retrospective ADHD symptoms during childhood (Ward et al., 1993). In the comparison of the general intellectual level, the measures were Full-scale IQ (FSIQ), Verbal IQ (VIQ), Performance IQ (PIQ), and [WAIS-III (Wechsler, 1997)]. Moreover, results on the four indexes were also compared: the Verbal Comprehension Index (related to Verbal IQ) and the Perceptual Organization Index (related to the nonverbal IQ), as well as the two indexes

loading on executive functions (EFs): the Working Memory Index and the Processing Speed Index (Weschler, 1997).

3.3 STUDY II

3.3.1 Participants

The included participants were the same 60 adult males with ADHD and severe SUD as in Study I. Of the 71 patients referred for an assessment, 47 were found to have ADHD. Additional 13 assessed patients, who had an ADHD diagnosis prior to admission to the Hornö SiS Institution, were also included in the study. At the time point for follow-up, 30 patients had received pharmacological treatment for ADHD and 30 patients had not.

3.3.2 Procedure

3.3.2.1 Rehabilitation plans

An individualized rehabilitation plan, based on the clinical and psychosocial assessments and the patients' own motivation for voluntary rehabilitation after completing compulsory care, was carried out for all patients. The rehabilitation options were 24-hour care in rehabilitation institutions, family homes, and supported housing, or outpatient care for patients having their own accommodation and a sufficient level of psychosocial functioning. All rehabilitation options included, or were combined with, psychiatric treatment and drug screening, except for those patients in support housing who refused parallel psychiatric treatment and/or only needed an accommodation.

3.3.2.2 Pharmacological treatment

All patients diagnosed with ADHD who were interested in starting a pharmacological treatment for ADHD were referred to a neuropsychiatric clinic or a clinic for addiction disorders in the patient's hometown. In all referred cases, the patient's local clinic was contacted in order to initiate the pharmacological treatment (to be prescribed by the local clinic) during the compulsory care period at the SiS Institution. Thus, the opportunities for the patients to receive pharmacological treatment for their ADHD depended on the local clinics' routines and prerequisites.

3.3.2.3 Long-term follow up

The follow-up data were collected from February, 2008, to March, 2009. The time between discharge from the institution and the follow-up ranged between 6 and 45 months (Md = 16 months, M = 18.4 months, SD = 9.79). In all cases, except for those patients who no longer had any contact with the social services, information was obtained from the patients' local social workers. When possible, interviews with the patients were also conducted, either in face-to-face meetings or by phone. The questions posed to the social workers and/or the patients who could be reached were semi-structured.

3.3.3 Measures

The outcome measures were *current status of substance abuse*, *rehabilitation status*, *accommodation*, and *employment*.

The *current abuse status* was categorized as (1) no known substance abuse, (2) no abuse due to compulsory care (imprisonment, forensic care, or a new period of compulsory care due to severe SUD), and (3) ongoing substance abuse.

Rehabilitation status: Patients who did not require rehabilitation due to good psychosocial functioning were defined as having a combination of no substance abuse, independent accommodation (which, in some cases, included supportive housing without psychiatric treatment), and current employment. Voluntary rehabilitation included long-term stays at an abuse rehabilitation center (24-hour care), a rehabilitation-oriented family home, or supportive housing that included regular psychiatric care. Compulsory care was defined as imprisonment, forensic care, or a new period of compulsory care for substance abuse at the time of the follow-up assessment. No rehabilitation due to other reasons included all patients who did not meet the rehabilitation criteria defined above, including patients exhibiting ongoing drug abuse, homeless patients, and those who could not be tracked, neither through their social workers nor the tax authority's population registers. However, for four of these patients, it was possible to obtain information from their former local social workers regarding some aspects of their current social situation.

The *accommodation status* was categorized as (1) independent accommodation, (2) rehabilitation center or family home (24-hour care), (3) supported accommodation, and (4) compulsory care, as defined above.

Employment status included two main categories: employed and unemployed. Employed was defined as all forms of structured and regular work or studies and unemployed was divided

into subcategories related to the causes of unemployment (compulsory care, being in voluntary rehabilitation, sick leave, and other reasons).

3.4 STUDY III

3.4.1 Participants

Forty patients were included in the study on DBT-based skills training. The exclusion criteria were an IQ < 70, severe psychiatric comorbidity, such as psychosis, and/or suicidal behavior. Patients who displayed severe externalizing behavior, as well as patients who were assessed as not being able to attend a group treatment, were also excluded. Twenty-three patients were previously assessed for ADHD and 17 were assessed at the SiS Institution Hornö.

3.4.2 Procedure

3.4.2.1 Treatment setting

All the participants were treated on a ward established for patients with ADHD at the SiS Institution Hornö. The ward staff had all been trained in the principles of DBT-based treatment and coaching. Every participant in the treatment program was assigned to a coach for daily support and for motivational interventions. One of the coaches, all of whom were ward staff, was always present at the treatment sessions. To encourage attendance at the sessions and for demonstrated treatment-related efforts, the participants received some modest rewards, e.g., a preferred activity with the ward staff.

