Graduate thesis

NTNU
Norwegian University of Science and Technology
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The role of sleep problems in the development of emotional and behavioral problems in adolescents with ADHD: A three-year prospective study in a clinical sample.

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Abstract

Background: There is insufficient knowledge about how sleep problems affect adolescents with ADHD and whether sleep problems aggravate comorbid difficulties and functional levels in a long-term course. The aim of the present study was to examine if sleep problems affect the level of comorbid emotional and behavioral problems in adolescents with ADHD compared to adolescents with ADHD without sleep problems.

Methods: This prospective study obtained data from a health survey in the Department of Child and Adolescent Psychiatry, St. Olavs hospital, Trondheim University Hospital, Norway. At baseline, 257 adolescents with ADHD between the ages of 13 to 18 were included and filled out a self-report about sleep problems. At follow-up three years later 200 subjects participated in a psychiatric interview (Kidde-SADS). Information about emotional and behavioral problems was obtained by parent reports on the Child Behavior Checklist (CBCL).

Results: Analyses showed that sleep problems predicted more internalizing problems and externalizing problems three years later when controlling for age, sex and ADHD-symptom score.

Conclusion: Assessing and treating sleep problems is important to reduce emotional and behavioral problems in adolescents with ADHD in a long-time perspective.

1 Introduction

1.1 Attention Deficit Hyperactivity Disorder

Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurodevelopmental disorder in childhood and has a chronic course that persists into adulthood (Franke et al., 2018). ADHD is characterized by a behavioral pattern with attention problems, hyperactivity and/or impulsivity that decreases function in daily life, in different situations and over time. This pattern of behavior is usually present from early preschool but may become more apparent in late childhood.

In ICD-10 (World Health Organization, 1992), the disorder is classified as hyperkinetic disorder. Impaired attention and hyperactivity are the main features and both must be present to make the diagnosis. Impaired attention is manifested by a lack of persistent task involvement and a tendency to move from one activity to another without completion. Overactivity is characterized by restlessness, noisiness, talkativeness and fidgeting, particularly in situations requiring calmness. Hyperkinetic children are often careless and impulsive, prone to accidents and more often face disciplinary difficulties because of thoughtless violations of norms and rules, not only because of a deliberately challenging. They often exhibit socially uninhibited behavior with a lack of normal caution and restraint, become unpopular with other children, and can become isolated as a result of the behavior. The behavioral symptoms have an early onset, usually during the first five years of life, and have a long duration. Impairment must be present in two or more settings (home, classroom, clinic). Cognitive disorders are common, and specific motor and linguistic developmental disorders are disproportionately frequent. Secondary complications include dissocial behavior and low self-esteem. There is a great deal of variation between individuals in the number and type of symptoms, frequency, intensity and impact on functioning in everyday life. The severity ranges from low to moderate and high.

The clinical presentation changes with age, and the impact on everyday function is greatly influenced by the course. Very young children are more likely to display externalizing symptoms such as hyperactive-impulsive behavior, while in middle childhood inattentive symptoms become more apparent, and by late adolescence and in adulthood inattention tends to persist, while the objective signs of motor hyperactivity decline (Franke et al., 2018).

DSM-5 (APA, 2013) divides ADHD into the following categories: *Combined type*, where both symptom criteria of attention deficit and hyperactivity/impulsivity are present. *Inattentive presentation*, where symptom criteria of inattention is present, but not criteria of hyperactivity/impulsivity. *Hyperactive/impulsive presentation*, where criteria of inattention is not present, only criteria of hyperactivity and impulsivity (Norwegian Directorate of Health, 2018d, American Psychiatric Association, 2013).

The DSM categories are somewhat more broadly defined and many practitioners in Europe, including Norway use the wider definition of the DSM-IV and DSM-5 in addition to the ICD-10 for clinical purposes. For example, the Norwegian Directorate of Health allows the use of stimulant medication in patients with severe attention problems without hyperactivity, designated DSM ADHD Inattentive type, even though such a patient would not strictly fulfill the ICD-10 criteria (Norwegian Directorate of Health, 2007; Taylor et al., 2004).

