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Sleep disturbances and psychiatric symptoms in school-aged children

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ACADEMIC DISSERTATION

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Contents

1. ABBREVIATIONS

ACG	Actigraphy
ADHD	Attention deficit and hyperactivity disorder
ANOVA	Analysis of variance
AS	Asperger syndrome
CBCL	Children’s behaviour checklist
CDI	Children’s depression inventory
CI	Confidence interval
CSRF	Children’s self-report form for sleep disturbances
DSPS	Delayed sleep phase syndrome
EEG	Electroencephalography
fMRI	Functional magnetic resonance imaging
INCL	Infantile neuronal ceroid lipofuscinosis
KSS	Karolinska sleepiness scale
NREM	Non-REM sleep
OR	Odds ratio
OSAS	Obstructive sleep apnoea syndrome
PET	Positron emission tomography
PSG	Polysomnography
RA	Rutter A2
RB	Rutter B2
REM	Rapid eye movement sleep
SD	Standard deviation
SDSC	Sleep disturbance scale for children
SL	Sleep log
SRBD	Sleep-related breathing disorder
TRF	Teacher’s report form
TQ	Teacher’s questionnaire

2. ORIGINAL PUBLICATIONS

This thesis is based on the following original publications referred to in the text by their Roman numerals:

I Paavonen EJ, Aronen ET, Moilanen I, Piha J, Räsänen E, Tamminen T, Almqvist F. Sleep problems of school-aged children: a complementary view. *Acta Paediatrica 2000, 89: 223-228.*

II Paavonen EJ, Almqvist F, Tamminen T, Moilanen I, Piha J, Räsänen E, Aronen ET. Poor sleep and psychiatric symptoms at school: an epidemiological study. *European Child and Adolescent Psychiatry 2002, 11:10-17.*

III Paavonen EJ, Solantaus T, Almqvist F, Aronen ET. Four-year follow-up study of sleep and psychiatric symptoms in preadolescents: relationship of persistent and temporary sleep problems to psychiatric symptoms. *Journal of Developmental and Behavioral Pediatrics 2003, 24: 307-314.*

IV Aronen ET, Paavonen EJ, Fjällberg M, Soininen M, Törrönen J. Sleep and psychiatric symptoms in school-age children. *Journal of the American Academy of Child and Adolescent Psychiatry 2000, 39: 502-508.*

V Paavonen EJ, Nieminen-von Wendt T, Vanhala R, Aronen ET, von Wendt L. Effectiveness of melatonin in the treatment of sleep disturbances in children with Asperger disorder. *Journal of Child and Adolescent Psychopharmacology 2003, 13: 83-95*.

3. INTRODUCTION

Epidemiological studies have shown that approximately one third of all children suffer from sleep problems (Blader et al. 1997; Kahn et al. 1989b; Rona et al. 1998; Simonds et al. 1984). Persistent sleep problems are also common, with the estimated prevalence rates ranging from 17% to 41% (Manni et al. 1997; Pollock 1994; Zuckerman et al. 1987). Finnish children have been reported to sleep less than children elsewhere in Europe (Tynjälä et al. 1993b). In addition, their average sleep duration has decreased in recent years (Tynjälä et al. 2002), suggesting that chronic sleep deprivation has become more frequent. Children's sleep disturbances have been linked with numerous somatic disorders, neurological illnesses and psychiatric disturbances (Ferber et al. 1995). The psychological and psychiatric sequelae of sleep disturbances and sleep deprivation are, however, still largely under debate.

Previous sleep studies have mainly focused on different clinical populations, while normative samples and population-based studies are rare. These studies have used different methodologies and definitions and have therefore yielded partly contradictory results. The relationship between sleep quality and psychiatric symptoms has not been studied extensively in children. The main objectives of the present study were to assess the prevalence of sleeping difficulties among school-aged children and to determine whether children with poor sleep quality have more psychiatric symptoms than those without sleep complaints. The effectiveness of melatonin to treat persistent sleeping difficulties in a sample of patients with Asperger syndrome was also evaluated.

4. REVIEW OF THE LITERATURE

4.1 What is sleep?

According to one definition, sleep is a readily reversible state of reduced responsiveness to and interaction with the environment (Bear et al. 2001). Although the function of sleep has always fascinated scientists, the basic question of why we sleep remains unanswered. Researchers are unanimous that while many bodily functions can recover during wakefulness only sleep seems to restitute cortical functions because during wakefulness the cortex always preserves a certain level of baseline activity (Horne 2000a). From a neurophysiological point of view, sleep is a specific state of brain alertness. It comprises two components: REM (rapid eye movement) sleep and non-REM sleep (NREM, also called slow wave sleep). While cortical activity is rather intense during the REM stage, slow wave sleep is characterized by diminished activity levels with large-amplitude, low-frequency electroencephalography (EEG) oscillations (Bear et al. 2001). According to alternations in the sleep EEG, slow wave sleep is further divided into four stages (S1-S4), moving in an ascending direction towards more synchronized cortical activity. The deepest two stages (S3-S4) are considered to constitute refreshing quiet sleep. During the night the five sleep stages alternate systematically (wakefulness > S1 > S2 > S3 > S4 > REM). One complete sleep cycle lasts approximately 90 minutes in adults, but in children, and particularly in infants, the periodicity is much shorter (Bear et al. 2001). Also the sleep architecture in infancy and early childhood differs from that in older children and adults, especially with regard to the amount of REM sleep: the younger the child, the higher the proportion of REM sleep (Anders et al. 1995).

4.2 Development of sleep structure in children

A newborn's sleep is fragmented and distributed evenly throughout the day and night. Adaptation to the 24-hour diurnal rhythm is a gradual process regulated largely by the maturation of the neural network (Handford et al. 1991). Circadian rhythm is typically not well established until 4 months of age (Armstrong et al. 1994), and this is reflected by the number of regular awakenings requiring parental intervention during the night. Almost one third (30.5%) of children <1 month of age wake up more than three times a night. Although the sleep gradually consolidates, nocturnal awakenings continue to be common even after the age of 3 months: 22% of 8-month-olds were reported to wake up every night and 10% more than three times a night (Zuckerman et al. 1987). As summarized in Table 1, approximately 50% of children continue awakening more than once a night at least until 2 years of age (Armstrong et al. 1994).

Table 1. Average frequency of nocturnal awakenings in children aged under 24 months.

Age	no awakenings	1-2 awakenings	>3 awakenings
<1 month	6.5%	63.0%	30.5%
1-3 months	33.3%	59.7%	7.0%
4-24 months	43.7%	44.6%	11.6%

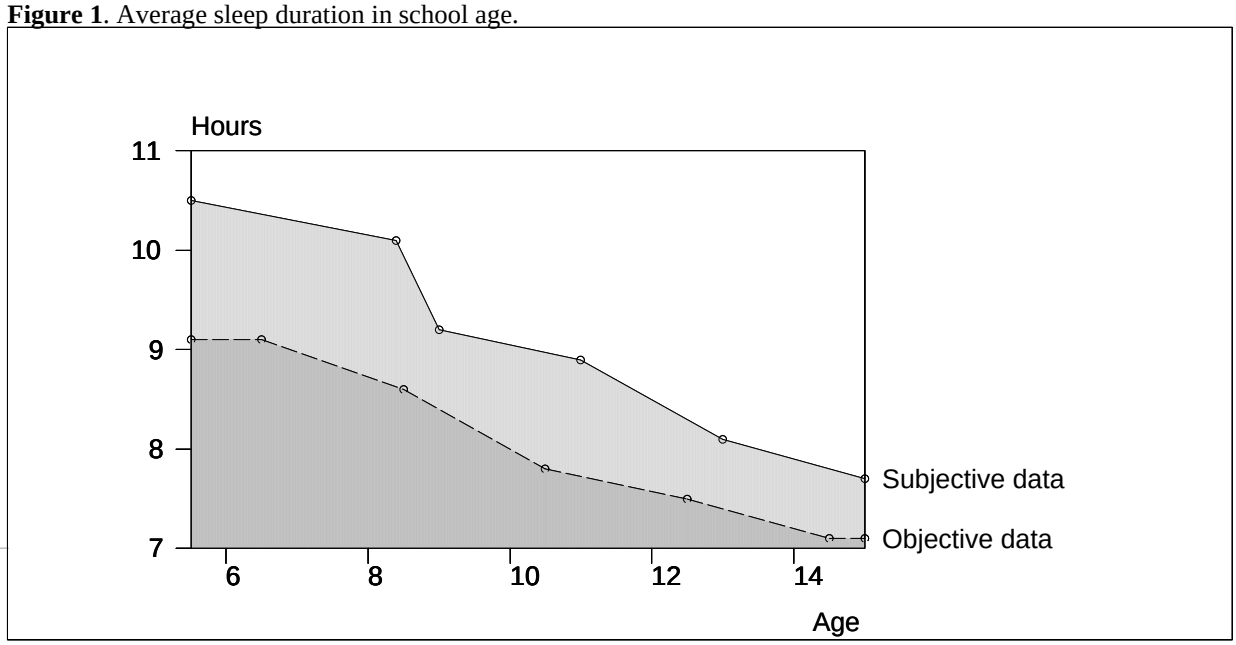
Adapted from Armstrong et al. (1994).

Sleep architecture changes as a function of age (Roffwarg et al. 1966). In newborns, the NREM and REM states are immature. The equivalent of NREM in neonates is “quiet sleep”, REM is “active sleep” and a mixture of these is “indeterminate sleep” (Stores 2001b). However, whether active sleep represents a precursor of REM or NREM is controversial (Horne 2000b). In any case, REM is particularly common in infants (<3 months), who spend as much as 50% of sleep time in REM (Roffwarg et al. 1966). Thereafter, the proportions of REM and indeterminate sleep begin to diminish (Anders et al. 1995), falling to a level of 20% by the age of 6 years and then remaining stable (Coble et al. 1984a; Roffwarg et al. 1966). The decreasing sleep duration in preadolescence therefore reflects a smaller amount of NREM stage IV sleep (Coble et al. 1984a).

A newborn may sleep as much as 16-18 hours a day (Stores 2001b), but diurnal sleep duration decreases rapidly during the first months of life, falling to approximately 13 hours at the age of 6 months and 12 hours at 2 years, as measured by PSG (Roffwarg et al. 1966). Monophasic sleep has usually developed by the age of 3- to 5 years, when the total sleep requirement is approximately 11 hours (Anders et al. 1995; Stores 2001b). Parent-estimated sleep duration of 5- to 6-year-olds is on average 10 h 30 min ± 50 min (Smedje et al. 1998;1999), which is almost 1.5 hours more than estimated by polysomnography (PSG); 6- to 7-year-old children were reported to sleep 9 h 6 min ± 54 min daily (Coble et al. 1984a). Sleeping habits of 5- to 6-year-olds are still relatively immature. For example, co-sleeping and bedtime resistance are common. As many as 64.8% of children are accompanied by someone at sleep onset at least occasionally, and 27.5% nearly every night. Most children (77.4%) sleep in their parents’ bed during part of the night at least occasionally, and 19.9% almost every night. Bedtime resistance appears occasionally in 52.1% of children, weekly in 19.6% and almost every night in 3.2%. Anxiety at bedtime is also common, occurring in 26.3% of children at least occasionally (Smedje et al. 1998).

Sleep duration continues to decrease at school age (Figure 1) (Tynjälä et al. 1993a). In an actigraph (ACG)-based study, 6- to 12-year-olds slept 9 h 5 min ± 34 min on average, but the range was large, from 7 h 20 min to 10 h 12 min (Aronen et al. 2001). This corresponds to the self-reported school-day sleep durations, which were 9 h 14 min among 9-year-olds, 8 h 51 min among 11-year-olds and 8 h 7 min among 13-year-olds (Tynjälä et al. 2002). Sleep requirements reach levels corresponding those of adults in late adolescence; 15- to 18-year-olds reported an average sleep duration of 7 h 54 min ± 1 h 9 min, as compared with the 7 h 26 min ± 1 h 11 min recorded for young adults (19-24 years) (Ohayon et al. 2000). Finnish 15-year-olds reported sleeping 7 h 50 min on school days (Tynjälä et al. 2002). However, based on PSG, the average sleep duration for 14- to 15-year-olds was 7 h 6 min ± 36 min which was almost one hour less than that based on subjective reports (Coble et al. 1984a).

Figure 1. Average sleep duration in school age.



Subjective data are based on Smedje et al. (1999), Saarenpää-Heikkilä et al. (1995) and Tynjälä et al. (2002). Objective data are based on Coble et al. (1984). Most of the exact figures are reported in the text.

Although questionnaire-based studies have often yielded higher mean sleep durations than those gathered from exact ACG or PSG measurements, objectively and subjectively estimated sleep latencies have been similar in all studies: in a PSG study of 6- to 15-year-olds, the mean sleep latency was 20±10 min (Coble et al. 1984a), in an ACG study of 5- to 12-year-olds 19±17 min (Aronen et al. 2001) and in a questionnaire study of 6- to 7-year-olds 19±16 min (Smedje et al. 1999). PSG- and ACG-measured sleep efficiencies have also been quite similar: 94±2% in children aged 6-15 years (Coble et al. 1984a) and 93±4% in children aged 6-12 years (Aronen et al. 2001), respectively.

4.3 Types of sleep disturbances

There are three types of sleep disorders: 1) dyssomnias, 2) parasomnias and 3) secondary sleep disturbances (Stores et al. 2001b). The term dyssomnia refers to problems with amount, maintenance or timing of sleep, or with impaired wakefulness. The parasomnias constitute a group of problems related to arousal, partial arousal or sleep stage transition. These problems can disrupt sleep but usually do not result in excessive sleepiness. The secondary sleep disturbances, on the other hand, are related to underlying psychiatric, neurological or other medical disorders (Kryger et al. 2000). In Finland, two classifications for sleep disorders are available, the ICD-10 and the DSM IV. The sleep diagnoses in the ICD-10 belong to the categories F51 (“Nonorganic sleep disorders”) and G47 (“Organic sleep disorders”). The former category is further divided into dyssomnias and parasomnias. The DSM IV classification is presented in Table 2. No specific criteria exist for children, but the ICD-10 emphasizes that children’s sleeping problems are not necessarily related to sleep quality, rather to parents’ inability to control bed-time.

Table 2. Classification of sleep disturbances according to the DSM IV.

DSM IV	Code
Dyssomnias:	
Primary insomnia	307.42
Primary hypersomnia	307.44
Narcolepsy	347
Sleep-related breathing disorders	780.59
Circadian rhythm disturbance	307.45
Unspecified dyssomnia	307.47
Parasomnias:	
Nightmares	307.47
Sleep terrors	307.46
Sleep walking	307.46
Undefined parasomnia	307.47

The term insomnia refers to an inability to sleep, a lack of refreshing sleep or an impairment in sleep quality. It is thus used to describe a wide range of alternations in the amount and type of sleep loss or perceived sleeplessness, including difficulties in initiating or maintaining sleep as well as non-restorative sleep (Littner et al. 2003a). According to Morin (2000) “insomnia is a complex, heterogeneous condition that can be symptomatic of an underlying medical, psychiatric or substance abuse disorder. Or, it can be a syndrome in itself”. Buysse and Ganguli (2002) in turn emphasized that “insomnia can refer to short sleep duration, secondary sleep disturbances, difficulty falling asleep or experience of unrefreshing sleep”. Therefore, unlike for many other disorders, no exact criteria to define insomnia exist. While subjective perception of the presence of a problem is regarded as the cornerstone of the diagnosis, clinical definitions also maintain that the sleep impairment should cause significant distress or impairment in social, occupational or other central areas of functioning. According to DSM IV, for instance, a sleep disturbance must persist for over three weeks and markedly impair well-being and/or the ability to function. It is worth noting that in the case of young children the term “sleeplessness” is sometimes used interchangeably with “insomnia” because children may not be old enough to complain about lack of sleep (Wiggs et al. 2001).

Hypersomnia refers to an increased need for sleep and is closely related to daytime somnolence (Anders et al. 1997; Vgontzas et al. 1999). Narcolepsy is characterized by excessive sleepiness and a spontaneous tendency to fall asleep throughout the day. The four classical features of narcolepsy include cataplexy, hypnagogic hallucinations, sleepiness and sleep paralysis (Vgontzas et al. 1999). The aetiology of the syndrome seems to be related to low levels of a specific neuropeptide, hypocretin-1 (also called orexin) (Krahn et al. 2001). Among children, it is a rare condition (Dahl et al. 1994). Sleep-related breathing disorders (SRBD) refer to obstructive sleep apnoea syndrome (OSAS) and sleep apnoea, both of which are characterized by repeating episodes of upper airway obstruction, which can cause a reduction in blood oxygen saturation (Anders et al. 1997; Vgontzas et al. 1999). Dissimilar to insomnia, there are well-established PSG-based criteria to define sleep breathing disorders. In adults, OSAS typically presents with snoring and excessive somnolence and is closely related to obesity, but the manifestations in children are different (Kirjavainen et al. 1995; Marcus 2000). The most common circadian rhythm disorder is delayed sleep phase syndrome (DSPS), which is characterized by an inability to fall asleep at an appropriate time (Apter et al. 1999). This in turn leads to sleep deprivation and tiredness if sleep can not be extended in the morning (Vgontzas et al. 1999).

Parasomnias (sleep-wake transition disorders, episodic disturbances of sleep) constitute a group of sleep disorders that represent recurrent episodes of behaviour/physiological changes occurring during different stages of sleep (Partinen et al. 1988). They include sleep starts, sleep paralysis, rhythmic movement disorder and restless leg syndrome (occurring during sleep onset); bruxism, sleepwalking, confusional arousals and sleep terrors (occurring during light NREM); nightmares (occurring during REM), and sleep talking and enuresis (not related to any specific sleep stage) (Stores 2001a).

For children's sleep disturbances, no simple consensus exists on how a sleep problem should be defined or assessed. A clear definition would aid in distinguishing normal variation in sleep quality from clinically significant problems; however two major problems exist: 1) sleeping difficulties include several subcategories, all of which have different aetiologies but potentially similar consequences and 2) boundaries between normality and pathology are vague in many of the categories. The lack of consensus on a definition for sleep disorder has been a marked disadvantage in paediatric sleep research and has likely resulted in investigators applying their own criteria (Table 3). Although quantifying insomnia, for instance, can be considered arbitrary, only explicit definitions enable reasonable comparisons of results gathered in different studies. The lack of exact definitions can also lead to misclassification bias. For example, some of the parent-reported difficulties may represent sleep-related behavioural problems, such as bedtime resistance, which is not necessarily a sign of insomnia. Making a distinction between a sleep problem/sleep complaint and the cause of the problem, the sleep disorder, is important (Stores et al. 2001b), but many of the previous studies on children's sleeping difficulties have simply focused the symptoms.