The treatment project started in September, 2011, and ended in December, 2014. Due to circumstances related to events at the institution, there was a couple of long breaks in the treatment project.

3.4.2.2 The skills training program for ADHD

The treatment program was based on the manual (B. Hesslinger, Philipsen, A., Richter, H., 2010), but was adjusted somewhat in order to facilitate the reading and understanding. The group leaders were licensed psychologists working at SiS Institution Hornö.

3.4.3 Measures

3.4.3.1 Background and demographic data

Data on the psychosocial background were obtained from the assessments documented in the participants' case files and from a structured interview prior to the treatment, based on a form that covered both psychosocial background and present life situation.

3.4.3.2 *Feasibility*

The criteria for good *feasibility* were defined as the percentage of completers (attending at \geq 75% of the sessions) of the treatment being 60% or more of the patients allocated to treatment.

3.4.3.3 *Treatment acceptability*

A Treatment Credibility Scale (TCS) (Borkovec, 1972), administered before and after the treatment, was used to measure expectation for improvement and treatment credibility. In order to measure the participants' confidence and satisfaction with the treatment, the patient evaluation form from the manual (B. Hesslinger, Philipsen, A., Richter, H., 2010) was used. Included items are specificity of the treatment program, increased knowledge of ADHD, increased ability to cope with their ADHD, experience of having opportunities to make their own suggestions during the sessions, and willingness to take part in a similar group in the future. A ranking of the most helpful treatment elements was also included.

3.4.3.4 *Efficacy-related measures*

The Current ADHD-Symptom Scale – Self Report Form (R. A. M. Barkley, K.R., , 1998) and a Staff Report form (modified from the Self-Reported Form for ward staff) were administered before and after the treatment program. The scale includes 18 symptom items for ADHD, corresponding to criteria for ADHD in the DSM-IV, and eight symptoms of externalizing behavior (such as irritability and anger outburst). The Current ADHD-Symptom Scale is scored from 0 to 3. To assess psychiatric symptoms, a short version of the SCL-90-R was used (Degoratis, 1983), scored from 0 to 4. General well-being was measured with a visual analog scale (VAS), ranging from 0 (worst) to 10 (best) (B. Hesslinger et al., 2002).

3.5 STUDY IV

3.5.1 Participants

Forty patients who were included in the DBT- based skills training program, described in Study III, were followed up.

3.5.2 Procedure and Measures

Six months after discharge from compulsory care, the patients' local social workers were contacted by letter with an attached short questionnaire and/or a telephone interview.

3.5.2.1 The DBT-based skills training

The recruitment and treatment setting, as well as the structured skills training groups, are described in Study III. The Swedish version of the original German manual (B. Hesslinger, Philipsen, A., Richter, H., 2010) was adjusted to the patient population. Otherwise, the general structure of the sessions and the included themes were the same as in the manual.

3.5.2.2 Outcome measures

1. Substance abuse status [categorized as (1) no known substance abuse at the time of follow-up, (2) no abuse due to imprisonment, forensic care, a new period of compulsory care for substance abuse, or (3) ongoing substance abuse and (4) deceased].
2. Rehabilitation status [categorized as (1) voluntary rehabilitation (rehabilitation center (24-hour care), rehabilitation-oriented family home or supportive housing in combination with outpatient psychiatric care and outpatient care), (2) compulsory care, defined as imprisonment, forensic care, or a new period of compulsory care for substance abuse, (3) neither voluntary rehabilitation/ treatment, nor compulsory care].
3. Accommodation [categorized as (1) rehabilitation center, supported housing, (2) independent accommodation, and (3) no permanent housing].
4. Employment [categorized as (1) employed or studying, (2) on sick leave, and (3) neither employed, studying, nor on sick-leave].

4 RESULTS

4.1 STUDY I

In the comparison between the ADHD/SUD group ($n = 60$) and the general SUD group ($n = 120$), it was found that both groups had an unstable family background, low educational level, and little work experience, as well as no significant differences between the ADHD/SUD group and the general SUD group. A few statistical trends pointed towards a higher percentage of unstable family backgrounds in the ADHD/SUD group than in the general SUD group ($p = .10$) and towards a lower percentage of work experience in the ADHD/SUD than in the general SUD group ($p = .10$).

Symptoms of depression and anxiety were frequently reported in both groups (85.0% in the ADHD/SUD group versus 84.2% in the general SUD group, *n.s.*), as well as self-reported psychotic symptoms, such as hallucinations, mainly referable to drug-induced psychotic symptoms or psychotic episodes (58.3% in the ADHD/SUD group and 64.2% in the general SUD group, *n.s.*).

The ADHD/SUD group had a significantly higher degree of compulsory care during childhood (mostly due to substance abuse and/or antisocial behavior) compared to the general SUD group ($p = .04$). Moreover, imprisonment was significantly more frequent in the ADHD/SUD group than in the general SUD group ($p < .001$). No significant differences were found in previous adult psychiatric care. Data on special education in primary school was not available in the general SUD group. A between-group difference was found in the preferred abused substance ($p = .05$). In the ADHD/SUD group, the stimulant drugs, amphetamine and cocaine, were preferred in 53.3%, compared to 30.8% in the general SUD group. Alcohol and benzodiazepine were preferred more often in the general SUD group (21.7%, compared to 9.0% in the ADHD/SUD group).