Population prevalence depends on whether the definition of Hyperkinetic Disorder in ICD-10 or AD/HD in DSM-5 is used. In addition, there is a wide variation in symptom severity and whether the symptoms cause disruptions in everyday life function. The prevalence also varies with age and gender (Norwegian Directorate of Health, 2018a). It is estimated that Hyperkinetic Disorder in line with ICD-10 has a prevalence of 1-3 % in children and adolescents, while AD/HD in line with DSM-5 occurs in around 5% in childhood and 2.5% in adulthood. A Norwegian registry study found an ADHD prevalence rate of about 3% in 11-year-old children (Suren et al., 2012). However, about 5.5% fulfilled the DSM-criteria in a large Norwegian epidemiological study (Ullebo, Posserud, Heiervang, Obel, & Gillberg, 2012)

Sex differences in the rates of ADHD are prominent but change throughout development in both clinical and community settings (Larsson, Dilshad, Lichtenstein, & Barker, 2011). Earlier findings suggested that around 80% of ADHD cases in child and adolescent clinics were male, whereas in adult clinics the proportion of males were closer to 50% (Kooij et al., 2010). In more recent studies findings report an increasing amount of females being diagnosed with ADHD. In Norway 1:3 of the children and adolescents with ADHD referred to a European cohort study were females (Noevik et al., 2006). One possible reason for the predominance of males in child clinics is the greater hyperactivity-impulsivity levels they

show compared to females, who are more likely to display predominantly inattentive symptoms and less overt disruptive behaviors.

1.2 Treatment

Treatment of ADHD includes information about the diagnosis, environmental modifications, parent training programs and medical treatment (Norwegian Directorate of Health, 2018b). Information about the diagnosis and adapting the environment to the child´s or the adolescent's needs is the first step. It is recommended to create a treatment plan for each individual with ADHD/Hyperkinetic Disorder.

1.2.1 Medical treatment and side effects

Medical treatment is the most effective option to relieve symptoms and improve daily functioning, when the above measures have not had sufficient effect. Most relevant for people with ADHD is stimulant drugs, which has shown effect on core symptoms, resulting in less hyperactivity, increased ability to concentrate, targeted problem solving and improved impulse control (Matthijssen et al., 2019). The active substance most frequently used is methylphenidate, which is the first drug of choice in children and adolescents (Cortese et al., 2018; Felleskatalogen AS, 2017)

Common side effects of stimulants are sleep problems and decreased appetite. Methylphenidate, compared to no intervention, increased the risk of insomnia and sleep problems such as difficulty falling asleep, and also decreased appetite (Storebø et al., 2018). Another study also demonstrated a general association between increased methylphenidate dose and increased sleep problems in children with ADHD. However, a substantial proportion of children with pre-existing sleep difficulties no longer had sleep problems on the highest dose of methylphenidate, which suggest that methylphenidate dose titration should not be avoided solely on the basis of a child´s premorbid sleep problems (Becker, Froehlich, and Epstein, 2016).

If symptoms and function in everyday life improves, but unfavorable side effects are present but mild, it is recommended to continue treatment because of the positive effect (Norwegian Directorate of Health, 2018b). Long-term use of medical treatment is not well evaluated, therefore it is important to assess other factors that can affect ADHD over the lifespan.

1.3 Comorbidity

ADHD is characterized by substantial comorbidity over the life course including behavioral problems, anxiety, depression, substance abuse and accidents (Franke et al., 2018).

More than 50% of children and adolescent with ADHD have additional difficulties (Norwegian Directorate of Health, 2018c). During adolescence, ADHD is associated with low academic achievement due to learning disabilities, a common comorbidity that either affects specific problems within the areas language, reading, writing, motoric or non-verbal skills, or affect general learning ability. A minimum of 1/3 has additional learning disabilities (Arnold, Hodgkins, Kahle, Madhoo, & Kewley, 2020). Aside from this ADHD in adolescence is also associated with interpersonal difficulties, substance use disorders, mood disorders and anxiety disorders continuing into adult life (Barkley, Fischer, Smallish, & Fletcher, 2006; Thompson, Molina, Pelham, & Gnagy, 2007). A large sample of Norwegian adults with ADHD was recently studied to look at comorbidity. Results shows that both men and women had a four to nine times higher prevalence of anxiety, depression, bipolar and personality disorders, schizophrenia and substance use disorder than the remaining adult population (Solberg et al., 2018), indicating the potential for introducing preventive measures in young people with ADHD.

1.3.1 Sleep disorders & insomnia

Sleep is a basic human need and is critical to both physical and mental health. How much we sleep is individual and varies with age. Lack of sleep or poor sleep quality can give rise to fatigue, decreased energy, irritability and problems focusing. The ability to make decisions and mood stability can also be affected. Sleep problems often coexist with symptoms of depression or anxiety and can exacerbate depression or anxiety (American Psychiatric Association, 2017; Olufsen, Sørensen, & Bjorvatn, 2020)

Sleep disorders involve problems with the quality, timing and amount of sleep, which cause problems with functioning and distress during the daytime. Insomnia is the most common among the different types of sleep disorders.