Table 3. Definitions of children's sleep disturbances.

Reference	n	Age	Inf	Method	Criteria	Prevalence
Archbold et al. (2002)	1038	2-14	P	PSQ	Significant IS: >2/4 IS symptoms (yes/no)	18% significant IS 41% any IS
Blader et al. (1997)	987	5-12	P	Quest	Depends on symptom frequency: bedtime resistance, SOP >3/week	27% bedtime resistance 11.3% SOP
Camhi et al. (2001)	452	3-14	P	Quest	Current problem with falling asleep, staying asleep or waking too early	16.8 %
Johnson et al. (2000)	822	6,11	P	CBCL, TRF	SP sometimes or often	6.4% at age 6 8.8% at age 11
Kahn et al. (1987)	972	8-10	P	Quest	Poor sleep: sleep latency >30 min & >1 awakening >2 times a week; other SPs not defined	14% Poor sleep 43% Any SP
Liu et al. (2000)	2004	6-12	P	CBCL	SP sometimes or often	6.1% trouble sleeping 14.0% too little sleep 43.8% any SP
Morrison et al. (1992)	943	15	C	Int	>1 SP at least 4 times/week	33.4% SP
Owens et al. (2001)	494	4-11	P	CSHQ	Whether or not the SP represents a problem	37.0% any SP 15.1% bedtime resistance
Ohayon et al. (2000)	3294	15-21	C	Phone int	DSM IV criteria, not defined exactly	4% insomnia 25% some symptoms
Pollock (1994)	13135	5,10	P	Rutter A	Any sleeping difficulty (no/mild/severe)	22.1% mild 1.4 % severe
Rona et al. (1998)	14372	5-11	P	Quest	Disturbed sleep at night: cries and needs attention	1.8 % >1/week 6.4% <1/week
Simonds et al. (1982)	309	5-18	P	Quest	SP >1 time/week	27.6% restless sleep
Zuckerman et al. (1987)	308	0.7,3	P	Semistr int, BSQ	8 mo: sleep onset > 1 h or waking up >3/times a night or any problem severely disturbing mother's sleep; 3 yrs: sleep onset >1 h or waking at night >3/ week	18% at age 8 months 29% at age 3 years

BSQ Behavioural Screening Questionnaire, C Child, Inf Informant, Int Interview, IS insomnia, CSHQ Children's Sleep Habits Questionnaire, CBCL Children's Behaviour Checklist, DIMS Disorders of initiating and maintaining sleep, P Parent, PSQ Parent Sleep Questionnaire, Semistr int Semistructured interview, SOP Sleep onset problems, SP Sleep Problem, TRF Teacher's Report Form.

In clinical settings where detailed interviews and various screening methods are readily available this may not be a significant problem, but for research purposes well-established criteria should be developed. Forthcoming studies should therefore aim at thorough and consistent description of the methodologies and criteria used. Despite the need for explicit criteria for "pathological sleep disturbance", sleep should not viewed as a biological phenomenon only. While the biological representatives of sleep are always objectively measurable, the quality of sleep may not. For the individual with a sleep disturbance, the problem may be relevant regardless of whether or not objective findings are made. As a consequence, PSG, for example, is not recommended for routine evaluation of insomnia (Littner et al. 2003a).

4.4 Aetiology of sleep disturbances

Since the alternation of sleep-wake states is a complex neuronal process, many internal and external factors can interfere, impairing sleep quality. In fact, any factor that activates the ascending reticular activating system leads to an increased arousal level and a decreased propensity to fall asleep. Various environmental factors have been reported to affect sleep quality in children. These include noise and household over-crowding (Liu et al. 2000), and the use of drugs and stimulants (Mick et al. 2000), or alcohol (Tynjälä et al. 1999). Moreover, temporary infections (Camhi et al. 2000) and chronic physical illness can impair sleep (Liu et al. 2000). Examples include for example asthma (Camhi et al. 2000; Diette et al. 2000; Stores et al. 1998a), allergies, atopic dermatitis (Dahl et al. 1995; Kahn et al. 1987; 1989a) and migraine (Bruni et al. 1997; 1999).

Certain behaviours and habits are also related to sleep disturbances. For example, high quantities of TV viewing and TV viewing at bedtime, have adverse effects on sleep (Owens et al. 1999). Moreover, bedtime resistance (Blader et al. 1997; Smedje et al. 1998) and co-sleeping (Latz et al. 1999; Lozoff et al. 1984; 1996; Madansky et al. 1990) have been correlated with sleep onset problems. Of 5- to 6-year-olds, 91.4% of night-wakers were reported to move to their parents' bed at night >3 times/week, while only 17.6% of other children did so (Smedje et al. 1998). Although some authors have cited co-sleeping as the cause of sleeping problems (Madansky et al. 1990), findings in cross-sectional studies do not necessarily imply causality. Co-sleeping may be a consequence of a waking problem (Lozoff 1995).

Among children, social interaction and temperament characteristics may play a stronger role in the establishment of sleep quality than among adults. Infant temperament has been associated with the propensity to display sleeping problems (Scher et al. 1992). In 5-year-old children, an emotional personality type was associated with sleep disturbances (Owens-Stively et al. 1997), and persistent sleep problems were associated with temper tantrums and maternal ratings of "hard to manage" (Zuckerman et al. 1987). In adolescents, neuroticism has been found to be closely related to the propensity for disrupted sleep (Gau 2000), whereas good self-perception was related to higher sleep quality (Tynjälä et al. 1999). Fears (Blader et al. 1997) and emotional stress (Verlander et al. 1999) have also been linked to sleep disturbances.

Children's sleep quality can also be affected by problems in child-parent interaction. All children with sleep disturbances and 57% of others were reported to have insecure maternal attachments (Benoit et al. 1992). Moreover, maternal anger regarding an infant's demands and doubts about parenting were correlated with infant sleep disturbances (Morrell 1999). In adolescence, sleep disturbances have been found to be associated with poor parental and peer relations (Liu et al. 2000), as well as with poor home atmosphere (Tynjälä et al. 1999). Strictness and physical punishment were also closely linked to sleeping difficulties (Liu et al. 2000), while laxness in parenting and ineffective limit setting were not related to increased frequency of behavioural sleep disturbances (Owens-Stively et al. 1997).

Finally, maternal psychiatric morbidity has been associated with children's sleep disturbances. Maternal depression (Armstrong et al. 1998; Johnson et al. 2000; Zuckerman et al. 1987) and mothers' affective problems (Stoleru et al. 1997) are reported to increase children's sleep

disturbances. Moreover, persistent sleep problems were closely related to maternal affective illness (Stoleru et al. 1997; Zuckerman et al. 1987).

4.5 Methods to measure sleep quality

Two objective research methods are available for studying sleep: polysomnography (PSG) and actigraphy (ACG). The former is based on EEG recordings, while the latter utilizes information about motor activity. Hence, while PSG provides detailed information of the alternations of sleep-wake states and the five sleep stages, ACG can only give an estimate of sleep quality (American Sleep Disorders Association 1995b). PSG is therefore considered the gold standard of sleep research. PSG recordings are usually done in a sleep laboratory. In addition to the EEG measurements, electro-oculogram, electromyogram and ECG recordings are obtained (Himanen et al. 2001). The data is handled in small epochs and usually scored according to Rechtschaffen-Kales criteria (Rechtschaffen et al. 1968). Complete information collected though the night is compressed into parameters describing sleep quality. The most common indication for PSG is a clinical suspicion of a sleep breathing disorder (Chesson et al. 1997). Due to the nature and amount of information collected, PSG requires extensive resources and the scoring of one full night's data takes several hours.

Polysomnography as a diagnostic instrument in epidemiological studies of children's sleep disturbances has some shortcomings. First, the instrumentation required makes PSG impractical or infeasible in epidemiological research. Second, as PSG scoring is dependent on subjective rating of EEG registration, inter-informant discrepancy can be a problem (Collop 2002). Third, PSG recordings usually require a stay in the sleep laboratory, which can alter sleep quality. Indeed, this change in sleeping environment has been described to disturb normal sleeping habits (often called as "first night effect") of adults (Reynolds et al. 1992; Riedel et al. 1998) as well as children, particularly young children (Coble et al. 1984a). Moreover, some children can experience the instrumentation and the stay in a sleep laboratory as stressful (Anders et al. 1995), and may be completely unable to comply with the procedure. Some people with insomnia can paradoxically sleep better in the sleep lab than at home (Littner et al. 2003a). As a result, a proportion of sleep problems may go undetected in the sleep lab. In fact, according to a recent consensus statement, PSG is indicated only for evaluation of selected sleep disorders (Chesson et al. 1997).

The use of actigraphs is based on the finding that sleep-wake states can be derived relatively well from variation in motor activity levels (Littner et al. 2003b). Motor activity diminishes when a subject falls asleep and increases again on arousal. An actigraph is a small wrist-worn (or waist-worn) device that registers and stores data on motor activity. It counts hits of accelerations greater than 0.1 g in preset time intervals, usually in one-minute epochs. Different variables describing sleep quality (such as mean diurnal activity, mean nocturnal activity, sleep duration, sleep efficiency and sleep latency) can be calculated from the diurnal variation of activity. Although sleep stages can not be differentiated using motor activity data, ACG data and PSG recordings are otherwise reported to correlate very well in healthy controls (de Souza et al. 2003). The minute-by-minute agreement between EEG and actigraphs scores is reported to be 91.2% in adolescents and 89.9% in children (Sadeh et al. 1989). In healthy adults, ACG data combined with subjective reports seem to generally correlate well with PSG findings (Kushida et al. 2001; Lockley et al. 1999). A consensus report has therefore concluded

that sleep quality can be adequately estimated using actigraphs, especially when combined with subjective data (American Sleep Disorders Association 1995a; Sadeh et al. 1995a).

Some methodological issues concerning the use of actigraphs deserve comment. First, its sensitivity in detecting wakefulness is rather low, making it less reliable for detecting disturbed sleep (Littner et al. 2003b). Some subjects with sleep onset problems can lie quietly in bed for long periods and can be falsely registered as being asleep by actigraphs. ACG consistently overestimated sleep quality in adults with sleep onset problems (Kushida et al. 2001). Nocturnal movements can also be misinterpreted as wakefulness (Lockley et al. 1999), leading to an underestimation of sleep quality (de Souza et al. 2003). The accuracy of ACG (defined as the correlation between ACG and PSG ratings) appears to be lower in sleep disordered patients than in healthy controls (Sadeh et al. 1995a). In fact, ACG is not indicated for routine diagnosis of any sleep disorder (Littner et al. 2003b). Second, some inconsistent inter-individual differences between the correspondence of PSG and ACG can exist both among children (Sadeh et al. 1995a) and among adults (Lockley et al. 1999). Third, the question of how many registration nights are needed to get reliable sleep estimates is controversial. Although a recent review of practice parameters concluded that three would be the minimum (Littner et al. 2003b), one study of children suggested that as many as five nights might be necessary (Acebo et al. 1999). Due to these limitations, ACG can only give an estimate of sleep quality. Despite this, the simple use of the device has made actigraphs popular in sleep research, especially in situations where PSG is not feasible.

The third way to assess sleep quality and quantity is to use subjective estimates: questionnaires or interviews. In epidemiological studies, this is often the only reasonable alternative. While questionnaires are easy to develop and analyse, this is simultaneously their disadvantage; their validity and reliability are often poorly characterized. Subjective sleep estimates may be considered too inaccurate and unspecific for research purposes, as compared with objective methods. This problem can be countered using standardized questionnaires. Several sleep questionnaires aimed for completion by parents have been reported and validated, including the Children's Sleep Behaviour Scale (Fisher et al. 1989), the Children's Sleep Disturbance Scale (Bruni et al. 1996), the Paediatric Sleep Questionnaire (Chervin et al. 2000) and the Children's Sleep Habits Questionnaire (Owens et al. 2000b). However, none of these questionnaires has been validated against PSG or ACG. Several authors have used either their own, non-validated questionnaires (Blader et al. 1997; Kahn et al. 1989b; Smedje et al. 1998), or other standardized questionnaires that include some sleep items, such as the Children's Behaviour Checklist (Johnson et al. 2000; Liu et al. 2000), Rutter A (Pollock 1994) or an undefined questionnaire (Rona et al. 1998). Only one questionnaire has been designed to be filled out by children themselves (Owens et al. 2000c).

A disadvantage in using parental reports for studying children's sleep problems is that parents may not be aware of their child's sleep quality. While this problem is acknowledged by most authors (Smedje et al. 1998; Stoleru et al. 1997), comparisons of reports of sleep quality provided by parents and children have been rare. Parent's observations of OSAS were found to be neither sensitive nor specific in predicting the severity of obstructive sleep apnoea in children (Preutthipan et al. 2000). Children's self-reports did, however, correlate better than parental reports with objective sleep measures and teacher's reports (Aronen et al. 1996; Owens et al. 2000c). Mothers' (with affective disorders) ratings of children's sleep problems were not correlated with any psychiatric symptoms, while children's own ratings of sleep disturbances were associated with both anxiety and mood problems (Stoleru et al. 1997).

In child psychiatry, many investigations have shown that children and parents often disagree especially about issues that are abstract or ambiguous, such as internalizing symptoms (Barrett et al. 1991; Bird et al. 1992; Grills et al. 2003; Ivens et al. 1988; Puura et al. 1998). To aid child psychiatric diagnostics, multi-informant approach has recently been emphasized (Jensen et al. 1999). This approach is considered to decrease false-negative responses and to enable in more reliable data on the presence of various symptoms to be obtained (Grills et al. 2003). This might also be true in the case of sleep disturbances.

However, when informants disagree, scoring may constitute a significant problem (Grills et al. 2003). In the case of sleep problems, this problem is likely to be very relevant because not only the two informants but also subjective and objective measurements can be discrepant (Littner et al. 2003a; Rosa et al. 2000; Seidel et al. 1984). In fact, subjective perception of insomnia can be independent of objective findings (Rosa et al. 2000). Moreover, patients with chronic insomnia had similar daytime sleep tendency to those without sleep complaints, and better sleep quality associated paradoxically with greater daytime sleep tendency. Only the personality profile of subjects with insomnia was more deviant than that of normal controls (Seidel et al. 1984).

If a multi-informant approach is selected, it should be accompanied by an explicit algorithm for combining information across the methods to guarantee comparability of results gathered in different studies. Basically, there are four alternatives to approach this problem: 1) Keeping the results separate is often the easiest alternative, but the most relevant information (the actual prevalence of the problem) may be missed. 2) Simple aggregation of all positive test results is based on ignorance of discrepancies; the symptom is considered to be present when it is reported by either informant. The main problem with this approach is the high number of false-positive reports. 3) Inclusion of only consistent information leads to a marked decrease in the false-positive rate. Clearly, the specificity (true negative rate) increases, but at the cost of diminished sensitivity (true positive rate). 4) Selection of a primary informant (Loeber et al. 1989) resembles the first alternative, but the criteria for the selection can be difficult to set. While comparisons with objective methods would be useful, they have rarely been made. (Bird et al. 1992; Loeber et al. 1989)

4.6 Prevalence of sleep problems

Sleep disturbances are among the most common complaints throughout childhood. According to clinical paediatricians they are the fifth leading concern of parents, following illness, feeding, behavioural problems and physical abnormalities (Mindell et al. 1994). Different sleep problems are characteristic of different ages, but sleeplessness seems to be the most common sleep disorder at all ages (Wiggs et al. 2001). Toddlers typically display behavioural sleep disturbances, whereas by school age, different forms of insomnia, such as prolonged sleep latency, night waking and early-morning waking, predominate (Blader et al. 1997; Kahn et al. 1989b).

Estimates of the prevalence of different sleep problems have varied largely, particularly with regard to school-aged children, ranging from 1% to 42% (Blader et al. 1997; Kahn et al. 1989b; Rona et al. 1998; Simonds et al. 1984; Smedje et al. 1999). As mentioned earlier, these studies

have had little agreement on how to define sleep disturbance (Table 3). Studies without explicit definitions appear to yield higher estimates of prevalence than those with precise criteria. It is, indeed, likely that wide ranges in the prevalence rates reflect methodological differences as well as different cultural perceptions of sleep disturbances rather than true differences in prevalence. A significant limitation of all of these studies is that they have been based on parental reports alone.

The highest prevalence rates reported for insomnia and parasomnia have been 41% and 38%, respectively, whereas sleep-disordered breathing (11%) and daytime sleepiness (14%) appeared less often (n=1038, 2-14 years) (Archbold et al. 2002). Another study found bedtime resistance to be the most common sleep disturbance (27%), while sleep onset problems (11%) and nocturnal awakenings (7%) were more infrequent (n=987, 5-12 years) (Blader et al. 1997). Of 5-year-olds, 22% were reported to have a sleep disturbance, which in 1% was characterized as severe (n=13135) (Pollock 1994). In a Swedish sample, 26.9% of 5- to 6-year-old children had sleep onset difficulties, night waking or breathing disturbances (Smedje et al. 1998). A larger sample of 5- to 7-year-olds revealed lower rates: difficulty falling asleep >3 times a week in 5.6%, night waking in 15.5%, snoring in 7.5% and nightmares at least 1-2 times a week in 3.1% (Smedje et al. 1999).

Much lower prevalence rates have also been found; according to one study, disorders of initiating and maintaining sleep affected 17% of children (n=452, 3-14 years) (Camhi et al. 2000), while another reported that 14% displayed sleep walking, 14% got too little sleep, 13% slept too much, 12% had nightmares, 6% had trouble sleeping and 4% had enuresis (n=2004, 6-12 years) (Liu et al. 2000). Sleeping difficulties were reported to affect 6% of 6-year-olds and 9% of 11-year-olds (Johnson et al. 2000). The lowest frequencies reported for a sleep problem occurring at least once a week are 4% for 5-year-olds and 1% for 9-year-olds (Rona et al. 1998).

Sleep disturbances remain common during adolescence. One third of teenagers reported having at least one sleep problem more often than four times a week; no differences in prevalence were seen between the genders (n=943, 15 years). The most common types of problems were difficulties in falling asleep (10%) and staying asleep (2%), early awakening (3%) and the need for more sleep (25%) (Morrison et al. 1992). However, a DSM-IV diagnosis of insomnia was made for only 4% of adolescents, slightly more often for women than for men. At least one insomnia symptom (non-restorative sleep, difficulties in initiating sleep, early morning awakenings) was reported by one third of adolescents and daytime sleepiness by 20% (Ohayon et al. 2000).