In the comparison between the ADHD/SUD group and the ADHD/Psych group, it was found that the participants in the ADHD/SUD group reported significantly more ADHD symptoms in childhood as measured with WURS-25 ($M = 60.15$, $SD = 17.25$), compared to the ADHD/Psych group ($M = 50.83$, $SD = 24.38$) ($t [120] = 3.21$, $p = .002$, Cohen's $d = .60$). Furthermore, the ADHD/SUD group was found to have significantly poorer results on the full-scale IQ test ($n = 87$, ADHD/Psych, and $n = 51$, ADHD/SUD, $t [135.68] = 4.78$, $p < .001$, Cohen's $d = .79$). Similarly, further analyses of verbal IQ and nonverbal/performance IQ showed poorer results for the ADHD/SUD group: verbal IQ ($n = 86$, ADHD/Psych, and n

= 51, ADHD/SUD, $t[134.58] = 4.62$, $p < .001$, Cohen's $d = .77$), nonverbal/performance IQ (n = 86, ADHD/Psych, and n = 51, ADHD/SUD, $t[129.96] = 3.54$, $p = .001$, Cohen's $d = .60$). Analyses of the level of the four indexes of the WAIS-III showed a similar pattern of results, i.e., the ADHD/SUD group performed poorer on all indexes: verbal comprehension index, VCI (n = 86, ADHD/Psych, and n = 51, ADHD/SUD, $t[135.00] = 4.20$, $p < .001$, Cohen's $d = .70$); perceptual organization index, POI (n = 84, ADHD/Psych, and n = 51, ADHD/SUD, $t[127.60] = 3.70$, $p < .001$, Cohen's $d = .63$); working memory index, WMI (n = 83, ADHD/Psych, and n = 51, ADHD/SUD, $t[122.16] = 2.29$, $p = .129$, Cohen's $d = .40$); processing speed index, PSI (n = 84, ADHD/Psych, and n = 47, ADHD/SUD, $t[124.92] = 3.50$, $p = .002$, Cohen's $d = .60$). On controlling for FSIQ in an ANCOVA, the group differences in the working memory index (WMI) and speed of processing index (PSI) no longer reached statistical significance, indicating that there was no specific effect on EF in the ADHD/SUD group.

4.2 STUDY II

Thirty patients had received pharmacological treatment for their ADHD, while 30 had not. Twenty-two of those who had been treated pharmacologically at the time of follow-up had already started the pharmacological treatment for ADHD at the SiS Institution Hornö (with prescriptions from their local clinic) and eight at local out-patient clinics after discharge. Thirty patients had never started a pharmacological treatment for ADHD. The reasons why these patients never started treatment varied and are presented in Table 4.

Table 4. Reasons for not receiving ADHD medication after discharge from compulsory care

Reasons for not receiving pharmacological treatment of ADHD	N of 30 untreated patients
Declined referral for stimulant medication	6
Referral was rejected by the local clinic (lack of psychiatrist, requirement of two years of sobriety, diagnosis questioned)	4
Had not been called to an appointment with a psychiatrist after discharge	4

An unstable psychiatric condition	2
Did not show up for the appointment with the psychiatrist after discharge	3
Deceased	4
Missing information	7

No statistically significant differences between the pharmacologically treated and nontreated groups were found regarding growing-up conditions, IQ, educational level, work experiences, history of treatment interventions, or self-reported psychiatric symptoms at the time of assessment at SiS Institution Hornö.

Mortality

Five out of 60 patients (8.3%) had deceased (one in the pharmacologically treated group and four in the untreated group, n.s.). The mean age at death was 25.0 years (SD = 3.8).

Substance abuse status

Relapses into substance abuse were significantly less common in the patients in the pharmacologically treated ADHD group, compared to the group not treated for ADHD ($p = .01$).

Rehabilitation status

No rehabilitation due to good psychosocial functioning was more common in the pharmacologically treated group than in the untreated group (20.0% versus 10.0%). Voluntary treatment was more common in the pharmacologically treated group (36.7%) than in the untreated group (6.7%), whereas compulsory care was less frequent in the pharmacologically treated group (3.3%) than in the non-treated group (20.0%) ($p = .01$).

Accommodation

Twenty-one individuals in the pharmacologically treated group were staying at supporting housing (30.0%) or rehabilitation centers (26.7 %) according to their rehabilitation plan, compared to four (13.3%) in the untreated group. Nine (30.0%) of the individuals in the

untreated group were homeless or accommodated in compulsory care, compared to three (10.0%) in the treated group ($p = .028$).

Employment status

Thirty-six participants (60. %) were either in compulsory care or in voluntary rehabilitation, or on sick-leave. Thus, employment status was relevant for only 24 participants (15 in the treated group and 9 in the non-treated group). Of these 24 individuals, 20.0% in the treated group and 13.3 % in the untreated group had employment, while 30% in the treated group and 16.5% in the untreated group were unemployed ($p = .028$).