Insomnia involves problems falling asleep, multiple and long awakenings at night or early waking in the morning, or a combination of these. The diagnosis is based on the patient´s subjective experience of sleep and daytime functioning. There are no fixed lengths of periods

without sleep, but usually a 30 minutes time-limit is used, where the following can be counted as insomnia: Falling asleep takes more than 30 minutes, awakenings in the night last for more than 30 minutes in total, time for wakening in the morning is more than 30 minutes earlier than expected. In addition there must be a decreased daily function. Typical symptoms is tiredness, mood swings, reduced ability to concentrate, decreased cognitive or social function and increased anxiety concerning sleep (Bjorvatn, Sivertsen, Waage, Holsten, & Pallesen, 2018).

2 Aims

Bedtime activities and emotional problems have been shown to have moderating effects on the relationship between ADHD symptoms and sleep problems in children with ADHD (Tong, Ye, & Yan, 2018). Moderate positive correlations between sleep problems and reduced function has been demonstrated, but this issue has not been mapped in a long-term perspective. Therefore, there is insufficient knowledge about how sleep problems affect ADHD and whether sleep problems aggravate comorbid difficulties and functional levels in a long-term course (Virring, Lambek, Jennum, Moller, & Thomsen, 2017; Virring, Lambek, Thomsen, Moller, & Jennum, 2016). The aim of the present study was to examine if sleep problems affects the level of comorbid emotional and behavioral problems level in adolescents with ADHD compared to those without sleep problems.

3 Methods

3.1 Clinical sample

The study sample was a subsample from the Health Survey in the Department for Child and Adolescent Psychiatry (CAP), St. Olav's Hospital, Trondheim University Hospital, Trondheim, Norway. The CAP survey is a follow-up study. The objective is to examine the development and consequences of psychiatric and neurodevelopmental disorders from childhood and adolescence to adulthood (Ranøyen et al., 2018; Schei et al., 2018). Inclusion criteria were to have been referred to a CAP-clinic, have one attendance there in the time between February 15, 2009 and February 15, 2011, and be between the age of 13 and 18 (Schei et al., 2018). Exclusion criteria were major difficulties in answering the questionnaire because of psychiatric state, low cognitive function or lack of sufficient language skills.

During the two years of inclusion, 2032 adolescents were referred to one of the participating units. Of these, 289 were not included based on the exclusion criteria, and 95 were lost during

registration. The total number of invited participants was 1648. Among 717 participating at baseline (CAP survey baseline, T1), 54,8% were female (Schei et al., 2018). Among the included 717, 263 had been previously diagnosed with ADHD/Hyperkinetic disorder, 40.6% were female. Among these 263 adolescents, 257 answered the questions about sleep at T1.

The number of baseline (T1) participants agreeing to participate in the three-year follow-up (T2), were 648 out of 717. These subjects participated in a diagnostic interview, the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version (K-SADS-PL (Kaufman et al., 1997). Among the 256 diagnosed with ADHD at baseline, 200 (78%) participated in the follow-up, 40,5% in this group were female. Parents filled out the Achenbach Child Behavior Check-ist (CBCL, (Achenbach, 2001) at this time.

3.2 Procedures

At T1, the adolescents answered an electronic questionnaire and measured weight and height. Biological material and information was gathered from their medical journals. The questionnaire contained questions similar to the questions used for adolescents in The Health Study in Nord-Trøndelag, UNG-HUNT (Holmen et al., 2014; Junker, Bjørngaard, Gunnell, & Bjerkeset, 2014).

T2 included an electronic questionnaire and a telephone-interview. Medical doctors and psychologists interviewed the participants with the Kiddie-SADS-PL psychiatric interview. In addition, an electronic questionnaire was filled out by the parents. To provide information about behavioral and emotional problems, parents completed the CBCL.

3.3 Study design

This study is a prospective cohort-study.

3.4 Measures

3.4.1 Analysis/Baseline Population

The sample is based on the 263 participants diagnosed with ADHD/hyperkinetic disorder at baseline. Those without ADHD diagnosis were removed from the present study. The sample of adolescents with ADHD were either diagnosed with ADHD but not yet medicated, or diagnosed with ADHD and medicated. Sleep problems were examined using questions about

insomnia; *Sleep time after going to sleep* and *Early awakenings without going back to sleep*. 257 out of the 263 answered the questions about insomnia.