The few longitudinal studies that have been conducted on children’s sleep disturbances indicate that these problems are often persistent. For instance, 41% of children with a sleep problem at the age of 8 months still had a problem at 3 years (Zuckerman et al. 1987). Correspondingly, 48.5% of those with any kind of sleep problem at age 13 continued to have difficulties at age 15 (Morrison et al. 1992). Studies on preadolescents have, however, yielded conflicting results. While one study reported that a sleep problem at 5 years of age doubled the risk for a problem at the age of 10 (Pollock 1994), another could not establish any connection between the ages of 4 and 16 years (Klackenberg 1982). Persistent sleep disturbances are often considered more deleterious to development and well-being than transient problems, but this hypothesis remains to be proven. Longitudinal studies might also enlighten the causal relationships underlying sleep problems and co-existing psychiatric symptoms.

Approximately 30% of Finnish adolescents (11-15 years) had sleep onset problems at least once a week and 5% almost daily. Nearly 20% reported nocturnal awakenings more often than once a week (Tynjälä et al. 1999). Only 40% of 7- to 12-year-olds went to sleep before 23:00 every night of the week, and 15% of children stayed awake until 01:00 during weekends. Moreover, children were commonly alone at home at bedtimes: less than half of the children never went to bed without parents (parents not at home), and almost 20% of children went to bed without parents more than four times a week (Järventie 1999).

4.7 Sleep disturbances and well-being

Sleep quality is closely related to well-being (Härmä et al. 2000). Children's sleep disturbances often accompany various somatic illnesses as well as psychiatric and neurological disturbances (Ferber et al. 1995; Stores et al. 2001a). Poor sleep can also have a negative impact on mood (Poelstra 1984) and behaviour (Dahl et al. 1990a), and latent sleep disorders can in some cases manifest as psychiatric symptoms (Reite 1998). In adults, daytime sleepiness is related to impairments in work and social life and increased psychiatric disorders and risks for motor vehicle accidents (Ohayon et al. 1997). Although sleep disturbances and sleep deprivation can affect well-being in many ways, they are two separate concepts, both of which are individually associated with adverse daytime symptoms. While some sleep problems can lead to sleep deprivation, sleep deprivation can also be unrelated to the presence of sleep disturbances, especially in children. Inadequate bedtimes are one evident cause of sleep debt.

4.7.1 Effects of sleep deprivation

Among both adults and children, sleep deprivation is a widespread problem, which can have numerous negative consequences (Dement et al. 1993). Experimental studies on sleep deprivation in humans have described both the functions of sleep as well as the effects of sleep debt. As reviewed by Lamberg, these studies have roots in the year 1896, when researchers kept subjects awake for 90 hours, and found decreases in sensory acuity, reaction time, motor speed and memory (Lamberg 1996). Sleep deprivation affects primarily cerebral cortical functions (Horne 1985). Changes in brain activity in response to sleep deprivation have been registered using for example fMRI (Drummond et al. 1999) and PET (Wu et al. 1991). Changes in gene transcriptional activity in neuronal systems that control vigilance and sleep are known to contribute to the effects of sleep deprivation (Toppila et al. 1999), leading to reduction in arousal, which in turn can affect many aspects of behaviour (Bear et al. 2001). Mood alterations, impaired cognitive and motor performance and hormonal changes are possible sequelae of sleep deprivation (Horne 2000a).

Contrary to the assumption that "sleep is for the brain, not for the rest of the body", evidence has accumulated that sleep deprivation affects several physiological functions and the immune system (Horne 1988). Hormonal changes mimicking those typical of aging can result from sleep deprivation (Spiegel et al. 1999; Van Cauter et al. 2000; VanHelder et al. 1989). When sleep was restricted to 4 hours a night for a period of six nights, clear impairment in carbohydrate tolerance (decreased insulin response to glucose), increased sympathetic tone, decreased thyrotropin levels and increased cortisol secretions were observed (Spiegel et al.

1999). Sleep deprivation can also affect the cardiovascular system and blood pressure (Kato et al. 2000) as well as vigilance and reaction time (Gillberg et al. 1994). As a consequence, the risk for vehicle and work accidents increases (Ohayon et al. 1997). Up to 20% of all car accidents are estimated to be due to sleepiness (Horne et al. 1999). In contrast, 72-hour total sleep deprivation did not alter physical performance measured by a bicycle ergometer (Horne et al. 1984).

Even moderate partial sleep restriction impairs cognitive performance in healthy adults (Van Dongen et al. 2003), particularly affecting concentration, verbal learning and memory. For example, arithmetic performance, as measured by a serial subtraction test, was impaired by sleep deprivation and accompanied by decreased neuronal activity in the prefrontal cortex and parietal lobe areas on fMRI (Drummond et al. 1999). Moreover, one night's complete sleep deprivation deteriorated verbal learning and decreased activity in the temporal lobes. Simultaneous increase in activity in the parietal lobes was, however, associated with better performance (Drummond et al. 2000).

A relationship exists between memory, especially memory consolidation and sleep (Sejnowski et al. 2000). In one study, sleep loss also affected temporary memory (recency discrimination task) but not recognition (distinction between new and previously presented faces) (Harrison et al. 2000b). Moreover, 3 hours of "early sleep" dominated by NREM has been shown to improved performance in visual discrimination tasks, while "late sleep" had no such effect (Gais et al. 2000). Similarly, visual discrimination was found to improve on retest when individuals were allowed to sleep at least one complete night between testing occasions. However, individuals sleep-deprived after the first test occasion and then allowed to sleep as much as they wished showed no improvement (Stickgold et al. 2000).

As regards cognitive performance, sleep deprivation can at first be rather well tolerated among adults (Horne 1988). There is some evidence that long, tedious cognitive tasks with a low load are most sensitive to sleep deprivation (Horne 2000a), while motivating tasks or use of stimulants, such as caffeine, can mask the sleepiness (Horne 1988). Complex, rule-based convergent and logical tasks are often unaffected by short-term sleep deprivation but decision-making concerning something unexpected or novel can still be impaired (Harrison et al. 2000a). In addition to sleep duration, sleep continuity is important for alertness. Sleep fragmentation can have adverse effects similar to those of sleep deprivation, including decrements in psychomotor performance, cognitive function and mood (Stepanski 2002). Performance on simple mathematical tasks has been shown to be dependent on the number of sleep disruptions per night (Bonnet 1985; Downey et al. 1987).

Sleep loss also has deleterious effects on psychological well-being. The most predictable consequence of sleep deprivation is sleepiness, which can be considered a physiological reaction. Daytime sleepiness in adults affects deleteriously work and social life and has negative socio-economic impact (Ohayon et al. 1997). Approximately 20% Finnish children reported daytime sleepiness. Sleep disorders, irregular sleeping habits, somatic illness and depression were most predictive of daytime sleepiness, whereas the influence of life habits was smaller that was expected (Saarenpaa-Heikkila et al. 2000).

Cumulative partial sleep deprivation (experimental reduction of total sleep time by 33% to an average of 5 hours/night) has been reported to induce fatigue, confusion and tension and to increase scores of total mood disturbance, sleepiness, mood alternations (tension-anxiety,

bewilderment-confusion and vigour) and performance deficits, which continued beyond the restriction period of 7 days (Dinges et al. 1997). Mood is also often affected by poor sleep (Poelstra 1984). In children, feelings of anxiety and depression are more common in those who sleep less as compared with those with longer sleep durations (Sadeh et al. 1995b; Wolfson et al. 1998). Importantly, treatment of obstructive sleep apnoea can result in significant improvements in psychological and cognitive measures (Ali et al. 1996; Engleman et al. 2000; Lewin et al. 2002), suggesting a causal relationship between the daytime symptoms and the underlying sleep disorder.

Very few experimental sleep deprivation studies have been conducted among children. Two such studies aimed at detecting cognitive sequelae of sleep deprivation. The first showed that one night's complete sleep loss had similar effects in children (aged 11-14 years) to those previously shown in adults (Carskadon et al. 1981). Later partial sleep restriction was found to lead to impaired cognitive functions in verbal creativity, abstract thinking and concept formation. Routine performance (e.g. mean scores in visual, verbal and learning tasks), on the other hand, was maintained even after one full night's sleep restriction (Randazzo et al. 1998). Recently, shorter sleep duration has been demonstrated to be related to poorer performance on short-term memory tasks (Steenari et al. 2003).

Some children's studies indirectly suggest that both sleep deprivation and sleeping problems are associated with poorer academic performance. The less children sleep, the lower their school performance (Wolfson et al. 1998). Sleep-disordered breathing and snoring have also been related to inferior academic performance (Gozal 1998; Gozal et al. 2001). Moreover, some evidence indicates that untreated OSAS can lead to permanent neuropsychological deficits (Gozal et al. 2001). The developing brain may thus be especially vulnerable to the deleterious effects of sleep deprivation.

4.7.2 Somatic illness and sleep

A considerable proportion of children with disturbed sleep have medical conditions that can predispose to sleep disruption. Sleep disturbances at age 10 were mainly correlated with somatic symptoms (Pollock 1994). Somatic conditions associated with disturbed sleep include such infections as acute respiratory illness (Camhi et al. 2000), nocturnal hypoglycaemic episodes (Matyka et al. 2000), perception of pain and chronic pain syndrome (Lewin et al. 1999) and enuresis (Liu et al. 2000). Atopic diseases, such as cow's milk allergy (Kahn et al. 1987), and atopic skin disorders (Dahl et al. 1995) have been linked with sleep impairment in children. The authors speculated that metabolic changes or the physical discomfort caused by the intolerance might explain the relationship. Asthma has also been associated with sleep disturbance, an increase in psychological symptoms and a decrease in school performance (Camhi et al. 2000; Diette et al. 2000; Stores et al. 1998a), although contradictory findings have also been reported (Tirosh et al. 1993). However, this latter study concerned very young children (aged 4-48 months) and was based only on parental perception of nocturnal awakenings, which is a significant limitation.

4.7.3 Neuropsychiatric disorders and sleep

Several neurological disorders are associated with sleep disturbances (Zucconi et al. 2001). Such a link exists between sleep and attention deficit and hyperactivity disorder (ADHD) (Chervin et al. 1997; 2002a; Dagan et al. 1997; Marcotte et al. 1998; Stein 1999), autism (Diomedi et al. 1999; Elia et al. 2000; Hering et al. 1999; Patzold et al. 1998; Richdale 1999; Schreck et al. 2000; Taira et al. 1998), Asperger syndrome (Patzold et al. 1998), Tourette's syndrome (Dahl et al. 1990a), neuronal ceroid lipofuscinoses (Kirveskari et al. 2000), epilepsy (Stores et al. 1998c) and learning and/or motor disabilities (Jan et al. 1996). Epilepsy increases the risk for sleep disorders but also constitutes an important differential diagnostic alternative (Stores 2001c). Sleep disturbances in these syndromes are likely to have a multifactorial origin.

ADHD is a common neuropsychiatric disorder in which sleep disturbance frequently occur. Several questionnaire-based studies have reported increased rates of various sleep problems among children with ADHD (Chervin et al. 1997; Marcotte et al. 1998; Owens et al. 2000a; Stein 1999). ADHD patients also display more instability in their sleeping patterns than healthy children (Gruber et al. 2000). However, a recent questionnaire study reported that ADHD-related dyssomnias were actually more highly correlated with various confounding factors, while differences in sleep quality were inconsistently related to ADHD status (Corkum et al. 1999). Similarly, in another study, no significant associations between ADHD and sleep disturbances were found after controlling for co-morbidity (Mick et al. 2000). Nevertheless, both of these studies were based on parental sleep questionnaires, which may have biased the results. Findings of the few sleep studies using objective screening methods have been conflicting. One study found that ADHD patients had no greater sleeping difficulties based on a parental questionnaire than controls, but had significantly more ACG-registered sleep impairments (Dagan et al. 1997). A PSG-based study, by contrast, found no differences in sleep architecture between ADHD subjects and controls (Lecendreux et al. 2000).

Traditionally, the behavioural disorder has been thought to evoke the sleeping and settling problems, but suggestions have also emerged that the behavioural symptoms might actually be a consequence of an unrecognized sleep disorder. This is because the core symptoms of the disorder (inattention, hyperactivity) are also well-known sequelae of sleep deprivation in children. For example, almost one third of children with snoring or OSAS are hyperactive and inattentive, conditions which are ameliorated by adequate treatment of the sleep disorder (Ali et al. 1996; Engleman et al. 2000; Lewin et al. 2002). Children with certain parasomnias also tend to have problems with overactivity and concentration (Chervin et al. 2002b). Even in normative samples, sleep problems are significantly correlated with hyperactivity (Liu et al. 2000). Recent studies have shown that a significant number of ADHD children have OSAS (Chervin et al. 1997; 2002b), and up to 80% of ADHD children with habitual snoring (approximately one fourth of all children with ADHD) were estimated to benefit significantly from adequate treatment of the co-existing sleep disorder (Chervin et al. 1997). However, a recent review concluded that because most of the previous studies investigating the connection between sleep and ADHD had notable methodological limitations, thus producing partly contradictory results, the direction of causality is still unclear (Corkum et al. 1998). Whether the sleep problems in ADHD are primary or secondary remains to be determined in further studies.

Autism is a rare developmental disorder characterized by impaired social abilities, language delay and varying degree of psychomotor retardation (Filipek et al. 1999). Up to 65% of autistic children are reported to have sleep disturbances (Diomedi et al. 1999; Elia et al. 2000; Hering et al. 1999; Patzold et al. 1998; Richdale 1999; Schreck et al. 2000; Taira et al. 1998; Takase et al. 1998). These problems are usually with sleep onset and maintenance, and the frequency of parasomnias is not increased (Patzold et al. 1998; Richdale 1999; Schreck et al. 2000; Taira et al. 1998). However, contradictory findings have also been made. For example, in an ACG-based study, no differences in sleep quality were found between autistic children and controls. The authors suggested that parental over-sensitivity may account for reports of an association between sleep and autism (Hering et al. 1999). Nevertheless, it is also noteworthy that the validity of ACG is lower in patient samples (Littner et al. 2003b).

Asperger syndrome (AS) also belongs under the autistic spectrum of diseases. It is thought to be a multifactorial disorder, the development of which has genetic, neurological and sociocultural components (Gillberg 1995; Nieminen et al. 2000). The prevalence of AS has been estimated to be 0.4-0.7% (Ehlers et al. 1993; Kadesjö et al. 1999). AS is characterized by significant difficulties in social relationships, verbal and both fine and gross motor deficits, and bizarre and circumscribed targets of interest (Filipek et al. 1999; Gillberg 1995; Nieminen et al. 2000; Volkmar et al. 2000). Poor non-verbal communication skills and qualitative impairments in social interaction are essential features in AS, while language delay does not belong to the symptom profile. Normal intelligence quotient is required (Filipek et al. 1999). Psychiatric and neurological problems, such as ADHD and depression tend to co-exist in AS patients (Gillberg et al. 2000). Generally, people with AS, manage fairly well in normal life, but the risk for marginalization is considerable (Gilchrist et al. 2001; Green et al. 2000). Hence, supportive treatment and rehabilitation are often needed (Nieminen et al. 2000). From the clinical point of view, sleep disturbances are typical among people with AS, but studies are few (Godbout et al. 2000; Patzold et al. 1998). Sleep disturbances, such as sleep onset problems and nocturnal awakenings, manifest at a young age and usually persist for long periods. Moreover, for reasons that are not completely understood, these sleep disturbances can be resistant to treatment: behavioural modifications, for example, are often ineffective.

4.7.4 Psychiatric symptoms and sleep

In recent years, an increasing number of studies have reported associations between children's sleep disturbances and various psychiatric symptoms, including depression and behavioural problems (Aronen et al. 2000; Chervin et al. 1997; Corkum et al. 1998; Dagan et al. 1997; Dahl 1998; Marcotte et al. 1998; Morrison et al. 1992; Smedje et al. 2001). Post-traumatic stress disorder and abuse (Glod et al. 1997) have also been linked to disturbed sleep. A sleep disorder is in fact a classic symptom of major depression and post-traumatic stress disorder. Poor sleep has also been associated with mood alternations and irritability (Dahl 1996; Sadeh et al. 1995b). Moreover, low self-esteem (Sadeh et al. 1995b), anxiety (Johnson et al. 2000; Morrison et al. 1992; Sadeh et al. 1995b) and fears (Dollinger et al. 1996) have been found to be related to sleeping disturbances. Even shortened sleep duration has been associated with mood alterations, depressive feelings and anxiety (Wolfson et al. 1998). Finally, it is worth noting that sleep deprivation is also used in the treatment of depression, resulting in beneficial changes in approximately half of the patients (Giedke et al. 2002; Wirz-Justice et al. 1999).

In adults, sleep impairment has been strongly correlated with poor self-estimated health, and approximately 40.4% of those with insomnia also have a psychiatric disorder (Ford et al. 1989). Among adolescents, 67% of those with insomnia (or multiple sleep complaints) have clinically significant anxiety disorders or depression, as defined in the DSM III (Morrison et al. 1992). On the other hand, 73.2-76.5% and 67.6-77.4% of patients with an anxiety disorder or depression, respectively, have reported insomnia (Ohayon et al. 2000), and 75% of depressed adolescents complain of insomnia and 25% of hypersomnia (Ryan et al. 1987). As many as 30-40% complain of severe insomnia and extreme daytime fatigue (Dahl et al. 1990a). EEG studies of depressed adolescents have, however, yielded controversial results. For example, prolonged sleep latency and reduced REM latency have been reported in depressed adolescents (Dahl et al. 1996), but the abnormalities in sleep architecture seem not to be as consistent (Dahl et al. 1990b; Dahl et al. 1991b) as those reported in adults (Riemann et al. 2001).

Persistent sleep problems are sometimes considered most harmful to children's well-being and development, whereas temporary problems are thought to be of minor significance. However, only a few studies longitudinally examined the association between trouble sleeping and internalizing symptoms in children. In a recent study, parental reports of child's sleep disturbances at age 6 were not linked to increased incidence of depression at age 11 (Johnson et al. 2000). However, a connection was found between sleep disturbances and simultaneous anxiety/depression at 11 years. According to maternal reports, the risk was almost 7-fold. Similar results were reported in another study (Stoleru et al. 1997). Interestingly, insomnia seems to be a significant predictor of major depressive disorder in young adults (Ford et al. 1989). Those with complaints of insomnia had an almost 40-fold risk for developing major depression. Another study reported that individuals with a lifetime history of insomnia had a 2-fold risk for major depression (Breslau et al. 1996). A PSG-based study also lent support to these findings; adolescents at risk for developing major depression had preceding alternations in REM sleep architecture (higher density of REM and reduced REM latency) (Rao et al. 1996).