4.3 STUDY III

4.3.1 Feasibility

The number of patients with ADHD estimated to meet the inclusion criteria and informed and requested to be included in the treatment was 70. Thirty patients declined to participate, signifying a refusal rate of 42.9%.

Out of 40 patients who started the DBT-based skills training, 28 (70%) completed the treatment, all of whom had an attendance of at least 75% of the sessions. The mean number of attendances at the sessions among completers was 11.29 (SD = 1.0) (out of a maximum of 12) and, among non-completers, 4.17 (SD = 2.0). Of the 12 non-completers, one participant was excluded from the treatment program by the group leaders because of severe disruptive behavior. Other reasons for discontinuation were “did not get anything out of the treatment” ($n = 3$), “too restless and/or difficulty to concentrate” ($n=3$), were transferred to a voluntary treatment in their community ($n = 2$), increasing symptoms of depression and/or anxiety ($n = 2$), and absconded from the institution ($n=1$).

The non-completers of the treatment program were found to have a lower educational level (Completers: less than 9 years, $n = 4$; 9 years, $n = 16$; Secondary school, $n = 8$. Non-completers: less than 9 years, $n = 8$; 9 years, $n = 4$; Secondary school, $n = 0$. $\chi^2 = 14.5$, $p = .005$), more severe ADHD symptoms during childhood (WURS 25: Completers, $M = 58.27$, $SD = 11.76$; Non-completers, $M = 74.60$, $SD = 17.39$, $t = -3.26$, $p = .003$), and more current impulsive symptoms, according to the staffs’ ratings (the Current ADHD-Symptom Scale: Completers $M = 8.18$, $SD = 5.42$; Non-completers $M = 15.45$, $SD = 8.96$, $t = -3.11$, $p = .004$). No significant differences were found regarding employment , accommodation , marital

status, somatic illness, current pharmacological treatment for ADHD , other psychoactive medication, ADHD subtype, psychiatric comorbidity [Axis I and Axis II], other neurodevelopment disorders, preferred abused drug , drug screening, or full scale IQ (all p values $> .10$).

4.3.2 Treatment acceptability

There was a significant ($p = .021$) increase in the mean score on the Treatment Credibility Scale (TCS) from pre-intervention ($M = 5.7$, $SD = 1.87$) to post-intervention ($M = 6.34$, $SD = 1.89$).

According to the ratings on the patient evaluation form, the participants perceived the treatment as being ADHD-specific (mean score of 4.5, $SD = 0.51$, on a scale of 1–5). The lowest mean score, 3.2 ($SD = 1.16$), was observed for the item “Has achieved better control of the ADHD-related problems.” For the other three items, the average mean score was 4.0 ($SD = 1.14$ – 1.26). The patients rated the psychoeducation as the most helpful element in the treatment and, thereafter, the group leaders, followed by the group setting, and, lastly, the exercises. The participants’ mean summary evaluation of the treatment was 2.9 ($SD = 0.85$) on a scale from 1 (failed) to 4 (with honor).

4.3.3 Efficacy related measures

The ADHD symptoms ($p < 0.001$) and psychiatric symptoms ($p = 0.01$) were reduced from pre- to post-intervention in the self-ratings. General well-being increased significantly ($p < 0.001$). Contrarily, the staff reported no significant symptom reduction of ADHD symptoms from pre- to post-intervention.

The self-ratings were significantly correlated with the ward staff ratings only regarding externalizing behavior (in both the pre-and post-intervention ratings). No significant correlations were found in ADHD symptoms of hyperactivity/impulsivity or inattention.

4.4 STUDY IV

Twenty-eight out of 40 patients completed the treatment while 12 patients discontinued the treatment.

4.4.1 Substance abuse status

Known relapses into substance abuse were less frequent in the completers compared to the noncompleters, although this difference did not reach statistical significance ($p = .07$). One patient was deceased.

4.4.2 Rehabilitation status

Twenty-one of the completers (21 out of 28) were in some form of voluntary treatment (rehabilitation centers, supporting housing including treatment, or outpatient care), while the corresponding figure among the non-completers was one individual (1 out of 12) ($p = .001$). The number of patients in a new treatment period in compulsory care was the same in the two groups (two in both groups, either in prison or compulsory care for SUD).

4.4.3 Accommodation status

Eleven of the completers had an accommodation in rehabilitation centers or supporting housing, as compared to two of the non-completers. Eight of the completers and three of the non-completers had their own accommodation, while six of the completers and one of the completers lived with a relative (partner or parent). No one was homeless among the completers, as compared to two of the non-completers ($p = .23$).

4.4.4 Employment status

Among the completers, ten patients had employment, eight were on sick-leave and seven had neither employment nor were on sick-leave. The corresponding numbers for the non-completers were three (employment), one (on sick-leave), and four (neither employment nor on sick-leave). The difference between the groups was not significant ($p = .26$).

4.4.5 Clinical characteristics in completers and non-completers

The differences in clinical characteristics are described in study III. In summary, the non-completers were found to have more dysfunctions (lower educational level and more severe ADHD).

