



Relationships of Subjective Insomnia and Sleep Duration with Depression, Anxiety, and Pain Problems in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder

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Abstract

Objective:

This study examined the relationships of subjective insomnia and short and long nocturnal sleep duration with depression, anxiety, and pain problems in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods:

A total of 469 children and adolescents (97 girls and 372 boys; age, 6–18 years) who had received a clinical diagnosis of ADHD completed the eight-item Athens Insomnia Scale, Children's Depression Inventory-Taiwan Version, Multidimensional Anxiety Scale for Children-Taiwanese Version, and a questionnaire about sleep duration, pain-related dysfunction, and the severity of perceived pain. Their parents provided information on the children's current ADHD and oppositional symptoms, rated on the abridged Chinese version of the Swanson, Nolan, and Pelham Scale, Version IV. Multiple regression was conducted to examine the relationships of subjective insomnia and sleep duration with depression and anxiety. Logistic regression was applied to examine the relationships of subjective insomnia and sleep duration with pain-related dysfunction and the severity of perceived pain.

Results:

Subjective insomnia was positively associated with depression, anxiety, pain-related dysfunction, and severe perceived pain in the study population. Short nocturnal sleep duration was positively associated with depression, anxiety, and perceived pain. Long nocturnal sleep duration was positively associated with anxiety and perceived pain.

Conclusion:

Insomnia and short and long nocturnal sleep duration are associated with depression,

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anxiety, and pain problems in children and adolescents with ADHD. Sleep parameters should be routinely surveyed in this population to determine whether an intervention is necessary.

Keywords:

Anxiety, Attention-deficit/hyperactivity disorder, Depression, Pain, Sleep

Introduction

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [1], attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder with onset in the developmental period. Comorbid anxiety, depression, and pain problems are prevalent in children and adolescents with ADHD. Research has indicated that children and adolescents with ADHD are more likely to have depression than those without ADHD (14% *vs* 1%) [2]. Furthermore, more than one-third of adolescents with ADHD have comorbid anxiety disorders [3]. Studies have shown that, relative to ADHD alone, comorbid ADHD and depression result in greater psychosocial impairment [4] and higher suicidality risk in female adolescents [5]. Furthermore, individuals with comorbid ADHD and anxiety had worse overall functioning [6] and poorer psychosocial quality of life [7], and children with ADHD are more likely to have comorbid headaches [8] and recurrent abdominal pain [9]. Pain also has disabling effects on children with ADHD [10]. The results of previous studies thus support the conclusion that comorbid depression, anxiety, and pain problems warrant routine monitoring in children and adolescents with ADHD.

Not every child and adolescent with ADHD, however, has comorbid depression, anxiety, and pain problems, indicating that there may be risk factors that increase the possibility of them occurring. The roles of insomnia and sleep duration in comorbid depression, anxiety, and pain problems in this population thus warrant further study. Co-occurrence of sleep problems and short sleep duration with inattention and hyperactivity–impulsivity has also been documented in children [11], adolescents [12,13], and young adults [14]. A meta-analysis concluded that children with ADHD are more impaired than typically developed children on most subjective (and some objective) measures of sleep, such as bedtime resistance, sleep onset difficulty, night awakening, difficulty with morning awakening, sleep-disordered breathing, daytime sleepiness, sleep onset latency, and apnea and hypopnea [15].

Sleep problems not only have negative impacts on quality of life and social functioning [16] but are also significantly associated with health problems. Previous cross-sectional studies have indicated that youth with comorbid ADHD and depression [17] and anxiety may have sleep problems that are more severe relative to those with ADHD alone [18,19]. Prospective studies have shown that sleep problems can significantly predict greater depressive but not anxiety symptoms 1 year later in young adolescents with ADHD [20], that transient or persistent sleep problems at the baseline can predict behavioral and emotional problems 1 year later in children with ADHD [21], and that sleep problems at the baseline can predict emotional problems at 6 months (and vice versa) [22]. These results indicate that sleep problems should be a treatment target for depression and anxiety symptoms in individuals with ADHD.