3.4.2 Diagnosis of ADHD

Baseline

Diagnoses at baseline (T1) were collected from clinical charts and followed the ICD-10 multi-axial diagnostic system (i.e., axes I- VI) (World Health Organization, 1992). All diagnoses were made by a clinical psychologist or a child and adolescent psychiatrist based on all clinical information. The CAP clinic's standardized procedure for the assessment and diagnosis of hyperkinetic disorders is based on the National Guideline for Assessment and Treatment of ADHD (Norwegian Directorate of Health, 2007). This guideline, similar to other established ADHD guidelines (Subcommittee on Attention-Deficit/Hyperactivity et al., 2011), requires a clinical diagnostic interview based on the ADHD symptoms described in the ICD-10, and possible coexisting disorders, and a somatic assessment. It recommends the use of questionnaires filled out by the adolescent, their parent, and a teacher to obtain an ADHD symptom score. The ICD-10 diagnosis of hyperkinetic disorder is referred to as ADHD in this study.

The diagnostic criteria for hyperkinetic disorder are nearly identical to the DSM-IV-TR criteria for ADHD combined; however, specifiers such as mainly attention problems or mainly hyperactivity/impulsivity problems are not used in the ICD-10. The criteria for Hyperkinetic Disorder in ICD-10 for use in research are very close to the diagnostic criteria for ADHD in DSM-5 (Nyden et al., 2010; American Psychiatric Association, 2013).

Three-year follow-up

The KSADS-PL (Kaufman et al., 1997) was used for diagnosis at the three-year follow-up (T2). It is a well-established, semi-structured diagnostic interview designed to assess present and past episodes of psychopathology among children and adolescents on Axis I of the DSM-IV-TR. Diagnosis of ADHD included ADHD combined type, inattentive type, hyperactive/impulsive type and ADHD INA. Adolescents and young adults currently taking medication prescribed for ADHD were classified with a diagnosis of ADHD regardless of whether they fulfilled symptom criteria.

3.4.3 Insomnia

National guidelines recommend setting the diagnosis insomnia based solely on the patient's subjective experience of sleep and daytime functioning. Symptoms include either insomnia, multiple and long awakenings at night, or early waking in the morning, or a combination of these. There are no specific lengths for the periods without sleep for the diagnosis to be made. Nevertheless, a so-called 30-minute limit is often operated, with the following being considered as signs of insomnia: Sleep time of more than 30 minutes, awakenings at night of more than 30 minutes in total, wake-up time in the morning more than 30 minutes earlier than desired. In order to make the diagnosis, in addition to the sleep problems, a reduced function during the day is required (Bjorvatn et al., 2018).

The DSM-IV criteria for insomnia are defined as the subjective experience of difficulties in initiating or maintaining sleep or experiencing that sleep problems are impossible to change. The experience must be present for more than one month (Sivertsen et al., 2012). The questions about insomnia in the questionnaire at T1 are in line with this definition.

3.4.4 Baseline Measures

ADHD Rating Scale-IV

To assess the participants' symptom load at baseline we used the ADHD Rating Scale- IV (ADHD-RS-IV) parent version (DuPaul, Ervin, Hook & McGoey, 1998). This instrument is based on the DSM-IV criteria addressing ADHD symptoms. The scale is organized into two sections, each with its own sum score. There is a total of 18 items, where 9 items reflect symptoms of inattention and 9 items reflect hyperactivity and impulsivity, which may be answered by parent, guardian or grandparent (Kornør & Bøe, 2011). The score for each item ranges from 0–3, giving a maximum score of 27 for each dimension, and a total score of 54. A high score reflects a higher amount of symptoms (DuPaul, 2016).

3.4.5 Follow-up measures

Assessment of behavioral and emotional problems

To assess behavioral and emotional problems we used the Achenbach Child Behavior Checklist school-age version (CBCL 6-18), a questionnaire filled in by parents to describe competence and emotional and behavioral problems in youth 6-18 years of age.

The CBCL is a comprehensive mapping tool and is widely used in clinical work and research internationally. The validity of the CBCL as a screening instrument of emotional and behavioral problems in the child and adolescent population was demonstrated in a previous study (Nøvik, 1999), and the instrument has been widely used in other Norwegian studies (Kornør & Jozefiak, 2012), including studies of adolescents with ADHD (Schei, 2015).