5 DISCUSSION

5.1 SUMMARY OF THE MAIN FINDINGS

Compared to the general SUD group in compulsory care, the ADHD/SUD group had already been significantly more often in compulsory care during childhood or adolescence, as well as imprisoned more often as adults. The most common preferred abused substance in the ADHD/SUD group was stimulant drugs, while alcohol and benzodiazepine abuse was more common in the general SUD group. Compared to the ADHD/Psych group, the ADHD/SUD group reported more ADHD symptoms during childhood and performed poorer on all tests of general intellectual ability and executive functions.

The pharmacologically treated and the pharmacologically untreated groups were comparable with regard to the demographic and background characteristics. Overall, mortality was high; 8.3% of the participants had deceased at follow-up (one in the pharmacologically treated group and four in the untreated group; the between-group difference was not significant). The group that received pharmacological treatment for ADHD exhibited fewer substance abuse relapses, received more frequently voluntary treatments in accordance with a rehabilitation plan, required less frequent compulsory care, were more frequently accommodated in supportive housing or a rehabilitation center, and displayed a higher employment rate than the non-treated group.

The refusal rate for the DBT-based skills training was approximately 42.9%. Of those 40 who started the DBT-based skills training, 28 (70%) completed the treatment (attendance at $\geq 75\%$ of the sessions). The treatment acceptability was good. Both ADHD and psychiatric symptoms decreased from pre- to post-intervention in self-ratings, but not in staff ratings. The patients reported improved general well-being. The correlation between self- and staff-ratings was poor.

The six-month follow-up showed that the completers were more often in voluntary treatments, lived in their own accommodation or rehabilitation center and had less known substance abuse, as compared to the non-completers. However, the groups already differed in certain aspects at baseline, which has to be considered in the interpretation of the results.

5.2 THE COMPULSORY CARE CONTEXT

The main purpose of the compulsory care for SUD is to interrupt an often life-threatening substance abuse (Proposition 1987/88:147). The local municipalities and county councils are

responsible for the long-term rehabilitation after completion of the compulsory care, as planned on the basis of the assessments during the inpatient care, and in agreement with the local social service and the patient. Thus, neither more prolonged structured psychotherapies nor pharmacological treatment for ADHD is included as regular treatment interventions. Prescriptions of ADHD medications must be done by the local psychiatric or addiction clinics, but not all local clinics agree to prescribe stimulant medication during the patients' stay at the compulsory care institution.

The included studies in the present thesis indicate, however, that both pharmacological and structured psychotherapies in a compulsory care context may be beneficial for this high-risk patient group. The compulsory care setting may have facilitated the monitoring of the pharmacological treatment, as well as been supportive through daily feed-back. A monitored and stable medication for ADHD may have also reduced the risk of relapse during the vulnerable period immediately after discharge. The compulsory care context for substance abuse has similarities with a prison context since it involves a structured environment and treatment monitoring. Stimulant medication in prison inmates has shown both short-term improvement in ADHD symptoms and long-term improvements in several functions, such as psychosocial functioning (Ginsberg et al., 2012; Ginsberg & Lindfors, 2012). Thus, starting medication at the institution may be beneficial for this therapeutically challenging group.

Furthermore, the findings in Study III indicate that the DBT-based skills training program (B. Hesslinger, Philipsen, A., Richter, H., 2010) may be feasible in a compulsory care context. However, compared to an outpatient context (Hirvikoski et al., 2011), fewer patients are suitable for the skills training in a compulsory care context, not least due to an often low motivation for voluntary non-pharmacological treatments. Therefore, the feasibility criterion of an attrition rate of < 40% was set, as compared to <25 % in the outpatient setting. Compulsory care for SUD is *per se* an indication of low treatment motivation, since such care is always preceded by attempts to motivate to voluntary treatments in accordance with the Social Services Act. Thus, this patient group constitutes a great challenge to successful treatment, which has to be adapted to the patient group and the compulsory care context. Nevertheless, utilizing compulsory care for structured psychological treatment may be beneficial, since treatment programs such as DBT-based skills training are not likely to be feasible in an outpatient context for the current patient group.

5.3 CLINICAL CHARACTERISTICS

5.3.1 Antisocial behavior

A specific distinguishing characteristic, compared to a general SUD group without ADHD, was the early onset of antisocial behavior. The diagnostic assessments of the patients in Study I showed that 51.7 % in the ADHD/SUD group met the criteria for ASPD (American Psychiatric Association, 1994). In the assessments of the participants in Study III, the percentage of ASPD (American Psychiatric Association, 1994, 2013) was 55.0%, thus indicating that antisocial behavior is a salient characteristic in patients with ADHD and SUD in compulsory care. These percentages of ASPD in ADHD are in line with the findings in studies on treatment-seeking patients with ADHD and SUD (nearly 52.%) (van Emmerik-van Oortmerssen et al., 2014). Furthermore, ODD and/or CD in combination with ADHD has been found to be related to early onset of SUD (Z. Chang et al., 2012), as well as to a more severe course of SUD (August et al., 2006). However, CD during childhood and/or antisocial behavior without ADHD in adulthood has *per se* been proposed to be an independent and robust predictor of SUD (Couwenbergh et al., 2006; Hopfer et al., 2013; King et al., 2004; Rodgers et al., 2014; Saban et al., 2014; Westermeyer et al., 2005; Wilson & Levin, 2005).