Several issues concerning the association of insomnia and sleep duration with health problems in individuals with ADHD warrant further study. First, community-based studies have shown that compared with adolescents with average sleep duration, those with long nocturnal sleep duration were more prone to violence, alcohol and illicit drug use, and truancy [23], whereas long nocturnal sleep duration was found to be significantly associated with higher psychological well-being and quality of life [24]. Although one study showed that long sleep duration can predict the effect of stimulant medication on the improvement of executive attention in individuals with ADHD [25], another study found that long sleep duration was associated with increased odds of reporting ADHD [26]. No study has examined the relationship between long nocturnal sleep duration and health problems in children and adolescents who have received a clinical diagnosis of ADHD. Second, although prospective studies have found that short sleep duration can predict the diagnosis of ADHD [27] and subsequent development of depression and anxiety [28], to our knowledge, the relationships of short nocturnal sleep duration with depression and anxiety have not been examined in a clinical group

of children and adolescents with ADHD. Third, research found that community adolescents with subjective insomnia reported unsatisfactory pain-related quality of life, but the opposite was reported by those with long nocturnal sleep duration [24]. However, no study has examined the relationships of subjective insomnia and sleep duration with pain problems in children and adolescents with ADHD.

The aim of the present study was to examine the relationships of subjective insomnia and short and long nocturnal sleep duration with depression, anxiety, and pain problems in children and adolescents with ADHD. We hypothesized that the severity of subjective insomnia and short sleep duration are positively associated with the severity of depression, anxiety, and pain problems in this population. Given the lack of related studies, we tentatively hypothesized that long nocturnal sleep duration is negatively associated with the severity of depression, anxiety, and pain problems in children and adolescents with ADHD.

Methods

■ Participants

Participants were recruited from the child psychiatric outpatient clinics of two medical centers in Kaohsiung and Taoyuan, Taiwan. Children aged 6-18 years who had received a diagnosis of ADHD on the basis of the diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision [29] between November 2010 and October 2012 were invited to participate in the study. ADHD was diagnosed on the basis of multiple data sources, including (a) an interview with a child psychiatrist, (b) clinical observation of the participant's behavior, and (c) history provided by the mother and the results of the short Chinese version of the Swanson, Nolan, and Pelham Scale, Version IV (SNAP-IV) [30,31]. We interviewed with children and their parents to collect their histories of development and school adjustment and performance. We also reviewed children's medical records to collect their psychiatric and pediatric diagnoses and results of psychological assessment. Based on the results of interviews, clinical observation, medical records and psychological assessment, children were excluded from this study if they exhibited intellectual disability, bipolar disorder, difficulty communicating, or any cognitive deficit that prevented them from understanding the

study purpose or completing the questionnaires. In total, 553 children with ADHD and their parents were invited to participate. Among them, 469 (84.8%) agreed. No difference in sex ($\chi^2 = 0.924, p = .350$) or age ($t = -0.350, p = .780$) was observed between the children who participated and those who refused to participate in this study.

All participants and their parents received psychoeducation about the etiology, symptom presentation, and treatment strategies of ADHD. In addition, the parents received counseling about the skills required to manage children's ADHD symptoms and how to communicate with their children. The intervention for treating ADHD symptoms was medication in 390 participants (83.2%) and group cognitive-behavioral psychotherapy in 276 participants (58.8%). This study was approved by the Institutional Review Board of Kaohsiung Medical University Hospital.

Measures

Athens Insomnia Scale (AIS-8): We used the Taiwanese version of the eight-item AIS-8 to assess the severity of subjective insomnia over the last month [32,33]. Higher total scores indicate more severe insomnia symptoms and subjective sleep-related distress. The psychometrics of the Taiwanese version of the AIS-8 has been described elsewhere [33]. The Cronbach's alpha for the AIS-8 in the present study was .77.

Nocturnal sleep duration: Participants were asked, "How many hours of sleep on average do you usually get every night in the past one month?" Their responses were used to represent their habitual nocturnal sleep duration. The 2-week test-retest reliability and correlation between self-reports and parents' reports for the duration of nocturnal sleep (Pearson correlation's r) were .72 and .70 ($p < .001$), respectively [23]. We defined children and adolescents whose total sleep duration at night was one standard deviation (SD) below the mean sleep duration of all participants as "short sleepers," those whose total sleep duration at night was within one SD of the mean sleep duration as "average sleepers," and those whose total sleep duration at night was one SD above the mean sleep duration as "long sleepers."

ADHD and oppositional symptoms: The short version of the SNAP-IV-Chinese version was used to assess the severity of the mother-

reported DSM-IV-TR-derived inattention, hyperactivity-impulsivity, and oppositional symptoms in the month preceding the present study [30,31]. Each item is rated on a 4-point Likert scale, ranging from 0 (*not at all*) to 3 (*very much*). Higher total scores for the subscales indicate higher severity of mother-reported inattention, hyperactivity-impulsivity, and oppositional symptoms. In this study, the Cronbach's α of the three subscales ranged from .88 to .91.