A growing amount of evidence suggests a connection between sleep and externalizing problems. Questionnaire-based studies have shown significant correlations between conduct disorder scores and reports of sleep problems (Morrison et al. 1992; Owens-Stively et al. 1997). Objective NREM changes have also been found in preadolescents with conduct problems (Coble et al. 1984b). Moreover, children with OSAS and co-morbid bedtime resistance have been reported to display more externalizing symptoms than those with pure OSAS or no sleep disturbance at all (Owens et al. 1998). Although the authors suggested that co-morbid behavioural sleep disorder might have a significant effect on daytime behavioural consequences, their finding can also imply that bedtime resistance is a particular manifestation of the (primary) conduct problem, because the pure OSAS group did not have an increased number of behavioural problems.

A limited amount of research is available concerning causality between sleep and psychiatric problems. Clearly, sleep disturbances can reflect underlying psychiatric disorders, but sleep quality may also be easily affected by various adverse psychosocial factors. On the other hand, sleep disturbances, or at least sleep deprivation, can manifest as psychiatric symptoms (Reite 1998). Sleep disorder is a potential aetiological factor in psychiatric problems. For example, in many cases with ADHD the sleep impairment is secondary, but sleep deprivation can also cause problems similar to those in ADHD. A similar relationship seems to prevail between sleep and depression. Subjective sleep complaints often accompany depression, but sleep

deprivation can also produce symptoms typical of depression. The finding that sleep disturbances can precede development of major depression (Ford et al. 1989) makes it tempting to speculate that in some instances sleep debt can induce mood changes which eventually lead to onset of a major depressive disorder.

4.8 Treatment of sleep disturbances

Various methods have been used to treat children's sleep disturbances. These include sleep hygiene, bright light therapy, counselling, avoidance of factors that adversely affect sleep quality, behavioural therapy, melatonin therapy, pharmacotherapy, adenotonsillectomy and positive pressure oxygen treatment. Specific sleep disturbances usually require specific treatments: obstructive sleep apnoea, for instance, can be treated by a positive pressure oxygen mask or by tonsillectomy. Children's primary sleep disturbances are, however, mostly treated by behavioural interventions, supportive methods and counselling. If sleeping difficulties originate from short-term stress factors or anxieties, the duration of problems is usually brief and no specific treatment is needed (Anders et al. 1997; Dahl 1992; Mindell et al. 1993; Ramchandani et al. 2000; Stores 1996).

Several types of drugs are currently available to treat both children's and adults' sleep disturbances. According to one study, sedation is the most common treatment for children's sleep disturbances (Ramchandani et al. 2000). Up to 14.8% of American paediatricians prescribe pharmacological treatments for sleep disturbances despite data indicating that such a practice is often either useless or completely contraindicated (Mindell et al. 1994). Medication can not be considered the primary alternative for adults or children because of its potential side-effects and the risk for developing an addiction. As far as children are concerned, the indications for use of medication are even more limited than in adults. First, the effects of psychotropic substances on the developing brain are unknown. Second, although the short-term efficacy of drug treatment has been found to be similar to that of behavioural methods, when long-term efficacy was assessed it was worse (Ramchandani et al. 2000). Third, the results have mainly been based on studies with major methodological weaknesses, such as small sample sizes, heterogeneous patient populations, poorly defined outcome measures and non-blinded settings (Owens 2000). New alternatives for the treatment of severe sleep problems with less side-effects and good tolerability are thus clearly needed.

Melatonin has recently gained much interest among researchers and clinicians because paediatric data on this hormone secreted by the pineal gland (Bergstrom et al. 1998; Zhdanova et al. 1997), suggests high therapeutic potential with no side-effects (Gordon 2000; Jan et al. 1996). While melatonin in animals affects reproductive performance, its primary function in humans is not completely known (Brzezinski 1997). It appears to participate in circadian organization and regulation of diurnal rhythms (Arendt et al. 1999; Bergstrom et al. 1998; Kayumov et al. 2000; Zhdanova et al. 1997). During childhood melatonin levels drop by 80%, but in prepubertal children levels seem to be regulated by maturation and not chronological age (Bergstrom et al. 1998; Salti et al. 2000). Exogenous melatonin has a sleep-promoting effect, and hence, it is used to treat various sleep disorders (Arendt et al. 1999), particularly circadian phase disorders (Lewy et al. 1996). Administration of melatonin in low doses (0.5-3 mg) has been reported to decrease sleep latency and improve sleep quality in elderly people with chronic insomnia (Garfinkel et al. 1995) and in patients with DSPS (Dagan et al. 1998;

Kayumov et al. 2001; Lewy et al. 1996; Nagtegaal et al. 1998). Melatonin has been speculated to have long-term effects even after brief use (Masters 1996), but 91.5% of patients with DSPS have been reported to have a relapse after discontinuation (Dagan et al. 1998). More studies are therefore needed to determine the optimal length of treatment.

As summarised in Table 4, several melatonin treatment studies in children have reported beneficial effects of the hormone (Akaboshi et al. 2000; Dodge et al. 2001; Etzioni et al. 1996; Hatonen et al. 1999; Hayashi 2000; Jan et al. 1996; Jan 2000; Lapierre et al. 1995; Masters 1996; Miyamoto et al. 1999; Pillar et al. 1998a; Pillar et al. 2000; Robertson et al. 1997; Smits et al. 2003; Yamashita et al. 1999; Zhdanova et al. 1999). A recent review has concluded that melatonin offers a promising alternative to treat children's sleeping difficulties (Gordon 2000). The only study with negative results concerned infantile neuronal ceroid lipofuscinosis patients and was limited by a small sample size (Hatonen et al. 1999). Side-effects of melatonin have rarely been found, although a 14-year-old girl was reported to suffer from drowsiness and dizziness after taking an overdose (24-36 mg) (Balentine et al. 1997). Animal studies have, however, suggested that melatonin might have negative effects on pubertal development or reproductive function, and therefore it should be noted that its long-term safety has not been established in humans although its acute toxicity is remarkably low (Arendt 1997; Weaver 1997).

Table 4. Melatonin treatment studies in children.

Reference	Setting	Age (y)	n	Patient group	Dose (mg)	Side-effects	Outcome
Akaboshi et al. (1999)	CR	5	1	Mentally retarded	0.75	?	Marked improvement
Dodge et al.(2001)	RC	1-15	20	Developmental disabilities	5	None	Reduced sleep latency
Etzioni et al. (1996)	CR	14	1	Pineal tumour/ melatonin deficiency	3	?	Marked improvement
Hatonen et al.(1999)	OT		5	INCL	2.5, 5	None	Only subjective improvement
Hayashi et al. (2000)	CR	14	1	Autism	6	None	Sleep latency diminished
Horrigan (1997)	CR	17	1	Asperger syndrome	3	None	Marked improvement
Jan et al. (1996)	Rev	0-21	100	Developmental disabilities	2.5-10	None	Marked improvement in 80%
Jan (2000)	OT	1-11	10	Handicapped with circadian rhythm disorders	3	None	Dramatic response in 80%
Lapierre et al.(1995)	CR	5	1	Blind and retarded	0.5	None	Sleep wake rhythm normalized
Masters (1996)	CR		20	Psychiatric disturbances	3-6		All improved markedly
Miyamoto et al. (1999)	CR	4, 10	2	Rett syndrome	3-5	None	Marked improvement
Pillar et al. (1998)	CR	13	1	Psychomotor retardation	3	?	Marked improvement
Pillar et al. (2000)	OT	Avg 8	5	Psychomotor retardation	3	None	Marked improvement
Robertson et al. (1997)	CR	10	1	Bipolar disorder	12	?	Marked improvement
Smits et al. (2003)	RC	6-12	62	Sleep onset insomnia	5	Dizziness, mood/ appetite changes	Marked improvement
Zhadanova et al. (1999)	OT	2-10	13	Angelman syndrome	0.3	None?	Marked improvement
Yamashita et al. (1999)	CR	10	1	Rett syndrome	3	?	Marked improvement

CR Case report, RCT Randomized controlled study, OT Open trial, Rev Review.

The effects of melatonin have been reported to be immediate (Etzioni et al. 1996; Horrigan et al. 1997; Pillar et al. 1998a), in at least half of the cases (Jan et al. 1996). While discontinuing the medication may lead to recurrence of sleep problems (Horrigan et al. 1997; Miyamoto et al. 1999; Robertson et al. 1997), long-term treatment is often successful (Jan et al. 1996; Jan 2000; Miyamoto et al. 1999). Speculations have, however, arisen about whether melatonin is beneficial without substantial control over behavioural sleep routines, such as avoidance of napping, and standard bedtime rituals (Lord 1998).

5. AIMS OF THE STUDY

The study objectives were as follows:

1. To estimate the prevalence of sleep disturbances in school-aged children, as reported by the children and their parents.

2. To evaluate the course of sleep problems during a 4-year follow-up.

3. To estimate the correspondence between children's and parents' reports, and to establish how to best screen for sleep problems.

4. To assess relationships between sleep disturbances and psychiatric syndromes, particularly to determine how much sleep disturbances increase risk for significant mental health problems.

5. To assess whether melatonin is effective in treating sleep problems in children with Asperger syndrome. A specific aim was to determine whether improvements in behaviour and well-being occur in conjunction with amelioration of sleep disturbances.

6. SUBJECTS AND METHODS

Three different samples were used. First, the epidemiological sample consisted of nearly 6000 children (aged 8-9 years). Those who were from the Helsinki area were followed up for 4 years. Sleep problems were assessed according to parents' and children's reports, and teacher's reports were used as an independent information source on children's behaviour (I-III). Second, a sample of 61 children (aged 7-12 years) from ordinary schools was collected. Structured child psychiatric evaluation methods and two sleep questionnaires accompanied by actigraphic measurements were applied (IV). Third, the usefulness of melatonin in treatment of long-standing sleep disturbances in patients with Asperger syndrome (aged 5-17 years) was assessed (V).

6.1 Subjects

The first part of the study is part of the population-based epidemiological multicentre study (including all five University Hospital districts) on childhood psychiatric morbidity (the "LAPSET" study) in Finland. In this research project, all children with Finnish as their maternal tongue (93%) who were born in 1981 and registered in a school district constituted the sampling frame (n=60 007). A random sample of all school districts in Finland was drawn, and children in the selected districts constituted the primary sample. Severely mentally impaired children were excluded. The total number of eligible children was 6017, constituting approximately 10.0% of the age cohort in the country. The participation rate was very high; questionnaires were obtained from 5813 children (96.6%), while 2.2% failed or refused to attend and 1.2% could not be tracked down. The final sample consisted of 2946 boys (50.7%) and 2867 girls (49.3%). The socio-economic distribution and the demographic characteristics of the families were similar to those of the whole population in Finland, making the sample highly representative (Almqvist et al. 1999).

In the follow-up study, only children from the Helsinki area were considered. The initial sample size was 1320, which was approximately 8% of the respective age cohort of the area. The children were first assessed at the age of 8 years as described above, and the second assessment took place 4 years later, at the age of 12 years. A small proportion of the families (n=30, 2.3%) refused to participate or could not be located at the second time-point, therefore, questionnaires were administered to 1290 subjects, including 661 boys (51.3%) and 627 girls (48.7%).

The second sample included 61 healthy volunteers aged 7-12 years from ordinary schools in the Helsinki area who were recruited by advertising at schools. All consenting children in the target agegroup were eligible for the study. Written informed consent was obtained from both the children and the parents.

In the third sample, children with Asperger syndrome were studied. The subjects were obtained from the Asperger patient database of the Child Neurology Unit at the Helsinki University Central Hospital and the Helsinki Asperger Centre. The initial sample consisted of 68 children aged 5-17 years with a confirmed diagnosis of Asperger syndrome, who had been sent for assessment by a child neurologist. The diagnoses had been set according to criteria in the DSM

IV by an experienced child neurologist. One family could not be tracked down, but all of the other parents and children were sent a letter describing the study protocol, two basic sleep questionnaires and a set of background questions. Participants in the melatonin trial were selected on the basis of this initial screening.

6.2 Questionnaires

Children's Depression Inventory (CDI) was used as a self-report questionnaire (Kovacs 1985). It is a widely used and standardized measurement scale of childhood depression consisting of 27 items with three alternative statements of differing severity. Items are rated on a 3-point scale. From the Finnish version, one question concerning suicide was excluded for ethical reasons (it was thought to evoke worries/anxiety in children). Four questions concerning somatic symptoms, and one question concerning bullying were added.

Rutter A2 scale (RA) for parents comprises 36 statements 19 of which concern child's behaviour and psychiatric symptoms with three response options of differing severity ("does not apply", "applies somewhat", "certainly applies") (Rutter et al. 1970). Seven sleep questions are included on the RA. One question concerning bullying was added.

Rutter B2 scale (RB) for school teachers includes 26 items concerning child's behaviour, and problems (Rutter et al. 1970). Three response options of differing degree ("does not apply", "applies somewhat", "certainly applies") are provided. One item concerning bullying was added. The 26 original items are summarized and the total score is recorded. Children with a total score over 9 are considered to have a probable psychiatric disorder. Instead of using the Rutter's original sum-scores, we decided to perform factorial analysis to generate new independent scores. This was done because the original scale was rather old, and the symptom profile could have changed over the years. All items in the RB with three response options for psychiatric symptoms (items 1-27) were submitted to maximum-likelihood factorial analysis, followed by Varimax rotation. Four factors were extracted: externalizing behaviour, internalizing behaviour, hyperactivity and school refusal. Factor scores were calculated by the regression method and included all items (II).

Children's Behaviour Checklist (CBCL) is a parental questionnaire about various child psychiatric symptoms. It consists of 113 questions with three response options. A total score and eight subscores (withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, delinquent behavior, aggressive behavior) are calculated. The first three constitute the internalizing score, and the last two the externalizing score. The cut-off limits for borderline and deviant behaviour have been previously defined (Achenbach 1991a). The CBCL has been validated in different countries and is widely used as a screening instrument (Berube et al. 2001). In Finland, the validation process is ongoing.

Teachers' Report Form (TRF) is a standardized, well-documented questionnaire on children's behavior and mental health. A total score, internalizing and externalizing scores and eight subscores (withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, delinquent behaviour, aggressive behaviour) are extracted. The cut-off values for deviant and borderline behaviour have been previously defined (Achenbach 1991b). The TRF is a widely used and validated child psychiatric measurement scale (Berube

et al. 2001). Here, to assess risk for deviance, TRF scores were dichotomized using the cut-off value for borderline behaviour. If missing data on the TRF exceeded 20% on any sum score, that score was coded as missing, otherwise missing values were replaced by the mean score for the remaining items in the same category.

The sleep questionnaires used were the following: Children's Self-Report Form (CSRF) completed by the children themselves, Teacher's Questionnaire (TQ) completed by the teachers (Owens et al. 2000c) and Sleep Disturbance Scale for Children (SDSC) completed by the parents (Bruni et al. 1996). Karolinska Sleepiness Scale (KSS) was used to evaluate daytime sleepiness (Gillberg et al. 1994). Sleep logs (SL) were used for three consecutive nights during the actigraph measurements.

In the first sample, the CDI, RA, RB, CBCL and TRF were used. In the second sample, the CDI, CBCL, TRF and SL were used. In the third sample the CDI, CBCL, KSS, CSF, SL, TQ and SDSC were used.

6.3 Definitions of sleep problems

Sleep questions on the CDI, RA and CBCL were used in the epidemiological study. The CDI gives children the following three response options: "I sleep pretty well", "I have trouble sleeping many nights" and "I have trouble sleeping every night". In the RA, the parents are questioned: "is there any sleeping difficulty?" and the response options are "no", "yes mild" and "yes severe". The sleep question in the CBCL (item 100) asks "(are there) sleeping problems?" and responses are "does not apply", "applies somewhat" and "certainly applies". The two sleep questions (in the RA and the CBCL) are highly similar, and the wording of the items is almost identical. However, because the given response options are slightly different, both answers indicating the presence of a sleep problem were condensed into a "problems" category. Belonging in the "no sleep problems" group were all children for whom neither informant had reported sleep disturbances (n=3856). The "mild problems" group consisted of cases with either or both informants reporting mild sleeping problems (n=1515), while the "severe problems" group included those for whom at least one informant had reported severe problems (n=302). Finally, children with no or mild sleep problems were combined, leaving a dichotomous variable. Both informants were considered equally important, because there was a marked disagreement between children's and parent's reports of sleep. Approximately 95% of severe sleeping problems were reported by the child alone, with only 0.3% (n=17) of parents reporting severe sleep disturbances in their children. A persistent sleep problem was defined as a sleep problem reported by either the parent or the child at both 8 and 12 years of age.

6.4 Actigraph measurements

Sleep quality was assessed using actigraphs (American Sleep Disorders Association 1995a). Mini-motionlogger actigraphs (Ambulatory Monitoring Inc, New York, USA) were used. In one ACG-based study (IV), the activity monitor was worn at the waist in a small pouch attached to a belt, and in the other study (V), it was worn on the non-dominant wrist. It is noteworthy that actigraphs-based sleep measurements have been validated against PSG only

for wrist-worn activity monitors, and a recent consensus report stated that superiority of actigraphs placement has not yet been established (Littner et al. 2003b). Another report has, however, shown that wrist- and waist-worn monitors give highly correlated results (Paavonen et al. 2002).

The parents kept logs of monitor removal times, bedtimes and waking times, and were instructed to report as the bedtime the time when the child had finished reading or playing in bed, and was planning to go to sleep. Activity data were collected for continuous 72-hour periods on ordinary school days (IV-V). This is generally considered sufficient (Littner et al. 2003b), although some evidence suggests that 5-7 days might be required to get reliable estimates of sleep quality (Acebo et al. 1999). However, the authors had noted that the most common reasons for varying sleep parameters were illness, participant non-compliance and technical problems, none of which constituted a problem here. Illness was excluded when the measurement was initiated, and if a child became ill during the measurement period, the respective nights were excluded from further analysis. Compliance was high, because the study included only children who wanted to participate. Technical problems, such as monitor failure, did not occur during the measurement periods. However, a few nights were excluded from the analyses because of the inaccuracy of the sleep log kept by parents. “First night effect” may have contributed to the findings of rather low sleep efficiency and should be taken into account in forthcoming studies.