The problem-part of the CBCL 6-18 consists of 120 items, and is answered on a scale from 0 to 2, (0=not true, 1=partially or sometimes true, 2=fits very well or often). By summing up all answers a total problem score can be calculated on a scale from 0 to 240. The ASEBA data program calculates scores for eight narrow-band scales containing information about various symptom dimensions. The *Broad band* scale *Internalizing problems* includes the narrow-band scales Anxious/depressed, Withdrawn-depressed and Somatic complaints, while the broad-band scale Externalizing problems includes the syndrome scales Rule-breaking and Aggressive behavior.

In the present study the Internalizing and Externalizing scores are used to provide information about emotional and behavioral problems, respectively.

3.4.6 Statistical analysis

Descriptive statistics are reported as mean (standard deviation) for scale variables and count (percentage) for categorical variables. Proportions were compared using Pearson's chi squared test. Independent t-test was used to examine the difference in internalizing and externalizing problems in the groups with and without insomnia. Linear regression was used to assess the effect of sleep problems at baseline on emotional and behavioral problems (internalizing and externalizing scores) at the 3-year follow-up. Multiple regression was used to study the effect of insomnia, adjusting for age, sex and ADHD-RS scores at baseline.

Two sided p-value tests with $p < 0.05$ were taken to indicate statistical significance. 95% confidence intervals (Cis) were reported when relevant. Statistical analyses were conducted using SPSS version 26.

3.5 Ethics

Written informed consent was obtained from adolescents and their parents prior to inclusion, in accordance with the study procedures in the CAP survey. Study approval was given by the

Regional Committees for Medical and Health Research Ethics (Reference No. CAP survey: 4.2008.1393, present study Reference No.: 2011/1435), and by the Norwegian Social Science Data Services (Reference No. CAP survey: 19976).

4 Results

4.1 Descriptive data of sample

Baseline descriptive (T1)

Out of 263 participants with ADHD, 256 answered the questions about insomnia; Problems with falling asleep and/or problems waking up to early and not going back to sleep. There are 7 missing in this group that are not accounted for in the following descriptive. Descriptive of the sample at baseline and follow-up is presented in Table 1.

At baseline 105 (39.9%) reported to have insomnia. 40.6% of the participants were females (N=104). Baseline age ranged from 13 to 20. Four participants were over 18 years; three were 19 years old and one was 20 years old. Mean (SD) age at participation was 15.4 (1.7) years.

Out of 256 participants 11 adolescents used ADHD medication, 142 did not use medication, and 103 parents did not respond to the question whether the adolescents used medication or not.

55 % of the adolescents (N=141) lived with both parents. Almost 29% (N=73) lived with their mother, and only 4.7% lived with their father (N=12). A total of 30 adolescents did not live with any of their parents (N=30). 9 of these lived with their partner, 7 lived with their grandparents, 6 lived with their foster parents, 3 lived with their adoptive parents, and in total 4 lived either with friends or alone. There is one missing in the group of adolescents not living with their parents.

The parents of 154 participants filled out the ADHD-RS-IV. The range in ADHD-RS-IV inattention score was 2-56 and the mean score was 18.67. In ADHD-RS-IV *hyperactivity and impulsivity* the maximum score was 27, and the mean score was 11.67. The Maximum total ADHD-RS-IV score was 73. Mean score was 30.45.

Three-year follow-up (T2)

The study sample at follow-up included the adolescents who responded to the K-SADS (N=200). Age ranged from 16.0 to 23.2 years. Mean (SD) age was 18.2 (1.7). Parents of 140 participants answered the questions in the CBCL. Internalizing problem scores ranged from 0–50. Externalizing problem scores ranged from 0–38.

Dropout analysis (T2)

As we had 116 non-responders to the CBCL at T2, we performed a dropout analysis to compare responders to CBCL with non-responders. There were few differences in mean age (SD) 18.7 (1.5) and sex (40.5% were girls) between these groups. The findings are shown in Table 1.