5.3.2 Additional comorbidity

Due to the lack of established diagnoses in the general SUD group in Study I, the comparison with the ADHD/SUD group was based on self-reported data from comprehensive structured interviews documented in a database (DOK). One consequence of the self-reported data may be an unexpectedly high percentage of reported psychotic symptoms: 58.4% in the ADHD/SUD group and 64.1% in the general SUD group. However, this percentage also includes self-reported drug-induced psychotic symptom (such as psychotic paranoid symptoms related to abuse of central stimulants and hallucinations related to abuse of hallucinogens) or episodic psychotic symptoms, either on a single occasion or repeatedly, and either short-term or continuing for a longer time. In the ADHD/SUD group, 51.7% reported drug-induced psychotic symptoms and, in the general SUD group, the percentage was 41.0 %. These percentages may be compared to 14.9% of reported psychotic symptoms at the assessments at the SiS institution Hornö, according to the assessment data. The reported psychotic symptoms in the patients in the skills training groups (Study III) was 8 out of 40 (20.0%), 12.5% of which refers to psychotic episodes or drug-induced psychosis. It may be assumed that the percentage of psychotic symptoms reported in the assessments is more valid due to more thorough inquiries.

The rate of self-reported symptoms of depression/anxiety in Study I (85.0%) was higher than the rates for the established diagnosis of these disorders in Study III (77.5%). However, both these rates are in line with the rates of Axis I disorder over the life span in the ADHD population (between 65% and 89 %) (Sobanski et al., 2007; Sobanski et al., 2008) and a rate of more than 70.0% in patients with ADHD and SUD (Ginsberg, Hirvikoski, & Lindefors, 2010; van Emmerik-van Oortmerssen et al., 2014). In the general SUD group, self-reported symptoms of depression/anxiety were also high (84.2%).

5.3.3 Cognitive level

An additional distinguishing characteristic of the ADHD/SUD group, compared to an outpatient ADHD group without severe SUD, was a poor general cognitive capacity: IQ = 87 in Study I and IQ = 87.9 in Study III. At least two months passed between enrollment and completion of the detoxification and the psychological testing. It cannot be ruled out that such executive functions as working memory, response inhibition, processing speed, and mental flexibility were still affected by the severe substance abuse in some patients (Lundqvist, 2005, 2010; Verdejo-Garcia, Bechara, Recknor, & Perez-Garcia, 2006). However, it may also be assumed that cognitive impairments existed before an established abuse. Special education support, low school performance, and a low educational level were common findings among the ADHD/SUD patients. However, the relationship between the cognitive status at the time of assessment and all possible contributing factors, such as the long-term consequences of the substance abuse, the premorbid cognitive level, the low educational level, and unfavourable growing-up conditions, is complex and impossible to determine from the data in the present study.

5.3.4 Preferred abused substance

A difference between the ADHD/SUD group and the general SUD group (Study I) in the preferred abused drug was found: considerably more patients in the general SUD group reported alcohol as the preferred drug (21.7% vs. 6.7%), while the ADHD/SUD group more often preferred stimulants. However, it is clear from the drug screening (in both Study I and Study III) that these patients with ADHD and SUD may be regarded as polydrug abusers and that the use of benzodiazepines is very common (58.3% were positive for this drug in Study I and 85.0% in Study III). The choice of abused drug is, however, also dependent on the availability of the drug, which may change from time to time.

5.4 TREATMENT OUTCOME

5.4.1 Feasibility

The results in Study III showed that the attrition rate was 30% (12 out of 40 patients discontinued the treatment), while the attendance at sessions was high among completers (the mean attendance number was 11.29 sessions out of a maximum of 12), thus indicating that the treatment program was feasible and acceptable for most participants. High attrition in psychological treatments has been demonstrated in substance dependence in general (Aharonovich et al., 2006).

5.4.2 Treatment acceptability

Treatment acceptability in Study III refers to the participants' expectation for improvement and treatment credibility. Using the Treatment Credibility Scale (TCS) (Borkovec, 1972), it was found that the expectation for improvement/confidence in the treatment was considerably lower compared to what was found in a study on DBT-based skills training for ADHD in a psychiatric outpatient clinic (Hirvikoski et al., 2011). This applies to both the pre- and post-ratings. This may not be surprising, given the compulsory care context and the total clinical burden in the current study group. However, the treatment expectancy/credibility increased from pre- to post-intervention, which, hopefully, may indicate an increase in the individuals' propensity to participate in future psychological treatments.

In Study II, only six patients (10%) declined referral for stimulant medication, indicating that that pharmacological treatment was a more accepted treatment option than DBT-based skills training in this patient group.