Raw activity data were analyzed using ACT2000 and AW2 software (Ambulatory Monitoring Inc., New York, USA). Data were first inspected for accuracy in reported bedtimes and waking times as well as monitor removal periods. If any obvious discrepancy was observed between the activity data and the reported bedtimes, the night in question was excluded from further analysis. Sleep estimates (sleep duration, sleep efficiency, sleep onset latency, number of awakenings) were derived using the Sadeh sleep algorithm and were based on total activity counts obtained during 1-minute epochs (Sadeh et al. 1989). The down period was defined according to parental reports. The parameters used were sleep efficacy, number of awakenings, sleep latency, nocturnal activity and total sleep time. The data were averaged across the measurement days and then subjected to further statistical analysis.

6.5 Study protocols

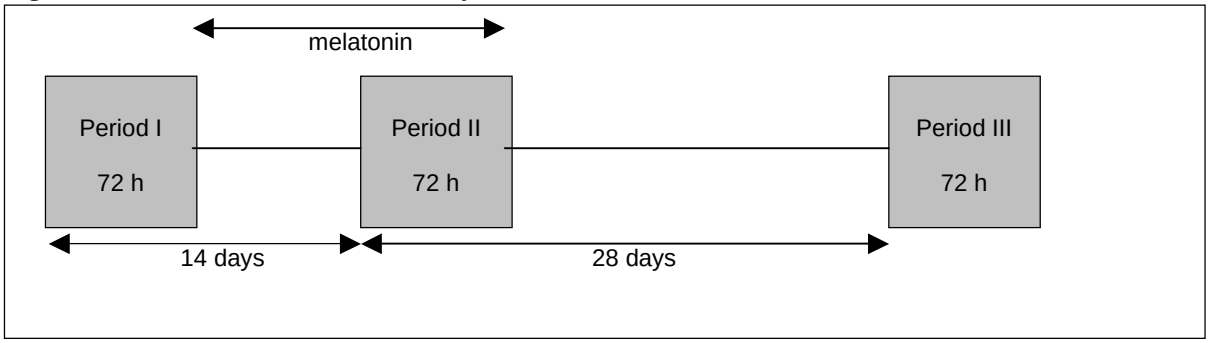
The epidemiological sample was initially recruited in 1989-1990 (T1) and followed up in 1994 (T2). At T1, the evaluation of children’s behaviour, emotions and sleep included administering the RA scale for parents, the RB for teachers and CDI for the children. The children filled out the questionnaires at school, and parents’ questionnaires were sent home, and asked to be returned to schools. At T2, a similar protocol was used, but children’s symptoms were assessed using the TRF, CBCL and CDI.

The second and third samples are questionnaire-based studies that include actigraph measurements. In the former, all eligible children participated ACG measurements during ordinary school week and the questionnaires were filled out during the measurement period. In the latter, all parents and children were sent a letter describing the study protocol, and the two questionnaires (CSRF and SDSC) and a set of background questions concerning sleeping habits were enclosed. The parents were instructed on what to do if the child had difficulties in

completing the questionnaire on his/her own. All children with severe sleep problems during the previous three months were eligible to participate. Exclusion criteria were 1) current psychotropic medication and 2) recent history of parental psychiatric morbidity. Informed consent was obtained from both the children and their parents. Consenting participants were then interviewed by phone. Severe insomnia was defined as continuous problems with sleep initiation or maintenance that disturbed either the child or the family such that the child was constantly tired or had symptoms that could be attributed to sleep deprivation.

Sleep quality and behaviour were first assessed before the treatment period (days 1-4) using an actigraph and questionnaires, then melatonin (3 mg) was started and used for 14 consecutive days 30 minutes prior to bedtime (days 4-18). The second assessment took place on the 12th treatment day onwards (days 15-18), and the third 3.5 weeks (days 43-46) after discontinuation of medication (Figure 2).

Figure 2. Flow chart of the melatonin study.



6.6 Response rates

The relevant response rates in the epidemiological study were the following: the sleep question in the CDI 97.8% (n=5685) and in RA 97.7% (n=5678), and for the RB 97.6% (n=5673). Cases with incomplete answers to the sleep questions, the RB or the background variables were excluded from multivariate analyses, leaving a total of 4531 participants. In the follow-up study, there were 862 (66.8%) sets of complete teacher ratings at T1 and T2, 867 (67.2%) sets of parent ratings and 1047 (81.2%) child ratings. Missing data were excluded test by test to best utilize the sample. However, in multivariate analysis, complete data across all measures were required, thus 598 (46.4%) cases were analyzed. The second sample initially included 61 cases with complete ACG and parental questionnaire data. The response rate for the TRF was 80.3% (n=49). In the melatonin trial, the response rate for the initial screening was 80.6% (n=54). Of the 54 families, 26 (48.1%) were interested in participating in the melatonin trial. Nine children were excluded due to the absence of a severe sleep problem and two because of other medications (melatonin or clonidine), leaving 15 children (13 boys, 2 girls).

6.7 Statistical methods

Parents' and children's reports were first analysed independently and then combined as described in Section 6.3. The three response options were then dichotomized such that the

alternatives of “often/always” and “mild/severe” were condensed into a “sleep problems” category because of the low frequency of parental reports of severe sleep problems. Moreover, misclassification bias was best avoided this way. The factorial scores were also dichotomized (cut-off mean + 2 SD, indicating a probable psychiatric problem).

A frequency analysis was done first. Prevalence estimates with 95% confidence intervals were calculated. Means and standard deviations were calculated for continuous variables. Simple comparisons were based on either t-tests or Mann-Whitney tests for continuous variables, and χ^2-tests or Fischer exact tests for categorical variables. The parametric test was selected when the distribution of the variable was normal. For dependent dichotomous data, the McNemar test was used, and dependent continuous data were compared using the Wilcoxon test. All p-values were two-sided, and the significance level was set at $p<0.01$.

Agreement between informants was estimated by calculating the kappa coefficient. In addition, the overall percentage of agreement, percentage of agreed occurrence and conditional probabilities of agreement were calculated. Conditional probability (probability of A given B) is calculated as follows:

$$p(A \mid B) = \frac{P(A \cap B)}{P(B)} = \frac{n_{ab}}{n_b}.$$

The conditional probabilities calculated were the probability of a positive response from a parent given a positive response from the child (P|C), the probability of a positive response from a parent given a severe sleep problem reported by the child (P|C2) and the probability of a positive response from a child given a positive response from the parent (C|P). Conditional probabilities of agreement given different types of sleep problems were also calculated.

Risk was estimated by calculating odds ratios with 95% confidence intervals. Multiple logistic regression analysis was used to control for potential confounding factors. Covariates in the models were gender, mother’s and father’s socio-economic class and mother’s education. Previous level of psychiatric symptoms (represented by the four factorial scores on the RB) was also controlled for in the follow-up study. The four categorical factor scores served as dependent variables. An ANOVA model for repeated measures was constructed to assess treatment effect.

7. RESULTS

7.1 Prevalence of sleep difficulties at the ages of 8 and 12 years

According to the parents, 21.7% (n=1261) of the children had some sleeping difficulties. Most of the reported problems were mild (n=1243, 21.4%) while severe sleep problems were reported for only 0.3% (n=18) of the children. The children reported slightly less sleeping difficulties than the parents: 17.7% (n=1030) reported some sleep problems. Mild problems were reported by 12.7% (n=736) and severe by 5.1% (n=294). When both the children's and the parents' reports were summarized, the overall prevalence of sleep difficulties rose to 32.0% (n=1859), and the prevalence of severe problems was 5.4% (n=312) (I).

According to the parents, dyssomnias were the most typical sleep disturbances among the children, with an overall prevalence rate of 17.3% (n=1006). This means that most of the children (79.8%) whose parents had reported sleep disturbances had difficulty with sleep initiation and maintenance. Sleep onset problems (11.1%, n=647) and nocturnal awakenings (7.1%, n=411) were particularly frequent, while too early awakening in the morning (2.3%, n=131) was less common. The overall frequency of parasomnias (nightmares, sleep-walking, night terrors) was 8.0% (n=465). The prevalence of nightmares was 5.4% (n=316), sleep-walking 3.3% (n=191) and night terrors 0.8% (n=42). Enuresis was also typical, with a rate of 9.5%. Multiple (at least two) sleep problems were present in 9.3% of the children (I).

Most of the sleep problems were more frequent in boys than in girls. Altogether, 34.3% of boys and 29.7% of girls had some type of sleep difficulty (χ^2=26.6, p=0.01). Severe sleep problems were almost twice as common in boys than in girls (6.7% and 3.9%, χ^2=26.6, p<0.01). The prevalence of multiple sleep problems was 11.0% among boys but only 7.6% among girls (χ^2=19.2, p<0.01). Boys also had more parasomnias (χ^2=11.1, p<0.01), nightmares (χ^2=9.7, p=0.02) and enuresis (χ^2=39.4, p<0.01), and they tended to wake up too early in the morning (χ^2=5.0, p=0.03) more often than girls (I).

Mother's education was not associated with the children's reports of sleep problems, but it was negatively correlated with parental reports of disturbed sleep (χ^2=12.8, p=0.01). The absolute difference was not, however, large: the reported rates decreased from 19.1% in the lowest socio-economic class (no education) to 17.9% in the highest class (academic education). Family composition was also associated with sleep problems (χ^2=17.6, p=0.01). Sleep disturbances were more prevalent in children from families with one biological parent and a cohabiting stepmother or stepfather (38.6%, n=115) and those who lived apart from their biological parents (the child was adopted or fostered) (51.3%, n=20) than in those who lived in families with both biological parents (32.4%, n=1519) or lone biological parents (28.8%, n=166). Illness in the family was also clearly associated with frequency of sleep problems (χ^2=26.5, p<0.01), whereas the number of children in the family, grandparents living in the family, other persons living in the family and being a twin were not associated with poor sleep (I).

During the 4-year follow-up period the prevalence of sleep disturbances decreased markedly according to parental reports, from 23.4% at the age of 8 years to 9.1% at the age of 12 years

($p<0.01$). However, according to children's reports, the prevalence remained steady at 18.7% and 18.8%. There was also a clear decrease in the combined prevalence (a sleep problem reported by either the child or the parent), from 34.2% to 25.6% ($p<0.01$), but this mainly reflects the diminished frequency of parental reports. Half of the children (50.4%, n=395) had no sleep disturbances at either time-point. Persistent sleep problems (reported by either informant) occurred in 12.0% (n=94) of children, with no gender differences being present. A sleep problem at the age of 8 years was a clear risk factor for a sleep problem later on (OR 1.85, 95% CI 1.33-2.56). In absolute numbers, every third child who had had sleep problems at the age of 8 years still had problems at 12 years (33.3%, n=94) (III).

7.2 Child-parent agreement

Children's and parents' reports of sleep problems were largely discrepant. Although the overall agreement percentage was high, 77% at the age of 8 years and 75% at the age of 12 years, this mainly reflects agreement on the absence of symptoms when occurrence of the symptom or disease is rather low. Consistent with this, the agreed occurrence was much lower, only 23.1% at the age of 8 years and 12.9% at the age of 12 years. Moreover, the kappa value was low, $\kappa=0.22$ at the age of 8 and only $\kappa=0.12$ at the age of 12. The disagreement was especially large with regard to severe sleep problems: parents reported severe sleeping problems for only 18 cases (0.3%), while according to the children the rate was 17-fold higher with 294 children (5.1%) reporting severe sleep disturbances. This means that if proportions are calculated from cases with sleep problems at 8 years, 23.1% of the sleep problems were reported by both the parent and the child, 44.7% by the parent only and 32.2% by the child only (the overall proportions being 7.4%, 14.3% and 10.3%, respectively) (I and III).

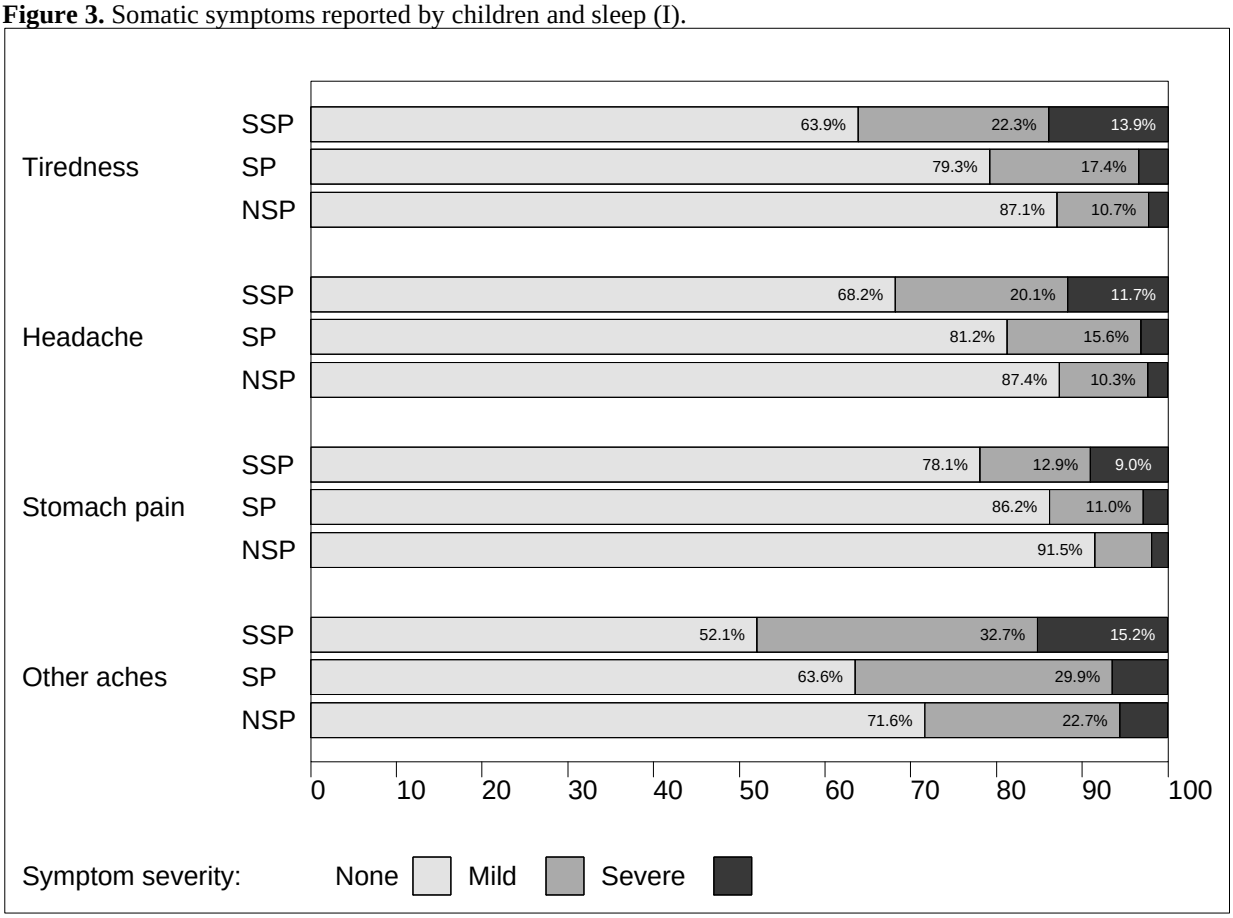
The probability of a positive response from a parent given a sleep problem reported by the child was P|C=0.42 (i.e. the likelihood of agreeing information was 42% if the child had reported a sleep problem), and for the reverse case C|P=0.34 (the likelihood of agreeing information was 34% if parent had reported a sleep problem). The conditional probabilities of agreement for different types of problems were the following: night terrors 0.38, sleep onset 0.38, night awakenings 0.37, nightmares 0.33, sleep-walking 0.28 and too early awakening 0.25. The disagreement is likely related to parental awareness; if the sleep impairment disturbs the parents, the discrepancy is lower. The probability of a positive response from a parent given a serious sleep problem reported by the child (P|C2) was 0.39 (I). The likelihood of persistent sleep disturbances was 0.26 for those for whom parental reports alone had been positive for sleep disturbance at age 8. Similarly, if the child had been the only one to report a sleep problem at age 8, the likelihood of having a sleep disturbance 4 years later was 0.31. However, when both the child and the parent had reported sleeping problems at age 8, the risk for long-term problems was significantly higher: 0.55 (III).

7.3 Sleep problems and other symptoms

Sleeping difficulties were correlated with several types of problems, as reported by children, parents and teachers. Many somatic symptoms were related to poor sleep (Figure 3)[1].

[1] The frequencies and all percentages can be found in the original paper which is referred to in the table heading.

Figure 3. Somatic symptoms reported by children and sleep (I).



NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

School attendance problems were generally uncommon but were significantly associated with severe sleep disturbances, the risk being 2- to 3-fold in cases with severe sleep problems as compared with those without sleep complaints (Table 5).

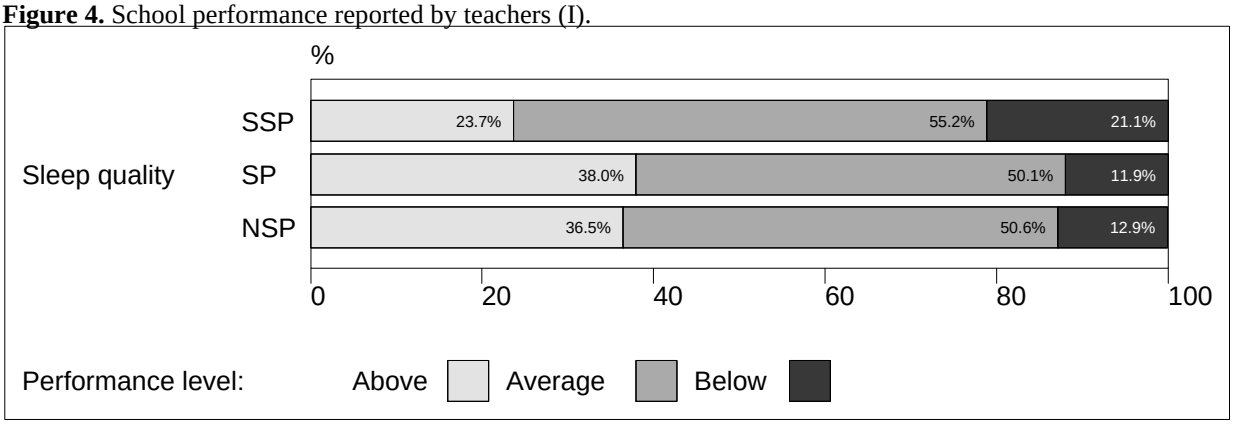
Table 5. School related problems reported by teachers (II).

% (n)	NSP	SP	SSP	p
Truant	2.1 (84)	2.1 (32)	6.8 (21)	<0.001
School tears	2.3 (89)	3.4 (53)	5.2 (16)	0.001
Absent from school	2.8 (109)	3.2 (50)	5.8 (18)	0.01

NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

School performance was also more frequently below average among children with severe sleeping problems as compared with those with no/mild sleeping problems (Figure 4).