Children's Depression Inventory-Taiwanese Version (CDI-TW): The self-report CDI-TW consists of 27 items assessing the severity of depressive symptoms in children and adolescents [34,35]. Respondents rate themselves according to how they feel and think, with each statement being scored from 0 to 2 [34,35]. The psychometrics of the CDI-TW was examined in a previous study on Taiwanese youths [34]. The Cronbach's alpha for the CDI-TW in the present study was .82. One item in the CDI-TW inquired about the participants' sleep disturbance. Because that the inclusion of the item in the CDI-TW inquiring the participants' sleep disturbance may confound the association between insomnia on the AIS-8 and depression on the CDI-TW, we excluded this item and summed the scores of the other 26 items for analysis. Higher total scores on the CDI-TW represent a more severe level of depressive symptoms.

Taiwanese version of the Multidimensional Anxiety Scale for Children (MASC-T): The self-report MASC-T consists of 39 items answered on a 4-point Likert scale [36,37]. Higher total scores on the MASC-T represent a more severe level of anxiety symptoms. The psychometrics of the MASC-T was examined in a previous study on Taiwanese youths [33]. The Cronbach's alpha for the MASC-T in the present study was .89.

Pain: Self-reported levels of pain in the chest, abdomen, neck and shoulders, back and extremities, and head, as well as pain-induced functional impairment in the month preceding the study were assessed using the Visual Analog Scale with ratings from 0 to 100. Those who rated their level of pain in any part of the body as 50 or higher were classified as experiencing severe perceived pain. Those who rated their level of pain-induced functional impairment as 50 or higher were classified as experiencing severe pain-related dysfunction.

■ Procedure and statistical analysis

Research assistants performed interviews using the research questionnaires to collect data from the study population. Parents completed the short Chinese version of the SNAP-IV. Data analysis was performed using SPSS 20.0 (SPSS Inc., Chicago, IL, USA).

We used multiple regression models to examine the association of subjective insomnia and sleep duration with depression and anxiety. We also used logistic regression models to examine the association of subjective insomnia and sleep duration with severe perceived pain and severe pain-related dysfunction. The effects of demographic characteristics and ADHD symptoms were controlled for in both models. A two-tailed p value of less than .05 was considered statistically significant in the multiple regression analysis. The odds ratio (OR) and the 95% confidence interval (CI) of the OR were used to represent the significance of the logistic regression analysis.

Results

The demographic and ADHD characteristics, subjective insomnia, sleep duration, depression, anxiety, and pain problems among the participants are shown in **Table 1**. The mean (SD) nocturnal sleep duration of all participants was 8.2 (1.2) hours. Regarding sleep duration, 121 (25.8%) participants were short nocturnal sleepers (nocturnal sleep duration, ≤ 7 hours), and 59 (12.6%) were long nocturnal sleepers (nocturnal sleep duration, ≥ 10 hours). Because that medication for ADHD may influence children's sleep, we compared the severity of insomnia on the AIS-8 and the proportions of participants with various sleep durations between the participants with and without receiving medication for ADHD. The results indicated that no significant differences in the severity of insomnia on the AIS-8 ($t = -.845, p = .399$) and the proportions of participants with various sleep durations ($\chi^2 = 4.753, p = .093$) between the participants with and without receiving medication for ADHD.

The multiple regression results regarding the associations of subjective insomnia and sleep duration with depression and anxiety are shown in **Tables 2** and **3**. The results showed that subjective insomnia was positively associated with depression ($\beta = .551, t = 13.396, p < .001$) and anxiety ($\beta = .444, t = 10.136, p < .001$).

Relationships of Subjective Insomnia and Sleep Duration with Depression, Anxiety, and Pain Problems in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder

Table 1: Demographic and ADHD characteristics, subjective insomnia, sleep duration, depression, anxiety, and pain problems (N = 469).

	n (%)	Mean (SD)	Range
Sex			
Girls	97 (20.7)		
Boys	372 (79.3)		
Age (years)		11.1 (2.8)	6-18
ADHD symptoms on the SNAP-IV			
Inattention		15.6 (5.6)	0-27
Hyperactivity/impulsivity		12.0 (6.7)	0-27
Oppositional		12.2 (6.1)	0-24
Subjective insomnia on the AIS-8		5.7 (4.1)	0-22
Sleep duration			
Average	289 (61.6)		
Short	121 (25.8)		
Long	59 (12.6)		
Depression on the CDI-TW ^a		14.3 (7.1)	0-41
Anxiety on the MASC-T		34.7 (17.5)	0-100
Severe perceived pain			
No	333 (71.0)		
Yes	136 (29.0)		
Severe pain-related dysfunction			
No	412 (87.8)		
Yes	57 (12.2)		