Table 1. Descriptive data of the study sample at baseline (T1) and follow-up (T2)

	N	Mean (SD)	%	Missing
T1				
Age	256	15.4 (1.7)	100	
Females	104		40.6	0
Insomnia	105		39.9	7
Medicated	200		78.1	56
(T1)	154		60.2	102
ADHD-RS inattention score	142	18.67 (6.91)		114
ADHD-RS hyperactivity/impulsivity scores	143	11.67 (6.76)		113
ADHD-RS Total score	139	29.93 (10.3)		117
T2				
CBCL participation (T2)	140		54.7	116
Age		18.2 (1.7)		
Females	57		40.7	
Medicated	66		47.1	
ADHD present	131		92.9	
CBCL internalizing score		11.3 (8.68)		
CBCL externalizing score		9.62 (7.85)		
T2 Dropout analysis	116		45.3	
Age		18.7 (1.5)		
Females	47		40.5	

Note. ADHD-RS: ADHD Rating Scale-IV. CBCL: Child Behaviour Checklist. ADHD presently includes “Partly in remission” and “Criteria for present diagnosis fulfilled”.

Insomnia

Out of 263 participants, 256 answered either or both questions about insomnia; *difficulties falling asleep at night* (N=255) and *early awakening and not falling asleep again* (N=253). 105 participants reported having difficulties falling asleep and/or early awakening. In Table 2, these numbers are presented as *Insomnia*. 75 participants answered yes to one of the questions about insomnia, accounting for 29.8% of the group. 28 participants answered yes to both questions about insomnia, 11.1% of the group.

52% of the participants answered yes either to the question *Difficulties falling asleep* (N=90) or *Problems with early awakenings and not going back to sleep* (N=43). Among the females (N=104) 43.3% had difficulties falling asleep. In the male group (N=151) 29.8 % reported that they struggled with falling asleep. In the group of participants reporting having problems with early awakening, 22.3% was females (N=103). In the group of males (N=150), 20 reported having problems with early awakening (13.3%).

Looking at the whole group jointly, 149 out of 252 participants reported no difficulties with neither falling asleep at night nor problems with early awakenings without going back to sleep. *Not insomnia* accounts for 59.1% of the group.

The proportion of females reporting insomnia was larger than for males, 53/104=51.0% versus 52/152=34.2%, p=0.007.

Table 2. Frequencies of adolescent reported sleep problems at baseline by gender (T1).

	Males	**Females**	**Total**	**Pearson Chi-Square/p**
	152	104	256 (100%)	
Difficulties falling asleep	45 (29.6%)	45 (43.3 %)	90 (35.1%)	
Early awakening	20 (13.2%)	23 (22.1%)	43 (16.8)	
Insomnia	52 (34.2%)	53 (51.0%)	105 (41%)	0.007

Note. Subjects with *Insomnia had Difficulties falling asleep* or *Early awakening or both sleep problems*.

We used an independent samples t-test to analyze the differences in internalizing and externalizing scores, the dependent variables in this study, between the groups with and without insomnia. The highest mean score was in the group with *difficulties falling asleep at night* (mean 13.3), where the difference in internalizing score was significant (p=0.018). We did not find a significant difference in the externalizing scores in the same group (p=0.518). When we analyzed both sleep variables jointly, (Table 3) we also found higher internalizing scores in the group with insomnia, compared to the group with no insomnia.

Table 3. Mean CBCL internalizing and externalizing scores at follow-up in adolescents with and without sleep problems at baseline

	N	Internalizing Mean (SD)	Externalizing Mean (SD)
Insomnia	84	13.28 (10.2)	10.7 (7.7)
No insomnia	54	10.07 (7.37)	9.32 (7.98)
p		.089	0.781

Regression analyses with internalizing and externalizing problems at three-year follow-up as dependent variable is shown in Table 4., Regression analysis adjusting for insomnia, age and sex is shown in Table 5a and adjusting for insomnia, age, sex and ADHD symptom score is shown in Table 5b. Unadjusted, insomnia affects internalizing problems significantly. Adjusted for age, sex and ADHD-RS-IV symptom score, insomnia significantly predicts higher externalizing problems.

Table 4. Regression analyses with Internalizing or Externalizing problems at the 3-year follow-up as dependent variable, and insomnia as covariate.

	N	B (SE se(b))	95% CI Lower	95% CI Higher	p
Internalizing	138	3.206 (1.499)	.243	6.170	.034
Externalizing	138	0.753 (1.374)	-1.964	3.469	.585

Table 5a. Multiple regression with Internalizing or Externalizing problems at the 3-year follow-up as dependent variable, and insomnia, age and sex at baseline as independent variables simultaneously.