Figure 4. School performance reported by teachers (I).



NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

The need for psychiatric consultation was higher in children with poor sleep than in others, both according to parents and teachers (Table 6).

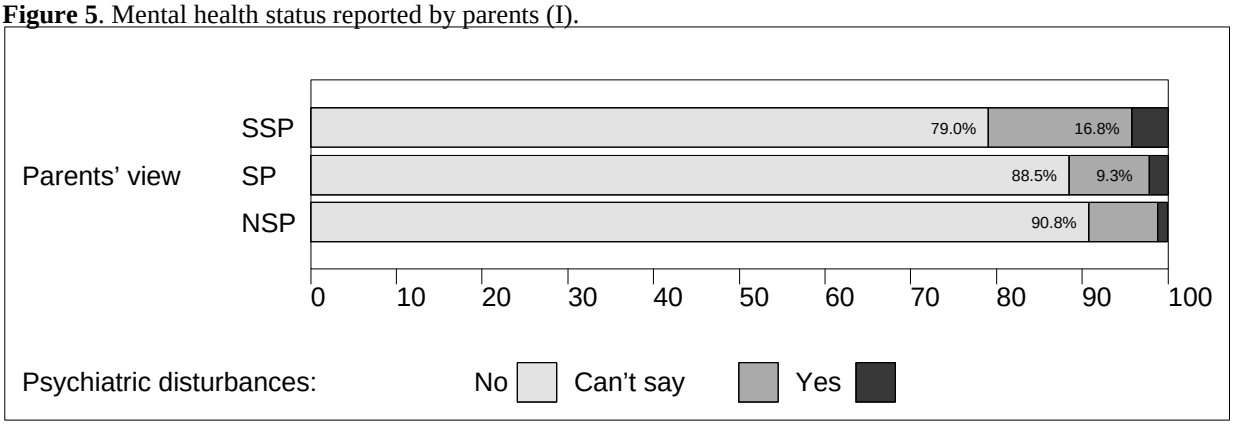
Table 6. Need for psychiatric counselling/consultation reported by parents and teachers (I).

% (n)	NSP	SP	SSP	p
Parent				
considered	2.0 (77)	4.9 (76)	5.8 (18)	
sought	1.9 (76)	4.4 (68)	6.1 (19)	<0.001
Teacher				
considered	2.4 (93)	2.6 (41)	4.2 (13)	
referred	2.0 (78)	3.5 (54)	6.5 (20)	<0.001

NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

Psychiatric morbidity was also more common among children with sleep disturbance than among those without any sleep complaints (Figure 5).

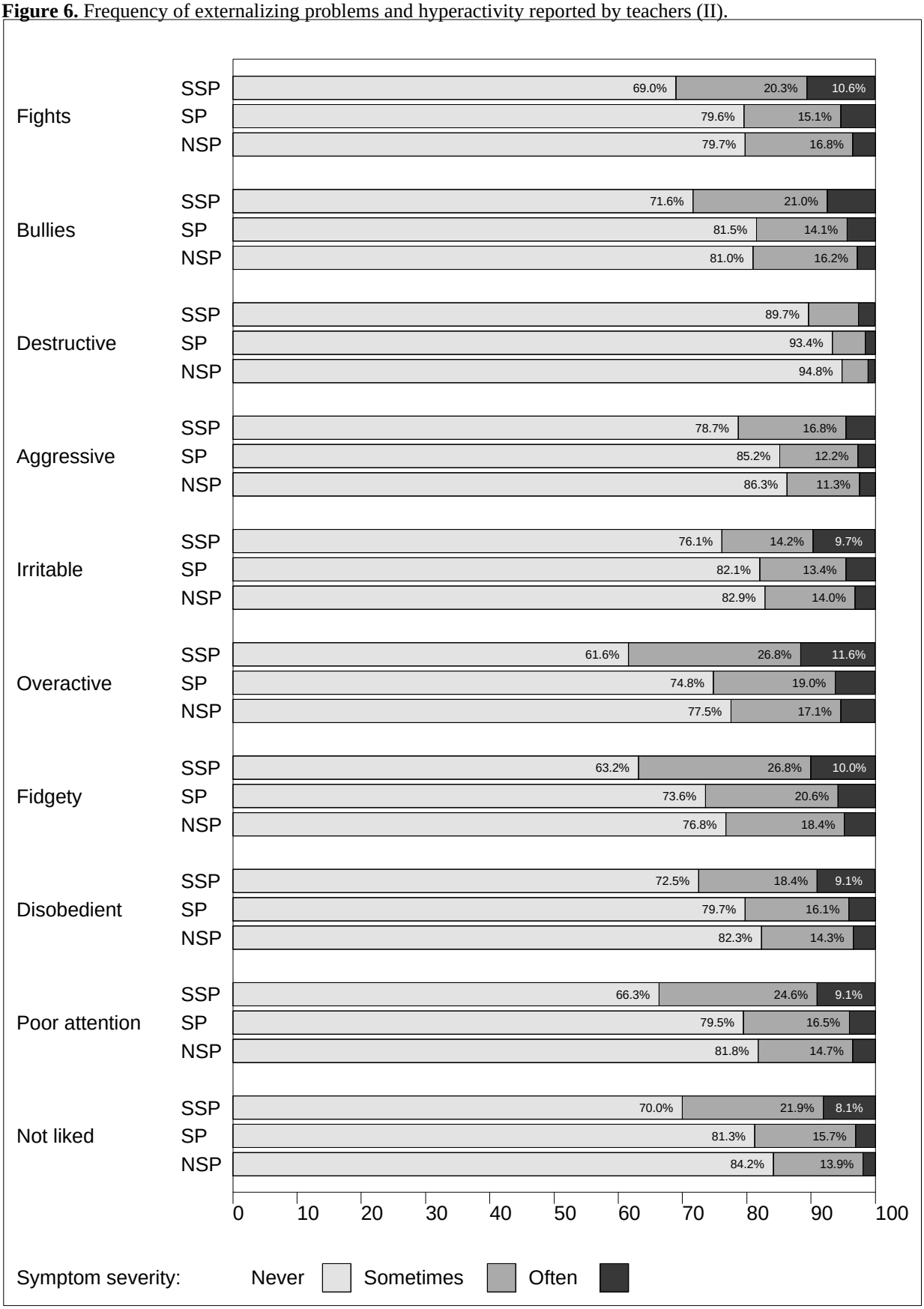
Figure 5. Mental health status reported by parents (I).



NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

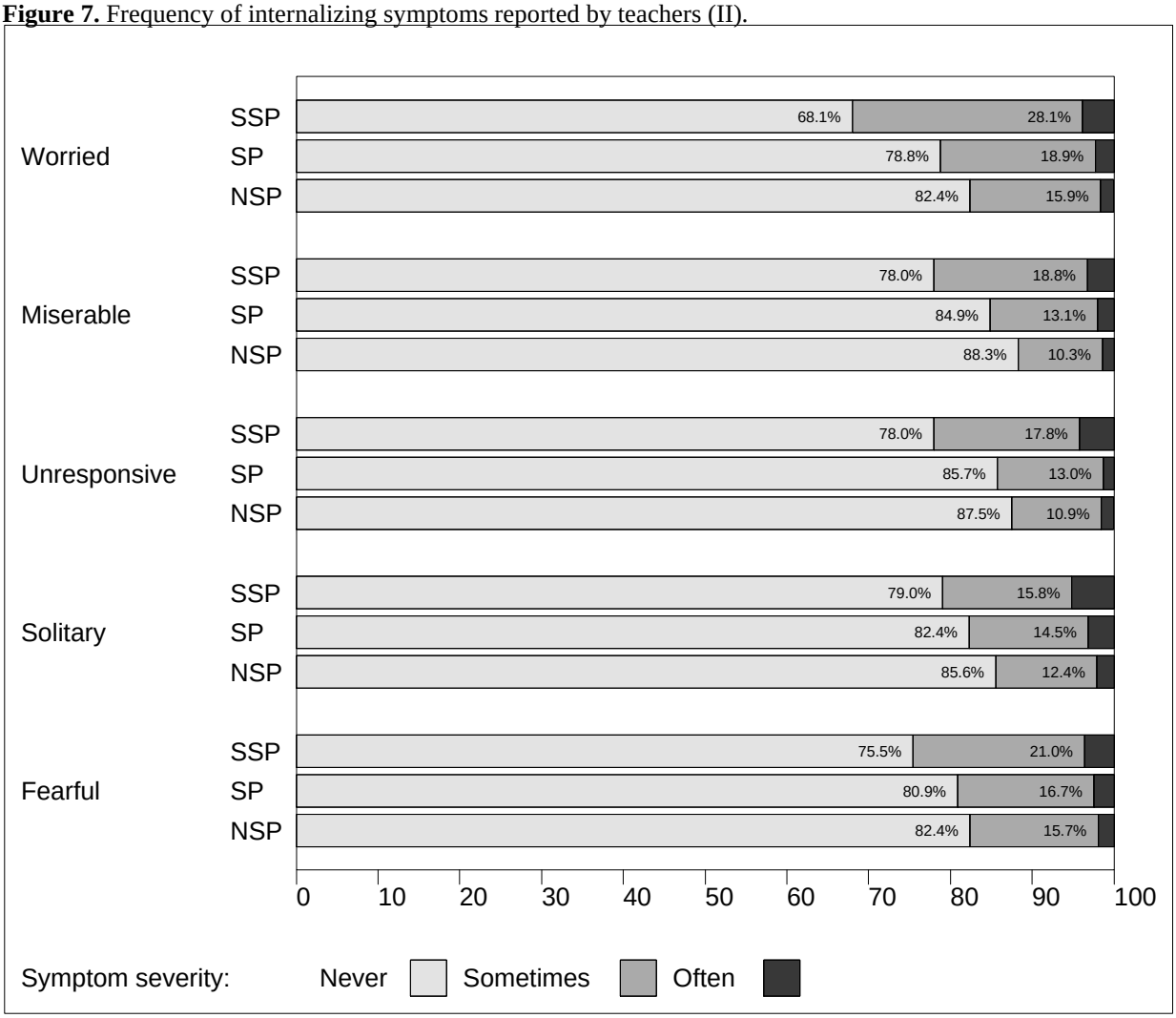
Both child- and parent-reported sleep problems were related to a broad range of mental health problems reported by teachers. The more severe the sleep problems, the higher the frequency of psychiatric symptoms. The association was strongest for hyperactivity, inattention and conduct problems (Figure 6), as well as for emotional problems (Figure 7). Many of these problems were almost two times more prevalent in children with severe sleeping problems than in those without any sleep complaints. Children with poor sleep were also 2.5-fold more likely to be bullied than others.

Figure 6. Frequency of externalizing problems and hyperactivity reported by teachers (II).



NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

Figure 7. Frequency of internalizing symptoms reported by teachers (II).



NSP no sleep problems, SP sleep problems, SSP severe sleep problems.

The mean total RB score was 3.61 in those without sleep complaints and 6.03 in those with severe sleep problems ($p<0.01$). The difference was larger in boys (4.91 vs. 7.25) than in girls (2.31 vs. 3.90) ($p<0.01$ for both). A deviant total score (over 9) was also more frequent in children with severe sleeping difficulties than in others. The respective odds ratio was 2.45 (95% CI 1.85–3.25) (II).

The incidence of significant psychiatric symptoms (indicated by deviant RB subscale scores) was higher in all children with sleep disturbances, but especially in those with severe sleep problems. Any sleep disturbances in both boys and girls significantly increased risk for emotional and behavioural problems, but not for hyperactivity and school attendance problems (Table 7).

Table 7. Unadjusted odds ratios for psychiatric problems (reported by teachers) in children with any sleep disturbances (II).

	Boys OR (95% CI)	Girls OR (95% CI)
Internalizing symptoms	1.86 (1.35-2.56)	1.51 (1.00-2.32)
Externalizing symptoms	1.52 (1.14-2.02)	2.14 (1.11-4.10)
Hyperactivity	1.05 (0.77-1.44)	0.82 (0.37-1.84)
School attendance problems	1.25 (0.79-2.00)	1.60 (0.99-2.58)

Severe sleep problems in boys significantly increased risk for all psychiatric problems, from 1.7- to 3-fold, and in girls they increased risk for behavioural problems almost 4-fold, and emotional problems 3-fold. Hyperactivity and school refusal were not associated with sleep problems in girls (Table 8). Children's reports of sleep disturbances were more predictive than parental reports of teacher-reported externalizing problems and school refusal, while parental reports were more predictive of hyperactivity (II).

Table 8. Unadjusted odds ratios psychiatric problems (reported by teachers) in children with severe sleep disturbances (II).

	Boys OR (95% CI)	Girls OR (95% CI)
Internalizing symptoms	2.37 (1.54-3.67)	2.83 (1.54-5.19)
Externalizing symptoms	1.74 (1.15-2.64)	3.93 (1.63-9.50)
Hyperactivity	2.03 (1.36-3.03)	0.49 (0.07-3.55)
School attendance problems	3.05 (1.80-5.18)	1.32 (0.53-3.31)

When significant background factors were taken into account, logistic regression models showed that all sleep problems were linked to both internalizing and externalizing problems. Severe sleeping problems were strongly associated with all subtypes of psychiatric problems (Table 9).

Table 9. Adjusted odds ratios for psychiatric problems (reported by teachers) in children with severe sleep disturbances (II).

	OR (95% CI)
Psychiatric disturbance	2.45 (1.85-3.25)
Internalising symptoms	2.74 (1.84-4.13)
Externalising symptoms	2.44 (1.59-3.75)
Hyperactivity	2.02 (1.30-3.13)
School attendance problems	2.53 (1.45-4.41)

The follow-up study showed that parental reports of sleep problems at age 12 were significantly linked to deviant internalizing score and anxiety/depression score. Children's reports of current sleep problems, on the other hand, were associated with higher total score as well as higher scores in emotional, social, thought and delinquent subscales (Table 10).

Table 10. Unadjusted odds ratios for psychiatric symptoms (reported by teachers) in children with parent- or self-reported sleep disturbances (III).

Deviant psychiatric symptom	Parent-reported sleep problem OR (95% CI)	Child-reported sleep problem OR (95% CI)
Total	1.73 (0.86-3.50)	2.04 (1.30-3.19)
Internalizing	2.46 (1.32-5.00)	1.93 (1.24-2.99)
Externalizing	1.58 (0.82-3.06)	1.38 (0.90-2.13)
Withdrawn	1.08 (0.25-4.75)	0.92 (0.31-2.74)
Somatic	0.87 (0.26-2.92)	1.81 (0.96-3.38)
Anxious/depressed	2.86 (1.11-7.34)	4.34 (2.23-8.43)
Social	1.24 (0.36-4.23)	5.12 (2.52-10.39)
Thought	1.02 (0.23-4.49)	2.51 (1.18-5.37)
Attention	3.49 (0.69-17.71)	0.43 (0.06-3.41)
Delinquent	0.46 (0.60-3.44)	2.08 (1.00-4.35)
Aggressive	0.75 (0.17-3.23)	1.79 (0.92-3.49)

Persistent sleep problems were also related to significant psychiatric symptoms at school, but the odds ratios were not much higher than those for current sleep disturbances. In fact, the symptom profile of children with persistent sleep problems was very similar to that of self-reported current problems. Only the risk for attention problems was higher in children with persistent problems (OR 3.08) than those with current problems (OR 0.43), although neither was significant (Table 11).

Table 11. Unadjusted odds ratios for psychiatric morbidity (reported by teachers) in children with persistent sleep disturbances (III).

Deviant psychiatric symptom	Persistent sleep problem OR (95% CI)
Total	2.21 (1.17-4.16)
Internalizing	1.91 (1.04-3.52)
Externalizing	1.61 (0.88-2.95)
Withdrawn	0.53 (0.07-4.11)
Somatic	1.74 (0.69-4.37)
Anxious/depressed	4.44 (1.90-10.38)
Social	5.85 (2.40-14.24)
Thought	2.07 (0.67-6.43)
Attention	3.08 (0.59-16.17)
Delinquent	1.72 (0.56-5.23)
Aggressive	1.77 (0.65-4.83)

Logistic regression analysis furthermore revealed that deviant total score at age 12 was significantly dependent on previous internalizing symptoms (OR 1.47), externalizing symptoms (OR 1.83), hyperactivity (OR 2.10) and current sleep disturbances (OR 2.45), but not on persistent sleep problems (Table 12). Deviant internalizing score was related to previous internalizing symptoms (OR 1.50) and current sleep disturbances (OR 2.92). Again, persistent sleep disturbances did not reach statistical significance, although the OR was slightly increased. Deviant externalizing problems were unrelated to the presence of current or previous sleep disturbances but were related to previous behavioural problems (OR 2.04), hyperactivity (OR 2.07) and school refusal (OR 1.49).

Table 12. Logistic regression model to predict symptomacity (reported by teachers) in children at the age of 12 years (III).