ADHD: attention-deficit/hyperactivity disorder; AIS-8: eight-item Athens Insomnia Scale; CDI-TW: Children’s Depression Inventory-Taiwan version; MASC-T: Taiwanese version of the Multidimensional Anxiety Scale for Children; SNAP-IV: Swanson, Nolan, and Pelham Scale, Version IV; SD: standard deviation.
^a: Excluded the item on sleep disturbance

Table 2: Association of subjective insomnia and sleep duration with depression.

	Depression								
	Model I			Model II			Model III		
	Beta	t	p	Beta	t	p	Beta	t	p
Sex	-.031	-.789	.431	-.027	-.557	.578	-.004	-.082	.935
Age	-.125	-2.819	.005	-.043	-.744	.457	.001	.019	.985
Inattention symptoms	.101	2.016	.044	.171	2.729	.007	.140	2.143	.033
Hyperactivity/impulsivity symptoms	-.088	-1.476	.141	-.147	-1.922	.055	-.067	-.863	.389
Oppositional symptoms	.070	1.409	.159	.119	1.924	.055	.109	1.642	.101
Subjective insomnia	.551	13.396	<.001						
Short sleep duration^a				.193	3.686	<.001			
Long sleep duration^a							.093	1.729	.085

^a: Average sleep group as the reference

Table 3: Association of subjective insomnia and sleep duration with anxiety.

	Anxiety								
	Model IV			Model V			Model VI		
	Beta	t	p	Beta	t	p	Beta	t	p
Sex	-.156	-3.727	<.001	-.163	-3.316	.001	-.158	-2.967	.003
Age	-.143	-3.034	.003	-.072	-1.243	.214	-.031	-.553	.580
Inattention symptoms	-.024	-.447	.655	.062	.985	.325	.039	.606	.545
Hyperactivity/impulsivity symptoms	-.058	-.910	.363	-.121	-1.582	.115	-.101	-1.314	.190
Oppositional symptoms	-.060	-1.132	.258	-.040	-.653	.514	-.006	-.093	.926
Subjective insomnia	.444	10.136	<.001						
Short sleep duration ^a				.167	3.196	.002			
Long sleep duration ^a							.164	3.085	.002

^a: Average sleep group as the reference

Compared with the participants with average sleep duration, those with short sleep duration had more severe depression ($\beta = .193, t = 3.686, p < .001$) and anxiety ($\beta = .167, t = 3.196, p = .002$). Moreover, compared with the participants with average sleep duration, those with long sleep duration had more severe anxiety ($\beta = .164, t = 3.085, p = .002$).

The logistic regression results regarding the associations of subjective insomnia and sleep duration with severe perceived pain and severe pain-related dysfunction are shown in **Table 4**. The results showed that subjective insomnia was positively associated with severe perceived pain (OR = 1.287, 95% CI = 1.208–1.370) and severe pain-related dysfunction (OR = 1.252, 95% CI = 1.165–1.345). Compared with those with average sleep duration, both the participants with short sleep duration (OR = 1.958, 95% CI = 1.177–3.257) and those with long sleep duration (OR = 1.613, 95% CI = 1.171–2.222) were more likely to have severe perceived pain, whereas no significant difference in the risk of severe pain-related dysfunction was observed between those with average and short sleep duration (OR = 1.760, 95% CI = 0.891–3.476) and between those with average and long sleep duration (OR = 1.507, 95% CI = 0.983–2.311).

Discussion

The results of the present study indicate that short nocturnal sleep duration is significantly associated with depression, anxiety, and perceived pain in children and adolescents with ADHD. Several potential pathways have been speculated to explain the associations between

short sleep duration and mental health problems [38,39]. First, sleep insufficiency is a stressor that may exacerbate depression and anxiety through impairing cognitive judgment, increasing irritability, and lowering the threshold for negative emotional responses. Sleep insufficiency may also increase youths’ somatic discomfort and lower their pain threshold. Second, sleep insufficiency may interact with numerous underlying vulnerability moderators (e.g., hopelessness and impulsivity) and make some adolescents less tolerant of negative emotional states. Third, sleep insufficiency, depression, anxiety, and pain may share a common neurobiological mechanism, particularly regarding decreased serotonin functioning.