5.4.3 Efficacy-related measures

The finding in Study III of significant symptom reduction in all measured parameters in self-ratings from pre-to post-intervention is in line with previous studies in psychiatric outpatient contexts (Hirvikoski et al., 2011; Philipsen et al., 2007). It may be assumed that the symptom reduction is not only attributable to the treatment program, but also to general/nonspecific therapeutic factors (Strupp, 1986). Furthermore, the staff ratings did not indicate a reduction of ADHD symptoms and the correlations between self- and staff ratings was poor. The scores on self-rated ADHD symptoms ($M = 32.7$) were, however, comparable with the scores in the psychiatric outpatient ADHD group ($M = 28.0$), using the same rating scale (Hirvikoski et al., 2011). The lack of a control group complicates the interpretation of the relatively low mean

score ($M = 17.82$) in the ward staff's ratings, as well as the interpretation of the reduction of symptoms.

5.4.4 Long-term outcome measures

Long-term functional goals for chronic conditions with a complex symptomatology, such as ADHD, may be expressed in terms of functional remission/recuperation and freedom from additional impairments (Rostain, Jensen, Connor, Miesle, & Faraone, 2013). Concrete and realistic goals are recommended for treatment planning in the clinical guidelines (National Board of Institutional Care, 2011). The functional long-term outcome measures in Studies II and IV, *Current abuse status*, *Rehabilitation status*, *Accommodation status*, and *Employment status*, are in line with these standpoints and may be regarded as relevant, given the patient characteristics and the clinical context. Furthermore, mortality is a relevant outcome measure, given the high mortality in this patient group.

In both Study II and Study IV, the aims were to explore the association between a specific treatment modality (pharmacological treatment in Study II and DBT-based skills training in Study IV) and the psychosocial outcome after discharge. However, the studies differed in several aspects, e.g., the follow-up periods were different, which may have affected the rehabilitation status at the time of the follow-up. The mortality rate may also be assumed to be lower in the six-month follow-up than after a mean follow-up time of just over 18 months.

In individuals with ADHD and SUD, pharmacological treatment of ADHD has exerted a moderate or negligible effect on ADHD symptoms. However, the effect of pharmacotherapy on substance abuse is uncertain (Castells et al., 2011; Cunill et al., 2014; T. E. Wilens, Monuteaux, et al., 2005). Long-term studies on pharmacological treatment for ADHD in patients with combined ADHD and SUD are scarce. In a retrospective naturalistic study of adults with ADHD, comorbid SUD has been found to increase the risk of discontinuation of the stimulant medication (Torgersen, Gjervan, Nordahl, & Rasmussen, 2012). However, on controlling for SUD (in a prison context), methylphenidate (MPH) was shown to reduce ADHD symptoms and improve global functioning, quality of life, and cognitive functions in adult male long-term inmates (Ginsberg et al., 2012). Study II also indicates that pharmacological treatment for ADHD may improve long-term psychosocial functioning. In all measured parameters, the psychosocial outcome was better in the pharmacologically treated group than in the untreated group. Furthermore, symptom reduction and decreased risks for relapses have been found in two recent trials in which higher doses have been administered to individuals with ADHD and SUD: (1) individualized treatment protocols up

to 180 mg/day with methylphenidate (Konstenius et al., 2013) and (2) treatment with extended-release mixed amphetamine salts (60 or 80 mg) in combination with cognitive behavior therapy (Levin et al., 2015).

The six-month follow-up in Study IV showed that the psychosocial outcomes were better in the completers than in the non-completers. It is not possible, however, to draw any firm conclusions as to whether the better outcomes were related to the skills training program, given that the completer *versus* non-completer groups differed in certain aspects at baseline. However, one conclusion is that it is important to consider the severely disabled patients' ability to benefit from the treatment since discontinuation may be experienced as an additional failure. An individualized treatment may be needed for the patients at risk for treatment discontinuation.

5.4.5 Mortality

Individuals with ADHD have a higher mortality rate than individuals without ADHD (Dalsgaard et al., 2015). In combination with SUD, ODD and CD, the mortality rate increases (ibid.). The mortality in individuals with substance abuse is also high (Fugelstad, Annell, & Agren, 2014; Nyhlen, Fridell, Backstrom, Hesse, & Krantz, 2011; Stenbacka et al., 2010). Among individuals treated in compulsory care for severe SUD between 1999 and 2003, 5.3% had died (6.0% of male patients) within 12 months after discharge from compulsory care. (J. Larsson, & Leiniö, T. L., 2012). A register study of individuals treated in Swedish compulsory care between 2001 and 2009 demonstrated eight-fold mortality compared to the general Swedish population (Hall et al., 2015). The mortality rate for all patients in Study II, with a mean follow-up time of 18 months, was 8.3%. Thus, the mortality in patients with ADHD and SUD in compulsory care must be regarded as very high. In the six-month follow-up study (Study IV), mortality was not treated as a general outcome measure due to the short follow-up time. Instead, 'Deceased' was included as a category within the substance abuse status. One person had deceased during the six-month follow-up period (2.5%).

5.5 LIMITATIONS

A limitation in Study I is that the number of undiagnosed ADHD patients in the general SUD group was unknown. Bearing in mind the high prevalence of ADHD in substance abusers (van Emmerik-van Oortmerssen, Vedel, et al., 2013), it may be assumed that some individuals in the general SUD group had an undiagnosed ADHD. The differences between

the ADHD/SUD group and the general SUD group may have been larger if undiagnosed ADHD in the general SUD group could have been entirely ruled out.