	Deviant total score OR (95% CI)	Deviant internalizing score OR (95% CI)	Deviant externalizing score OR (95% CI)
Current sleep disturbance	2.45 (1.20-4.99)	2.92 (1.58-5.38)	0.97 (0.54-1.76)
Previous sleep disturbance	0.92 (0.46-1.85)	0.78 (0.43-1.43)	1.56 (0.82-2.94)
Persistent sleep disturbance	2.18 (0.89–5.33)	1.82 (0.83-3.97)	1.80 (0.84-3.83)

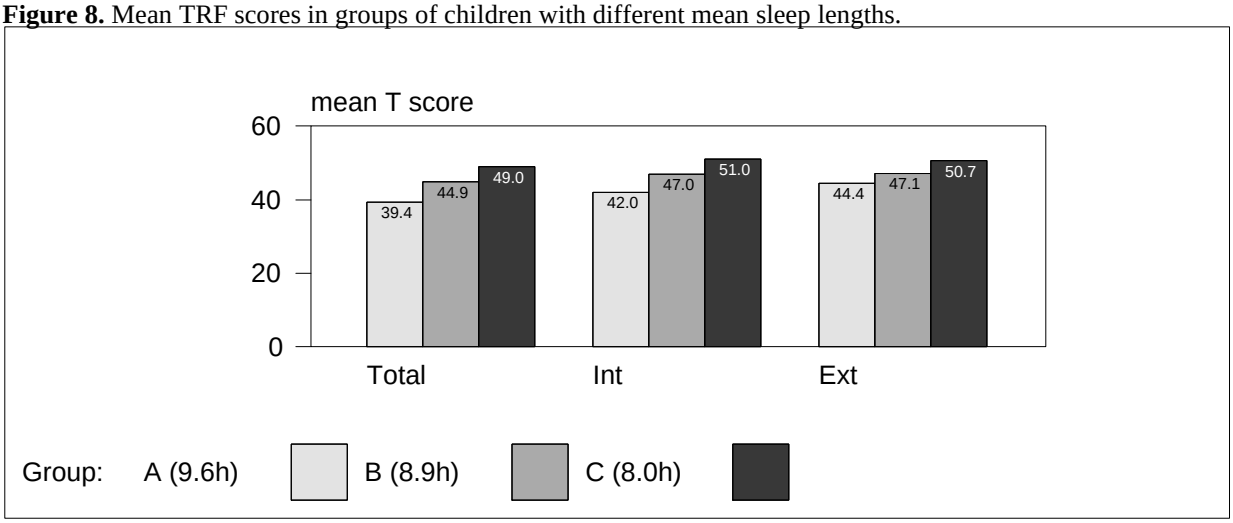
7.4 Actigraph-based sleep estimates and psychiatric symptoms

The actigraph-measured parameters describing sleep quality (sleep latency, sleep efficiency) were associated with some indicators of psychiatric symptoms. Although they were not correlated with the total score or any of the narrow-band symptom scores in the TRF, the six children who scored above the cut-off limit for the externalizing symptom T score in the TRF had significantly lower sleep efficiency than the other children (90.5% vs. 93.6%, $p=0.05$). Sleep latency was significantly correlated with aggressive behaviour ($r=0.33$, $p<0.05$), delinquent behaviour ($r=0.31$, $p<0.05$) and attention problems ($r=0.34$, $p<0.05$) in the CBCL, but sleep efficiency was not related to any elevated scores in the CBCL (IV).

7.5 Sleep duration and psychiatric symptoms

Shortened sleep duration assessed by actigraphs was significantly associated with behavioural problems and depression in the TRF (IV). Children were divided into three groups based on mean sleep duration: first group (n=16) 9 h 36 min, second group (n=24) 8 h 54 min and third group (n=9) 8 h. The mean TRF symptom scores in these groups were consistently higher the less the children slept (Figure 8). The differences were significant even when the two important confounders (age and season) were controlled (total score $p<0.01$, externalizing score $p<0.01$, internalizing score $p=0.03$). Children who scored above the TRF cut-off point slept less than the other children (8 h 28 min vs. 9 h 4 min, $p=0.02$). Sleep duration was also correlated with some of the narrow-band symptoms scores in the TRF, but not in the CBCL. These scores were aggressive behaviour ($r=-0.35$, $p<0.01$), delinquent behaviour ($r=-0.53$, $p<0.01$), attention problems ($r=-0.32$, $p=0.03$), social problems ($r=-0.38$, $p=0.01$) and somatic problems ($r=-0.51$, $p<0.01$).

Figure 8. Mean TRF scores in groups of children with different mean sleep lengths.

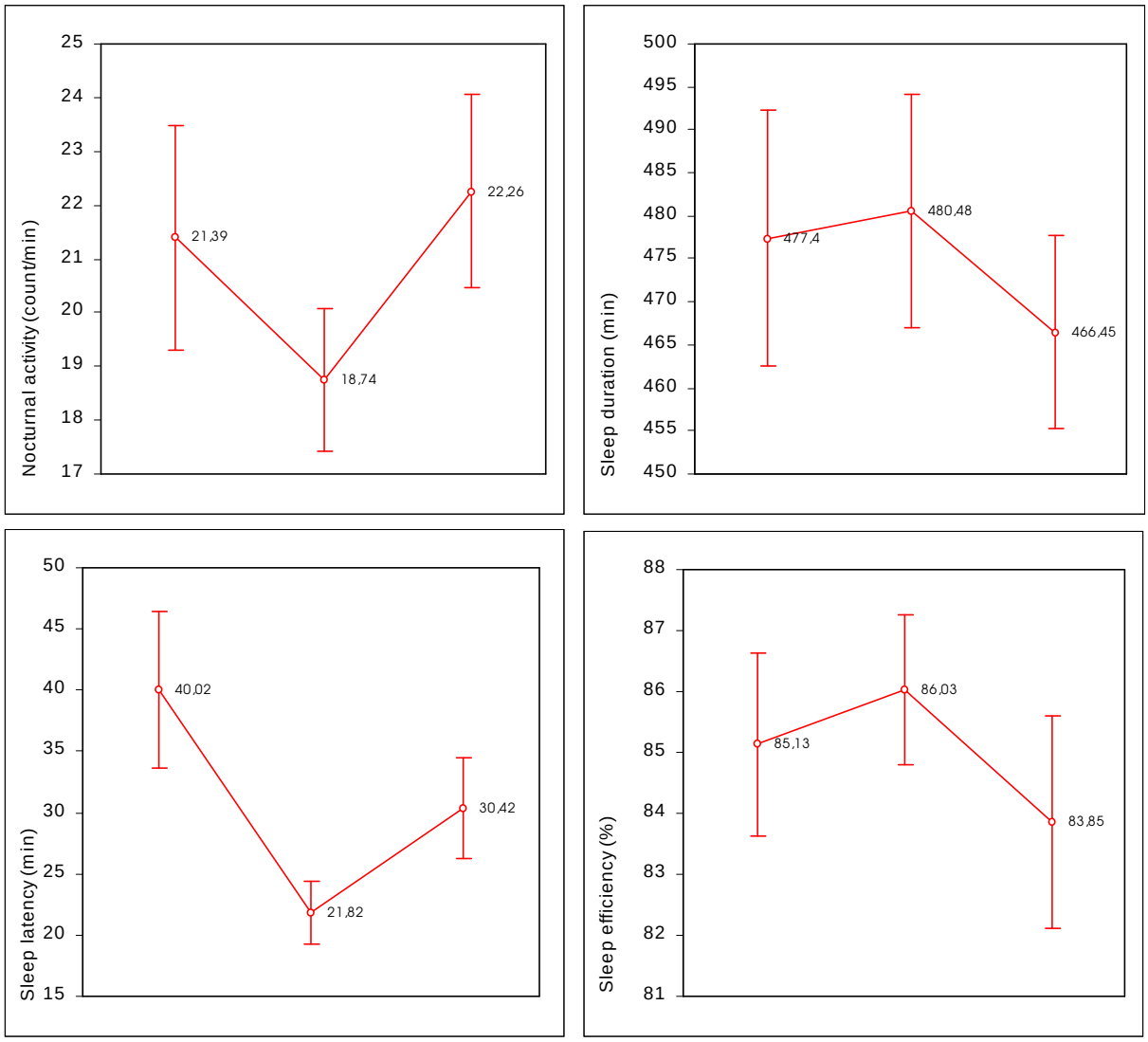


Tot Total T Score, Int Internalizing T score, Ext Externalizing T score.

7.6 Melatonin treatment in children with Asperger syndrome

Melatonin was found to be effective in treating sleep disturbances in Asperger children. All children subjectively reported that their sleep quality had improved “very much” or “rather much”. The objectively measured sleep parameters also improved. Mean nocturnal activity and sleep latency decreased significantly during the melatonin treatment period ($p=0.04$ and $p<0.01$, respectively), but no significant changes were found in sleep efficiency and total sleep duration. The number of awakenings increased slightly ($p=0.05$). Discontinuation of the medication led to a significant decrease in sleep duration ($p=0.03$), nocturnal activity rose again ($p=0.02$) and sleep latency and efficiency deteriorated somewhat ($p=0.06$ for both). Melatonin treatment had a significant overall effect on all values, except for the awakenings, as shown by the repeated measurement ANOVA model (Figure 9).

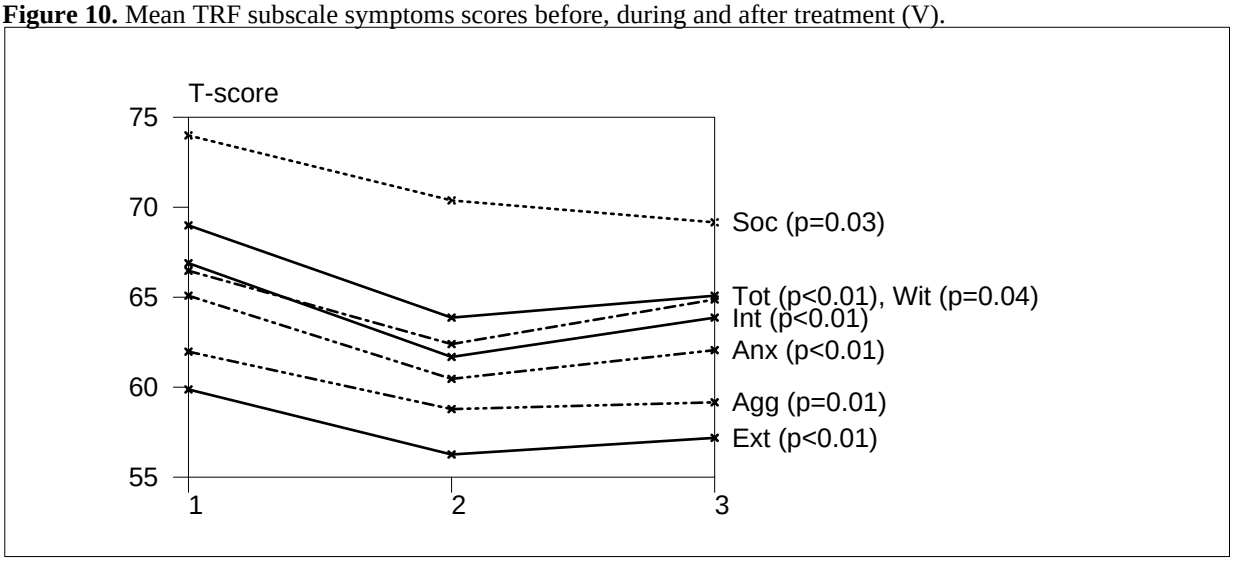
Figure 9. Effect of melatonin on actigraph-measured sleep parameters (V).



Clear inter-individual differences were present in the effectiveness of melatonin, with some cases responding better than others. During the treatment period total sleep duration increased in five cases, remained the same in nine cases and decreased in three cases. Two cases displayed a notable improvement in sleep efficiency, but no significant changes were found in the remainder. After the treatment period, sleep latency increased in most of the cases and remained steady or decreased slightly in the rest of the cases. Ten children experienced a significant reduction and two an increase in total sleep duration. Sleep efficiency deteriorated in five cases, but no changes were found in the rest of the children.

Most of the psychiatric scores in the CBCL showed significant improvement during melatonin treatment (Figure 10). Symptoms of depression, anxiety and withdrawn, in particular, decreased considerably, and behavioural measures decreased slightly. Scores reflecting attention problems and delinquency were not significantly affected by the treatment. Discontinuation of medication led to a slight increase in most scores, but these differences were mostly insignificant.

Figure 10. Mean TRF subscale symptoms scores before, during and after treatment (V).



Agg Aggressive, Anx Anxious/depressed, Ext Externalizing, Int Internalizing, Soc Social, Tot Total, Wit Withdrawn.

8. DISCUSSION

8.1 Prevalence

Sleep disturbances were prevalent in children aged 7-12 years. Up to 30% of children had some sleep-related problems, and in 5% the problems were severe. Less than half of the children had no sleep problems at the ages of 8 and 12 years. Most of the severe problems were reported by the children themselves. Insomnia, especially sleep onset difficulty, was the most typical problem. These results are rather consistent with many previous studies, but two earlier studies, using the same parental questionnaires as used here, found lower prevalence rates to ours: 8.8% in children aged 11-years (Johnson et al. 2000) and 6.1% in children aged 6-12 years (Liu et al. 2000), while one study reported a similar rate: 22% in children aged 5 and 11 years (Pollock 1994). Other studies have reported rates of 6% (Rona et al. 1998), 27% (Blader et al. 1997), 41% (Archbold et al. 2002) and 43% (Kahn et al. 1989b). Severe problems have been described in 1-5% of children (Kahn et al. 1989b; Rona et al. 1998), and significant insomnia in 18% (Archbold et al. 2002). The reported rates are largely heterogeneous, likely the probable consequence of varying definitions for a "sleep disturbance" and different screening instruments.

The proportion of long-term sleep disturbances of all sleep disturbances was high. The risk for long-term problems was 1.8-fold in children with sleeping problems at the age of 8 as compared with those without any sleep complaints. One third (33.3%) of children with a sleep disturbance at age 8 still had one at age 12. Similarly, sleep problems at the age of 5 have been reported to predict problems at the age of 10 (Pollock 1994). In toddlers 41% (Zuckerman et al. 1987) and in adolescents 48.5% (Morrison et al. 1992) of sleep disorders have been found to be persistent. Interestingly, persistence of sleep problems appears to be closely related to mothers' affective illness (Stoleru et al. 1997). In one study, mothers' depression was the only significant predictor of persistent sleep problems in toddlers (Zuckerman et al. 1987). Unfortunately, in our present study, we could not control for psychiatric morbidity in family.

The epidemiological study was based on a large representative sample with a very good response rate, thus providing valid information on children's psychiatric symptoms. One shortcoming of the study was, however, the lack of precise definitions in the sleep questions. As a consequence, the reported prevalence rates do not necessarily represent clinically significant problems. Another limitation was that we were unable to control for long-term medication and chronic illness. Nevertheless, the probability of these confounding factors being present in children is relatively low, and thus their effect on results is small.

8.2 Sleep disturbances and psychiatric symptoms

Relationships between sleep disturbances and psychiatric symptoms were assessed. As hypothesized, sleeping difficulties were associated with a large range of teacher-rated psychiatric symptoms, especially externalizing and internalizing symptoms and hyperactivity. Moreover, poor sleep quality was related to learning difficulties, school attendance difficulties

and somatic symptoms. Clear gender differences were present in psychiatric symptoms. Boys displayed more hyperactivity and school attendance problems than girls, while girls had more externalizing problems than boys. An important finding was that treatment of sleep disturbances was followed by a small but systematic decrease in emotional and behavioural symptoms. Theoretically, this was not surprising because sleep deprivation is known to have many adverse effects on well-being.

The association between sleep and psychiatric symptoms was recognized long ago (Dahl et al. 1990a; Reite 1998). Several sleeping difficulties, such as restless sleep, nightmares, night terrors, reluctance in going to sleep and sleep-related fears have been reported to be more prevalent in children referred to psychiatric clinics than in others (Simonds et al. 1984). Sleep onset problems have also been found to be related to psychiatric disorders in general, but risks were not assessed separately for different diagnoses (Blader et al. 1997). In a Finnish sample, children with mental health problems slept alarmingly little and simultaneous displayed sleep onset problems (Järventie 1999).

Internalizing problems, such as mood and anxiety disorders, have been linked with sleep disturbances in several studies (Gregory et al. 2002; Johnson et al. 2000; Manni et al. 1997; Sadeh et al. 1995b; Stoleru et al. 1997). The risk for significant internalizing symptoms has been reported to be as high as 7-fold among children with sleeping difficulties as compared with those without sleep complaints (Johnson et al. 2000). Although subjective complaints of sleeplessness are most typical (Ryan et al. 1987), sleep abnormalities have also been found using PSG, especially in those with suicidality, but the findings have not been consistent (Dahl et al. 1990a; 1990b; 1991b; Goetz et al. 1991). Sleep disturbance is in fact a traditional hallmark of depression in both children and adults.

The association between sleep and externalizing symptoms is also consistent with other studies (Chervin et al. 2003; Coble et al. 1984b; Gregory et al. 2002; Smedje et al. 2001). Conduct problems, for example, were 2-4 times more frequent among children with sleep-disordered breathing and periodic leg movement syndrome than in others (Chervin et al. 2003). A PSG-based analysis indicated that children with conduct disorders slept less, had lower sleep efficiency and had alternations in REM sleep characteristics (Coble et al. 1984b). Interestingly, we found externalizing problems to be strikingly prevalent among girls with sleep disturbances, which warrants future studies.

The relationship between hyperactivity and sleep has recently received much scrutiny among researchers, and many authors have reported increased rates of sleep disturbances in children with ADHD (Chervin et al. 1997; 2002a; Dagan et al. 1997; Dahl et al. 1991a; Marcotte et al. 1998; Owens et al. 2000a). Children with ADHD have, for example, more parent-reported bedtime resistance, sleep onset problems, sleep-related anxiety, daytime sleepiness, parasomnias and shorter sleep duration than control children (Owens et al. 2000a). However, some authors have failed to show similar relationships, and have suggested that these findings might be related to medication status or comorbidity (Corkum et al. 1998; 1999; 2001; Lecendreux et al. 2000; Mick et al. 2000). Moreover, many authors have reported increased rates of externalizing symptoms and hyperactivity among children with OSAS (Ali et al. 1996; Chervin et al. 2002a; Gozal 1998; Gozal et al. 2001; Lewin et al. 2002; Pillar et al. 1998b), and some have reported increased scores for hyperactivity in children with various sleeping difficulties (Smedje et al. 2001). Although we did not assess the presence of ADHD/OSAS, an

association was present between sleep disturbances and an increased prevalence of hyperactivity.

An interesting finding was the association between school attendance problems and severe sleeping difficulties. It has been previously emphasized that while some school-refusal children have clear psychiatric disorders, the majority do not. However, in one study all children with school refusal syndrome and no psychiatric disturbances were diagnosed as having a sleep-wake rhythm disturbance, suggesting that school refusal was closely related to the desynchronization of circadian rhythm (Tomoda et al. 1997). Therefore, some of the children with comorbid sleeping difficulties and school attendance problems may suffer from circadian rhythm disorders such as delayed sleep phase syndrome.

Both current and long-term sleep disturbances were associated with an increased level of psychiatric symptoms, but in contrast to what we expected, the long-term problems were no more harmful than current problems. Similar results have been recently reported by other investigators. No significant connection between persistent sleep problems and later psychiatric symptoms (Stoleru et al. 1997), nor sleep disturbances at age 6 and depression at age 11 (Johnson et al. 2000) were not found. However, a recent study did reported that sleep problems at 4 years of age were predictive of behavioural and emotional problems in mid-adolescence (Gregory et al. 2002), but the authors did not control for current sleep disturbances, which is a major shortcoming that can completely explain this discordant finding. Generally, the lack of connection between long-term sleep problems and subsequent psychiatric problems in children is in disagreement with findings in adults; sleep impairment appears to precede major depression in young adults (Breslau et al. 1996; Ford et al. 1989).