Contrary to our hypothesis, the results indicate that long nocturnal sleep duration is significantly associated with anxiety and perceived pain in children and adolescents with ADHD. This result is incongruent with that of a previous study that found long nocturnal sleep duration to be significantly associated with higher psychological well-being and quality of life in adolescents in the community [24]. The inconsistency between the present and previous studies indicates that the role of long nocturnal sleep duration in mental health may vary between youths with ADHD and their typically developed counterparts. Although further study is necessary to examine why the association between long nocturnal sleep duration, anxiety, and perceived pain develops, we suggest that the role of education systems be considered. Primary, junior high and high school students in Taiwan, Japan, and Korea must spend considerable time completing school assignments and studying for exams, which are a

Table 4: Association of subjective insomnia and sleep duration with pain problems.

	Severe perceived pain						Severe pain-related dysfunction					
	Model VII		Model VIII		Model IX		Model X		Model XI		Model XII	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Sex	.645	.369-1.125	.573	.332-.989	.648	.351-1.195	.970	.466-2.020	.686	.332-1.417	.781	.329-1.854
Age	1.098	1.001-1.206	1.173	1.060-1.296	1.187	1.063-1.324	1.062	.939-1.201	1.135	.991-1.300	1.112	.957-1.293
Inattention symptoms	.965	.914-1.019	.997	.945-1.051	1.014	.957-1.074	.978	.907-1.055	1.018	.945-1.096	1.033	.952-1.122
Hyperactivity/impulsivity symptoms	1.023	.971-1.079	1.017	.964-1.073	.981	.928-1.037	1.020	.952-1.093	1.015	.943-1.092	.971	.900-1.048
Oppositional symptoms	1.043	.993-1.095	1.050	1.002-1.102	1.047	.994-1.103	1.034	.970-1.103	1.031	.966-1.101	1.073	.996-1.155
Subjective insomnia	1.287	1.208-1.370					1.252	1.165-1.345				
Short sleep duration ^a			1.958	1.177-3.257					1.760	.891-3.476		
Long sleep duration ^a					1.613	1.171-2.222					1.507	.983-2.311

CI: confidence interval; OR: odds ratio
^a: Average sleep group as the reference

major cause of short nocturnal sleep duration for adolescents in these countries [40-42]. Children and adolescents with ADHD and long nocturnal sleep duration may experience difficulty complying with their school time schedule and awaking in the early morning; this increases their stress in daily life and leads to the development of anxiety. Moreover, both long nocturnal sleep duration and perceived pain might represent somatic discomfort. However, the validity of these explanations for the associations of long nocturnal sleep duration with anxiety and perceived pain requires further study.

In line with the results of previous studies [11-14], the present study found that subjective insomnia was positively associated with depression, anxiety, perceived pain, and severe pain-related dysfunction. Insomnia may share common neurobiological mechanisms with depression, anxiety, and pain, particularly regarding serotonin [43], norepinephrine functioning [44], and circadian clock genes [45]. Moreover, insomnia is a stressor that may worsen emotions through impairing cognitive judgment and impulse control [39,46].

Some limitations were encountered in this study. First, the cross-sectional design limited our ability to draw conclusions regarding the causal relationships between insomnia, sleep duration, and health indicators. Second, the study data were exclusively self-reported. The use of one data source could have influenced our findings and may have resulted in shared-method variance. Third, nocturnal sleep duration was not measured separately on weekdays and

weekends. Fourth, we did not specify the types of pain and painful event that participants had experienced, which should be included in further study.

Despite these limitations, the results of the present study support the conclusion that insomnia and short and long nocturnal sleep duration should be a treatment target in efforts to mitigate depression, anxiety, and pain problems in children and adolescents with ADHD. In recent years, several intervention models for sleep problems in children with ADHD have been demonstrated to be effective. For example, Better Nights, Better Days, a distance intervention for insomnia in school-aged children with and without ADHD, demonstrated a significant reduction in sleep problems and improved psychosocial functioning [47]. The brief behavioral sleep intervention program proposed by Hiscock, *et al.* [48] ameliorated ADHD symptoms and improved sleep, behavior, quality of life, and functioning in a community sample of children with ADHD [48]. Insomnia and nocturnal sleep duration should be routinely surveyed in children and adolescents with ADHD. Intervention programs should be provided for people in this population who have insomnia and short or long nocturnal sleep duration.