Dependent Variables	Independent Variables	B (SE(b))	95% CI L	95% CI H	p
Internalizing (n = 138)	Insomnia	2.633 (1.533)	-.399	5.666	.088
	Age	.407 (0.436)	-.455	1.270	.352
	Sex	-2.249 (1.500)	-5.215	.718	.136
Externalizing (n = 138)	Insomnia	1.157 (1.416)	-1.643	3.957	.415
	Age	-.487 (.403)	-1.283	.310	.229
	Sex	.194 (1.385)	-2.545	2.933	.889

Table 5b. Multiple regression with Internalizing or Externalizing problems at the 3-year follow-up as dependent variable, and insomnia, age, sex and ADHD-RS-IV score at baseline as independent variables simultaneously. (N=263).

Dependent Variables	Independent Variables	B (SE(b))	95% CI L	95% CI H	p
Internalizing (n =76)	Insomnia	3.819 (2.023)	-.215	7.854	.063
	Age	.411 (.628)	-.841	1.662	.515
	Sex	-3.041 (2.013)	-7.055	.974	.135
	ADHD-RS-IV total score	-.013 (.093)	-.198	.171	.885
Externalizing (n = 76)	Insomnia	3.801 (1.828)	.157	7.446	.041
	Age	-.147 (.567)	-1.278	0.983	.796
	Sex	-1.737 (1.818)	-5.363	1.889	.343
	ADHD-RS-IV total score	.044 (.084)	-.122	.211	.598

5 Discussion

5.1 Summary of main findings

In this study we assessed the prospective effect of insomnia on behavioral and emotional problems in adolescents with ADHD. Insomnia predicted higher behavioral problems three years later, when controlling for age, sex and ADHD-symptoms. Unadjusted, insomnia predicted higher emotional problems three years later. Insomnia reached near significance in predicting emotional problems three years later when adjusting for age, sex and ADHD symptoms.

The mean scores of emotional and behavioral problems in our sample of adolescents with ADHD were generally high compared to population scores. A new norm and cut-off scores for CBCL emotional and behavioral problems in the Danish population were published in 2012 (Henriksen, Nielsen, & Bilenberg, 2012). In the Danish study mean Internalizing scores for adolescent boys and girls were 5.0 (SD 4.9) and 6.0 (SD 5.9) respectively. Mean Externalizing scores were 4.7 (SD 5.4) and 4.9 (SD 6.1) The mean population score plus 2 SD (98$_{th}$ percentile) has been recommended as a cut-off for probable cases. CBCL population scores have been similar in the Nordic countries, including a previous Norwegian study (Nøvik, 1999). At baseline in our study the participants with ADHD already had high behavioral and emotional problem scores, and sleep difficulties further increased these problems. The results emphasize the negative effect sleep problems have on comorbid problems in adolescents with ADHD.

5.2 Insomnia and the effect on emotional and behavioral problems

Our findings indicate that difficulties with falling asleep at night has an impact on daily experienced emotions, but behavioral problems are also somewhat affected. There have been few studies clarifying how sleep contributes to heterogeneity of ADHD presentation and prognosis (Lunsford-Avery, Krystal, & Kollins, 2016). The systematic review by Lunsford-Avery et al. (2016) presents mixed findings, but overall it suggests associations between sleep disturbances and ADHD symptoms in the population. In adolescents with ADHD subjective sleep problems were associated with emotional symptoms, such as depression and anxiety. The systematic review also showed poorer clinical, neurocognitive and functional outcomes among adolescents with ADHD. Lack of sleep reduces our ability to focus and think clearly, it increases emotional distress and mood disorders (Medic, Wille, & Hemels, 2017). Actions and emotions may be more poorly regulated as a result.

A recent study from 2019 was the first to show that adolescents with ADHD have more variable sleep/wake pattern than their peers, using both objective and subjective sleep measures (Langberg et al., 2019). In our study only participants with ADHD were reviewed. We found that 41% of the adolescents with ADHD had sleep difficulties. A study from 2005 had almost the same numbers, where 37% of their sample described daytime fatigue and the need of more sleep (Brook & Boaz, 2005). Another study from 2014 found that sleep problems were prevalent among ADHD adolescents, where 74% reported problems with falling asleep at night (initial insomnia) and nocturnal awakenings (Fisher et al., 2014). This study also suggested a gender difference in reported sleep problems among ADHD teens, where males reported a fewer number of sleep problems compared to females. These findings are similar to our findings, where more females reported sleep problems, compared to the male participants. A dose-response relationship between sleep and symptoms of inattention and hyperactivity-impulsivity has been described, where shorter sleep durations raised the odds of having higher amount of ADHD-symptoms; higher for inattention scores than hyperactivity-impulsivity scores (Hysing, Lundervold, Posserud, & Sivertsen, 2016). The sleep variables used in our study do not describe length of in-bed-time, and sleep duration was not measured by actigraphy, which might affect the outcome. Intraindividual variability of sleep/wake patterns may be important for clinicians to assess and monitor as a part of treatment (Langberg et al., 2019).