In the field of psychiatry, sleep disturbances have traditionally been regarded as one manifestation of underlying psychiatric disturbances. As this study was cross-sectional in nature, drawing direct conclusions about causal relationships between sleep and well-being is not possible. In any case, the relationship is likely to be bi-directional (Dahl 1998). Sleep can obviously be affected by a variety of distressing factors, such as stress, social problems and family conflicts, as well as by underlying psychiatric and/or somatic illnesses. Sleeping difficulties are a common co-morbidity in depression, anxiety and post-traumatic stress disorder (Dahl et al. 1990a). On the other hand, sleep impairment can also influence mood and behaviour. Children with OSAS, for example, are reported to display more hyperactivity than control children (Chervin et al. 2001a), and long-term decreases in cognitive performance and irreversible neurocognitive deficits occur in children who have experienced sleep-disordered breathing during critical stages of brain development (Gozal et al. 2001). One possible linking mechanism between sleep and psychiatric status could therefore be sleep deprivation, supported by the association between short sleep duration and psychiatric symptoms (IV) and the amelioration of daytime psychiatric symptoms after melatonin treatment (V). However, as summarized by Dahl (1995) “it is often quite difficult to sort out the components of these problems (insomnia, hypersominia, excessive fatigue) with respect to decreased motivation, delayed circadian phase and the depressive symptomalogy”.

Some limitations in our study are worth noting. We could not control for maternal psychiatric morbidity, and this may have had an effect on results. Children’s self-reports have been associated with concurrent anxiety and mood problems, while (affectively ill) mothers’ ratings were unrelated to these symptoms (Stoleru et al. 1997). It is therefore possible that depressed mothers notice less problems in their children. Moreover, when parents suffer from sleep

deprivation, it can cause dysfunction in family life, which can further affect the psychiatric status of the child (Smedje et al. 1998). It is also important to note that although some children with sleep disturbances have psychiatric symptoms, others do not. A more detailed analysis of sleep quality might reveal subtypes of children especially prone to the adverse effects of poor sleep.

To conclude, psychiatric symptoms and sleep disturbances are closely intertwined. However, most of the sleep problems in children are mild and not strongly associated with psychiatric measures. Sleep disturbances can either reflect underlying emotional or psychological disturbances, or independently contribute to the development of these symptoms, in which case, the linking mechanism is presumably sleep deprivation. To confirm this, prospective follow-up studies, experimental studies, and treatment studies are needed. Even if the sleeping difficulty is a secondary problem, it may be a good indicator of psychiatric problems in clinical work. As suggested by Dahl and Puig-Antich (1990a), the possibility of depression should be assessed whenever a child presents with significant sleep complaints.

8.3 Sleep duration

The shorter the duration of sleep, the more psychiatric symptoms in general, and internalizing and externalizing symptoms in particular, children had. This finding is interesting because it may support the hypothesis that a significant proportion of the psychiatric symptoms associated with reports of poor sleep is related to the underlying sleep deprivation. Similar findings have been made in other studies. For example, children with conduct problems (Coble et al. 1984b) and high neuroticism scores (Gau 2000) are reported to sleep less than controls. Adolescents with shorter sleep duration reported more depression and tiredness than other children (Wolfson et al. 1998). Dahl (1996) concluded that lack of sleep manifests in children differently than that of adults; adults suffer mostly from tiredness, while children display more externalizing symptoms, such as the inability to stay seated and to concentrate, than just tiredness.

Comparison of previous cross-sectional studies suggests that children today sleep less than in the past (Tynjälä et al. 2002). Finnish children also seem to sleep approximately one hour less than their peers elsewhere else in Europe (Tynjälä et al. 1993b). Many children likely suffer from chronic sleep deprivation. An interesting question is whether this could eventually lead to an increase in children’s psychiatric symptoms. Another important question is how much sleep is enough? Because inter-individual differences in sleep requirements are large, it is impossible to give simple guidelines that would suit every child. Determining whether a child gets adequate sleep requires both direct and indirect information on sleep quality (e.g. symptoms of sleep deprivation, spontaneous awakening in the morning, tiredness, more sleep on weekends than on weekdays). Experimentally, total sleep time might be prolonged by one hour, and if this induces beneficial changes in daytime behaviour, the child has evidently previously slept too little.

Some public discussion has centred around whether school start times are too early. Generally, children appear to have increased daytime sleepiness in mid-puberty even in the absence of changes in total sleep duration (Carskadon et al. 1980), suggesting that biological need for sleep does not diminish during adolescence (Carskadon et al. 2002). The reduced sleep time

and delayed circadian rhythm in adolescence seem to be related to environmental factors (Carskadon et al. 1980; Gau et al. 2003). For these reasons children might be more prone to sleep deprivation in mid-puberty than at other ages and it has been suggested that psychosocial factors and changes in bioregulatory systems controlling sleep limit teenagers' capacity to adapt to early school schedule (Carskadon et al. 1998). Early school start times have indeed been associated with increased sleep deprivation and daytime sleepiness and poorer school performance (Carskadon et al. 1998). Children whose school started early complained significantly more about being tired throughout the day and having attention and concentration difficulties than those with a later school start time (Epstein et al. 1998). However, more studies are needed before any firm conclusions can be made about the effect of school start time.

8.4 Child-parent agreement and setting a diagnosis

As was hypothesized, a large disagreement was present between children's and parents' reports of sleep disturbance. Older children, in particular, were less likely to agree with their parents. This finding of discrepant reports is not new. One study reported that conditional probabilities (C|P and P|C) for the item "refusal to go to sleep without a major attachment figure" were only 0.44 and 0.27, respectively, while corresponding figures for the item "insomnia or hypersomnia" were 0.72 and 0.33 (Bird et al. 1992). Moreover, low kappa values of agreement for sleep disturbance were reported for all informant pairs: child-father 0.20, child-mother 0.02, father-mother 0.17. Another study reported a slightly higher agreement rate between parents' and children's reports of sleep onset problems, the kappa value was 0.49 (Barrett et al. 1991). The kappa values between a clinician's ratings and family members have also been low: clinician-child 0.36, clinician-father 0.42, clinician-mother 0.23 (Ivens et al. 1988).

We found that the conditional probabilities were related to the types of sleep disorders (varied from 0.38 in night terrors to 0.25 in too early awakening). Agreement tended to be higher for problems that were easier for parents to notice. Another study had similar findings: child-parent disagreement was largest on items related to insomnia such as sleep onset difficulties (parent- vs. child-reported prevalence rates being 4.9% and 26.2%) and night wakings (4.6% vs. 14.6%) (Owens et al. 2000c). These findings suggest that the disagreement is at least to some extent related to parental awareness.

We also found that children's self- reports of sleep problems correlated slightly more than parental reports with teacher–rated symptoms. Although the absolute difference was not large, it was consistent throughout the measures, suggesting that the children's reports of sleep quality are useful and do represent true (sleeping) problems. Respective to this, another recent investigation found low correlations between parents' reports of sleep disturbances and teachers' reports of behavioural problems, but a higher concurrence between children's self-reports and teachers' observations (Owens et al. 2000c).

One limitation in this study is that the intensity (frequency, duration, exact type) of the reported sleep disturbances was not explicitly defined. Hence, the discrepancy in the reports by children and parents could have been partially caused by differences in wording of the questions. These findings therefore require confirmation by studies with more detailed sleep questionnaires,

similar wording in questions for parents and children and objective measurements of sleep quality. Reasons for child-parent disagreement should also be evaluated.

In the field of paediatrics, parents are typically considered optimal informants. However, parents' abilities to interpret children's behaviour are not equal (Barrett et al. 1991; Bird et al. 1992; Edelbrock et al. 1986; Grills et al. 2003; Ivens et al. 1988; Jensen et al. 1999; Puura et al. 1998). There are a number of factors that can potentially contribute to the lack of correlation between children's and parents' reports. First, poor communication between the child and the parent is likely to decrease correspondence. Older children may not complain about problems with sleep to their parents. Second, assessment of their child's sleep quality can be difficult for parents because they may be unaware of how the child sleeps due to separate bedrooms. Third, parents' sensitivity to note various psychiatric problems is known to be affected by the nature or the quality of the symptom (Bird et al. 1992; Ivens et al. 1988). Their ability to adequately report internalizing symptoms, for instance, is low (Puura et al. 1998). Parents' stress or psychiatric morbidity can also hinder them from recognizing various symptoms in their children (Stoleru et al. 1997). Fourth, young children may be unable to reliably report about on such abstract issues as sleep. Their ability to understand the questions or to retrospectively report frequencies or times may be limited. The child's estimation of sleep quality may also be erroneous in the sense that the reported sleep problems may actually represent tiredness, sleep-related fears and other such issues.

The multi-informant approach is commonly applied in child psychiatry. However, as discussed in Section 5.4, when two or more informants are simultaneously used, the problem of how to combine discrepant information arises. Each of the alternatives has its own pros and cons. Although children themselves may be best aware of their sleep quality, determining whether a child is able to give valid information concerning herself/himself and how precise their estimates are is difficult. When in doubt about the child's ability to provide reliable information, parental reports should be considered primary. On the other hand, while parents are likely to be more exact and perhaps also more objective, the number of false-negatives can increase when the assessment is based only on parental reports. Naturally, this does not mean that the parent's report is unhelpful or not indicated, but rather that it should be combined with the child's own assessment. Owens et al. (2000c) pointed out, that problematic behaviour described by a parent may be particularly relevant in terms of further clinical evaluation. Parental perception has, after all, a strong influence on whether further clinical evaluation or treatment is sought.

To conclude, controversy over how children's sleep disturbances should be optimally screened or defined exists. For research purposes, objective measurement methods should be preferred whenever possible, but if sleep quality is investigated only by biological or physiological measures, one essential dimension of sleep would be ignored: the subjective experience of sleep quality. This warrants the use of more informants to avoid misclassification bias. When assessing children's sleeping disorders, both children's and parents' reports should be considered equally important, especially with older children, because parental reports often do not correlate well with children's own perceptions of the severity or even the existence of a problem. Objective methods, such as polysomnography and actigraphy, are also important in paediatric sleep research. Different screening methods should be viewed as complementary – not competing. As summarized by Lockley et al. (1999) "Even though all these methods attempt to measure sleep, they measure different things, i.e. subjective recollection of sleep, motor or electrical activity of the brain". If we were to use objective methods alone and assess

only features that can be objectively measured or quantified, many significant and interesting aspects of the sleep phenomenon would be overlooked.

8.5 Treatment

We found melatonin to be useful in treating severe sleep disturbances in children with Asperger syndrome. This is consistent with previous reports of melatonin being effective in paediatric patient populations (Etzioni et al. 1996; Horrigan et al. 1997; Jan et al. 1999; Jan et al. 1996; Jan 2000; Lapierre et al. 1995; Masters 1996; Miyamoto et al. 1999; Pillar et al. 1998a; Pillar et al. 2000; Robertson et al. 1997; Zhdanova et al. 1999). It appears to be effective also in autistic children (Hayashi 2000; Lord 1998). Some side-effects of melatonin, such as mild tiredness, awakening problems and headache, were noted during the first treatment days. One child dropped out because of the side effects. This is in contrast to most other studies, where no side-effects have been reported even in large patient populations (Jan et al. 1996). Moreover, the possibility of long-term side-effects can not be ruled out on the basis of these results (Arendt 1997).

The main shortcomings of this study were the small sample size and the lack of randomization. Therefore generalization of findings requires some caution. Because AS is a rare disorder, the target population was small, especially as only the most difficult cases were eligible. Further studies are needed the demonstrate the efficacy of melatonin in those with milder sleep disturbances and in other patients. Although several important confounding factors, including medication and somatic illness were controlled, no melatonin measurements were made, and thus we could not assess whether issues related to melatonin, such as absorption and secretion, had an impact on treatment efficacy. However, the role played by melatonin secretion would have been difficult to interpret for two reasons. First, the rate of melatonin secretion is known to vary largely even between healthy individuals (Laakso et al. 1990). Second, both relative/absolute melatonin deficiency (Akaboshi et al. 2000; Etzioni et al. 1996) and increased melatonin concentrations in children with fragile X have been associated with severe sleeping difficulties (Gould et al. 2000).

From the clinical point of view, sleep problems in AS are often persistent, severe and difficult to treat. Behavioural methods tend to be unsatisfactory or insufficient in treating children with autistic spectrum disorders (Anders et al. 1997; Robertson et al. 1997). Children with AS are known to display various symptoms, such as behavioural, attention and social problems (Gillberg et al. 2000), and our study suggests that these may be aggravated if a sleep disorder is present. Melatonin might offer an alternative treatment method, if its effectiveness can be proven in randomized blinded studies. Treatment of sleep disturbances should be provided for all children with significant sleep complaints to prevent the occurrence of sequelae. Individuals in risk populations should receive special consideration since sleep problems can worsen disruptive daytime behaviour, increase parental stress (Patzold et al. 1998; Richdale 1999), and aggravate other symptoms (Richdale 1999). Children with severe disabilities are also known to display more difficult daytime behaviour in association with sleep problems (Wiggs et al. 1999). Treatment may also carry prognostic benefits (Zucconi et al. 2001).

9. FUTURE PROSPECTS FOR SLEEP STUDIES

Many unanswered questions remain in the field of paediatric sleep research.

1. General lack of sleep research in children

Relatively little research has been carried out on school-aged children's sleep. Previous paediatric sleep studies have mostly focused on toddlers and adolescents. These results can not necessarily be extrapolated to all children since the nature and manifestation of sleep disturbances are likely to be different in different age groups.

2. Screening sleep problems

More studies are needed on screening sleep disturbances to enable adequate treatment alternatives to be devised for children's sleep disturbances. Clear cut-off limits should be defined for all age groups and standardized screening questionnaires developed. While children's and parents' reports often tend to disagree, studies assessing the meaning of this finding are rare. Moreover, very limited data are available on how children's and parents' reports of poor sleep quality correlate with results gathered by more objective methods.

3. Relationship between sleep and psychiatric disorders

Although sleeping difficulties are significantly associated with psychiatric symptoms and diminished cognitive performance, it is still an issue of ongoing debate whether they can actually cause particular daytime symptoms. To enlighten this issue, prospective studies, intervention studies and experimental studies are needed.

4. Sleep deprivation

Sleep deprivation appears to be prevalent among children. Despite strong indirect evidence for deleterious effects of sleep deprivation (Randazzo et al. 1998; Steenari et al. 2003) and the likelihood that children do not tolerate sleep deprivation as well as adults, experimental studies are rare. Pursuing this line of investigation may also facilitate our understanding of the nature of the connection between sleep disturbances and psychiatric symptoms.

5. Treatment of sleep problems

Treatments for paediatric sleep disturbances have been investigated very infrequently, and only a handful of randomized studies exist. This is rather surprising, since sleep quality can easily get affected by various environmental factors, including placebo effect. As a consequence of the lack of research in this area, many poorly studied treatment alternatives are currently offered for children.

10. SUMMARY AND CONCLUSIONS

Various sleep-related problems manifest during childhood. Many of these are mild, of short duration and without any noteworthy sequelae. However, some sleeping difficulties occur concomitantly with other problems such as psychiatric disturbances and neurological or somatic disorders. Moreover, sleep disturbances can by themselves have harmful effects on children's development and well-being. Objectives of this project were therefore 1) to evaluate the prevalence of children's sleep problems, 2) to investigate associations between sleep disturbances and psychiatric symptoms and 3) to evaluate the efficacy of melatonin as a treatment alternative for sleep onset problems in children with Asperger syndrome.

The results of these studies are based on three samples. The first comprised a large epidemiological cohort of 8- to 9-year-old children (n=5813), 1290 of whom were followed up over a 4-year period. The children and their parents and teachers filled out standardized child psychiatric questionnaires, including questions on sleep. The second sample consisted of a group of healthy preadolescents (n=61) whose sleep quality and behaviour were evaluated in detail: structured child psychiatric evaluation methods, actigraph measurements and sleep logs were used. The third study was an open trial with 15 children with Asperger syndrome. Actigraph measurements, sleep questionnaires and psychiatric questionnaires were used to monitor treatment effectiveness.

We found sleep disturbances to be prevalent in both boys and girls and their frequency to be more or less unaffected by age. Approximately 32% of 8-year-olds had some form of sleep disturbance, 5% severe sleep disturbances and 12% persistent sleep problems. Most sleep disturbances were more frequent in boys than in girls. Noteworthy is that children's and parents' assessments of sleep quality were largely in disagreement (72%), suggesting that children's own assessment is important in screening for children's sleep disturbances. Poor sleep quality was associated with mental health problems, inferior school performance and somatic complaints. In children sleeping poorly, risk for externalizing problems was 2.44-fold, for internalizing problems 2.74-fold, for hyperactivity 2.02-fold, and for school attendance problems 2.53-fold that of children without sleep complaints. Shorter sleep duration was significantly associated with both behavioural problems and depression. In children with AS, melatonin was effective in treating sleep onset problems. Treatment of sleep disturbance led to improvement of psychiatric symptoms, which worsened again after discontinuation of medication.

In conclusion, sleep-related problems in children appear to be highly prevalent, persistent and associated with scholastic problems, somatic complaints, psychiatric symptoms, especially emotional and behavioural symptoms, and hyperactivity. Although most sleep problems are mild in the sense that they are not correlated with increased psychiatric morbidity, a significant proportion of the children had here severe sleep problems that were linked to psychiatric problems. While cause-effect relationships can not directly be assessed from cross-sectional studies, it is reasonable to hypothesize that in a substantial proportion of children sleep deprivation is a possible linking mechanism between sleep problems and psychiatric symptoms. Alternatively, sleep disturbances may be a manifestation of underlying depression or other somatic disorders.

Several reports have found that sleep problems receive little attention in clinical practice. In a retrospective review of the medical records of 86 children with symptoms of chronic sleep disturbance a mere 16 of 103 sleep problems were discussed, with only 3 of these receiving adequate treatment (Chervin et al. 2001b). Moreover, almost half (47%) of parents (child <38 months) wished for more information on children's normal sleep behaviour (Armstrong et al. 1994). Recent studies have also shown that parents rarely seek help for their child's sleep problems (Stores et al. 1998b). These findings suggest that more effort should be directed at screening sleep problems in clinical work, helping parents to recognize the sleep disturbances and providing adequate guidance for their children when needed.

Because children can be more prone than adults to suffer from the consequences of poor or inadequate sleep, the prevalence of children's sleep disturbances is a cause for concern for parents and educators alike. Both sleep deprivation and sleep disturbances have numerous adverse effects, including mood alternations and decreased cognitive performance. Sleep-related problems can constitute a considerable and growing health problem among children and should thus receive more attention. New investigations should be aimed at developing effective screening instruments and studying treatment options and recommendations, and more resources targeted at the early recognition of sleep-related problems in the paediatric population.

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