The proportion of missing data was relatively high in the pharmacologically nontreated group in Study II. However, in accordance with clinical experience and anecdotal information from their social workers, these patients were assumed to have relapsed into substance abuse. Thus, the differences between the pharmacologically treated group and the non-treated group would be even greater if this assumption is correct.

The generalizability of the results in all studies included in the present thesis may be limited due to the extensive clinical burden in the patient group. Thus, the results may not characterize the total population of individuals with ADHD and comorbid SUD. The generalizability may also be limited by the study context of compulsory care. However, individuals who exhibit a high symptom severity of both ADHD and SUD, in addition to other comorbid psychiatric disorders, are often met in other compulsory care settings, such as forensic care and institutional youth care, and also in voluntary outpatient and inpatient addiction and psychiatric clinics (Klein et al., 1997; Rosler et al., 2004; Torok et al., 2012).

The lack of a control group is the major limitation in Study III. The primary aim was, however, to evaluate whether the treatment program was at all feasible, given the compulsory treatment context, the severely impaired patient group, and the resource allocation demands that the treatment program made on the SiS Institution. In study IV, it was not possible to draw any causal conclusion concerning the relationship between the DBT-based skills training and the psychosocial outcome due to the baseline differences between completers and non-completers, as well as the lack of a control group.

6 CONCLUSIONS

A conclusion drawn from Study I is that ADHD in combination with SUD is a particularly disabling condition, comprising poor general cognitive ability, severe psychosocial problems (including early and persistent antisocial behavior) and other co-existing psychiatric conditions. These findings suggest that undiagnosed ADHD with comorbid SUD constitutes a high risk for the development of an extensive clinical burden. This burden is, in turn, associated with high risk behaviors, including increased risks for accidents, criminality, drug overdoses, and mortality, as well as family burdens and high societal costs.

The long-term follow-up study showed that only 30 (out of 60) patients were medicated for ADHD, which indicates that the availability of pharmacological treatment was poor. This may be regarded as especially worrisome, given the severity of the clinical impairment in the group and the indication of treatment benefits with regard to the psychosocial outcome.

It is a challenging task for clinicians to balance the pharmacological needs of the patients with ADHD and severe SUD with the risk of drug misuse and diversion. The compulsory care context may facilitate the initiation of pharmacological treatment through the structured treatment setting, including monitoring to prevent misuse or diversion of the medication. Furthermore, initiating the pharmacological treatment at the compulsory care institution may have reduced the risk of relapse during the vulnerable period immediately after discharge.

Pharmacological treatment appears to be a more preferable treatment modality than structured psychotherapy in ADHD/SUD patients. However, the DBT-based skills training program for ADHD was also feasible and acceptable and may have contributed to symptom reduction in some patients in compulsory care. Discontinuation of a voluntary treatment program in a compulsory care context may be an adverse prognostic sign in this patient group.

7 FUTURE DIRECTIONS

The studies in the present thesis refer to the population of men with ADHD in compulsory care for SUD. However, women with ADHD and SUD in compulsory care have not been clinically characterized. Moreover, studies that evaluate the long-term psychosocial outcomes of pharmacological treatment for ADHD have not been conducted on women with ADHD and severe SUD after discharge from compulsory care. Therefore, studies including both women and men are necessary to further characterize individuals with ADHD in compulsory care due to SUD. Likewise, treatment studies including both men and women with ADHD in compulsory care due to SUD are desirable.

For patients with combined ADHD and SUD, additional efforts are needed to develop treatment strategies that both meet the patients' need for adequate pharmacological treatment and reduce such risks as misuse and diversion. (Bukstein, 2008; Kollins, 2008; Mariani & Levin, 2007; Upadhyaya, 2007). Future studies on these topics may be helpful for clinicians in their dilemma concerning treatment of this patient group. The trials with individualized treatment protocols in incarcerated men with ADHD and SUD (Konstenius et al., 2013) and with extended-release mixed amphetamine salts in combination with cognitive behavior therapy in patients with ADHD and cocaine use disorder (Levin et al., 2015) are encouraging since they have demonstrated both fewer relapses in substance use and ADHD symptom reduction.

More studies on psychological treatment programs adapted to the clinical characteristics of patients with ADHD and SUD are needed. Replications of studies on programs also targeting the antisocial behavior, such as the Reasoning and Rehabilitation ADHD Program (Emilsson et al., 2011; Young et al., 2013), would be valuable for patients with ADHD in compulsory care due to SUD.

Both ADHD and substance abuse are independently associated with an increased risk for mortality (Barbatesi et al., 2013; Dalsgaard et al., 2015; Fridell & Hesse, 2006; Johnson, Finney, & Moos, 2005; Nyhlen et al., 2011). Study II demonstrated a very high mortality in patients with ADHD who had been treated in compulsory care for SUD. A more comprehensive mortality study that compares ADHD/SUD patients in compulsory care with general SUD patients without ADHD would increase our knowledge of the risks in this patient group.

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