The prospective associations between baseline sleep variables and ADHD-symptoms indicates increased internalizing problems three years later, but not higher externalizing problems. Becker et al. (2020) recently posted a study with similar outcomes, where adolescents with ADHD showed greater depressive symptoms and lower positive affect when they were restricted sleep in three weeks, compared to a three-week period of sleep extension. The parents also reported greater negative affect and emotion dysregulation among the adolescents during sleep restriction (Becker, Tamm, Epstein, & Beebe, 2020). When adjusting for age, sex and ADHD-RS insomnia predicted worsened externalizing problems. Similar to these findings another study found that sleep problems significantly predicted general externalizing behavior problems, and depressive symptoms one year later (Becker, Langberg, & Evans, 2015). Both our findings indicate that insomnia predicts worse emotional and behavioral problems in a long-term perspective, when adjusted for age, sex and ADHD-symptoms.

In our study we did not take into account depression among the adolescents, as a dependent factor alone, as the CBCL Internalizing score includes depressive symptoms, as well as symptoms of anxiety and somatic problems. Depression is closely related to sleep problems, and is both a predisposing and precipitating factor in the development and maintenance of sleep problems over time (Talbot, McGlinchey, Kaplan, Dahl, & Harvey, 2010). Hysing et al. (2016) found that depressive symptoms accounted for more of the association between sleep and the inattentive subscale than for the association between sleep and the hyperactivity-impulsivity subscale. The association between sleep and ADHD symptoms was still significant after accounting for depressive symptoms, thus the association could not be solely explained by depression (Hysing et al., 2016). Our study show similar results, but by using only parent-reports we did not manage to pick up depression in the same way as we might have if we had used self-reports by the adolescents themselves. Thus, we may have underestimated the level of depressive symptoms in these adolescents. Furthermore we do not know based on these results what type of emotional problems had the most impact on the sleep problems.

The connections between sleep, emotional problems and function in daily life can be somewhat complex and complicated. There is a question about directions of effects and whether sleep disorder itself can lead to emotional problems and significant impairment in daily functioning. Some studies have shown that sleep disorders lead to several disabilities in daily life and over time. In children, behavioral problems and cognitive functioning are associated with sleep disruption. For adolescents, sleep disruption impacts psychosocial health, risk-taking behavior and school performance (Medic et al., 2017). A study using data from UNG-HUNT looked at sleep problems as a potential health factor affecting the risk of high school dropout. The results showed a dose-response relationship between insomnia and the risk for high school dropout (De Ridder et al., 2013). Children and adolescents with ADHD already struggle with school and dropout from school will make it even harder for them to catch up with their peers. As one of many potential benefits, preventing sleep problems might prevent adolescents from dropping out of school.

5.3 Strengths and limitations of the study

Strengths of the present study included a study population at baseline which consisted of a relative large number of participants, and we were able to control for several confounding

variables. Outcome measures were attained from diagnostic interviews and standardized questionnaires used in several studies, which makes our study comparable with other studies using the same measures.

A limitation of the study is the high amount of cases with missing information about emotional and behavioral problems in the follow-up. However, we performed a dropout-analysis to compare the groups and found no big difference between the groups. Another limitation is the lack of self-report about emotional problems from the adolescents. Parents may be at risk of underreporting the adolescents' emotional problems, as these are not as visible as behavioral problems. At the same time, parents are often the best informants about their child´s behavioral problems. Finally, the use of self-reports over short periods will not capture changes within the individuals over time, thus our participants may not have had sleep problems during the three years before follow-up.

5.4 Conclusion

We found a relationship between sleep difficulties and the burden of comorbid problems in children and adolescents with ADHD. Our results indicate that there should be an increased focus on the assessment of sleep problems and preventive measures among adolescents with ADHD during diagnosis and treatment. Initiating specific treatment options might contribute to less comorbid difficulties in this patient group. Increased knowledge of the subject and changed focus from the start of treatment may contribute to reduced symptoms and better functioning later in life in children and adolescents with ADHD.

6. Conflict of interests

Torunn Stene Nøvik received a speaker´s fee from Medice during the last year. The remaining authors declare that they have no competing interests.

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