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References

- American Psychiatric Association. Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC, American Psychiatric Association (2013).
- Larson K, Russ SA, Kahn RS, *et al.* Patterns of comorbidity, functioning, and service use for US children with ADHD, 2007. *Pediatrics* 20127(3), 462-470 (2011).
- Biederman J, Faraone SV, Spencer T, *et al.* Gender differences in a sample of adults with attention deficit hyperactivity disorder. *Psychiatry Res* 53(1), 13-29 (1994).
- Blackman GL, Ostrander R, Herman KC. Children with ADHD and depression: a multisource, multi-method assessment of clinical, social, and academic functioning. *J. Atten. Disord* 8(4), 195-207 (2005).
- Cho SC, Kim JW, Choi HJ, *et al.* Associations between symptoms of attention deficit hyperactivity disorder, depression, and suicide in Korean female adolescents. *Depress. Anxiety* 25(11), E142-6 (2008).
- March JS, Swanson JM, Arnold LE, *et al.* Anxiety as a predictor and outcome variable in the multimodal treatment study of children with ADHD (MTA). *J. Abnorm. Child. Psychol* 28(6), 527-541 (2000).
- Klassen AF, Miller A, Fine S. Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. *Pediatrics* 114(5), E541-547 (2004).
- Paolino MC, Ferretti A, Villa MP, *et al.* Headache and ADHD in Pediatric Age: Possible Physiopathological Links. *Curr. Pain. Headache. Rep* 19(7), 25 (2015).
- Holmberg K, Hjern A. Health complaints in children with attention-deficit/hyperactivity disorder. *Acta. Paediatr* 95(6), 664-670 (2006).
- Parisi P, Verrotti A, Paolino MC, *et al.* Headache and attention deficit and hyperactivity disorder in children: common condition with complex relation and disabling consequences. *Epilepsy. Behav* 32(1), 72-75 (2014).
- Paavonen EJ, Raikkonen K, Lahti J, *et al.* Short sleep duration and behavioral symptoms of attention-deficit/hyperactivity disorder in healthy 7- to 8-year-old children. *Pediatrics* 123(5), e857-e864 (2009).
- Gau SS, Chiang HL. Sleep problems and disorders among adolescents with persistent and subthreshold attention-deficit/hyperactivity disorders. *Sleep* 32(5), 671-679 (2009).
- Hysing M, Lundervold AJ, Posserud MB, *et al.*

- Association between sleep problems and symptoms of attention deficit hyperactivity disorder in adolescence: results from a large population-based study. *Behav. Sleep. Med* 14(5), 550-64 (2016).
14. Gau SS, Kessler RC, Tseng WL, *et al.* Association between sleep problems and symptoms of attention-deficit/hyperactivity disorder in young adults. *Sleep* 30(2), 195-201 (2007).
 15. Cortese S, Faraone SV, Konofal E, *et al.* Sleep in children with attention-deficit/hyperactivity disorder: Meta-analysis of subjective and objective studies. *J. Am. Acad. Child. Adolesc. Psychiatry* 48(9), 894-908 (2009).
 16. Craig SG, Weiss MD, Hudcok KL, *et al.* The functional impact of sleep disorders in children with ADHD. *J. Atten. Disord* (2017).
 17. Mayes SD, Calhoun SL, Bixler EO, *et al.* ADHD subtypes and comorbid anxiety, depression, and oppositional-defiant disorder: differences in sleep problems. *J. Pediatr. Psychol* 34(3), 328-337 (2009).
 18. Accardo JA, Marcus CL, Leonard MB, *et al.* Associations between psychiatric comorbidities and sleep disturbances in children with attention-deficit/hyperactivity disorder. *J. Dev. Behav. Pediatr* 33(2), 97-105 (2012).
 19. Hansen BH, Skirbekk B, Oerbeck B, *et al.* Comparison of sleep problems in children with anxiety and attention deficit/hyperactivity disorders. *Eur. Child. Adolesc. Psychiatry* 20(6), 321-330 (2011).
 20. Becker SP, Langberg JM, Evans SW. Sleep problems predict comorbid externalizing behaviors and depression in young adolescents with attention-deficit/hyperactivity disorder. *Eur. Child. Adolesc. Psychiatry* 24(8), 897-907 (2015)
 21. Lycett K, Sciberras E, Hiscock H, *et al.* Sleep problem trajectories and well-being in children with attention-deficit hyperactivity disorder: a prospective cohort study. *J. Dev. Behav. Pediatr* 37(5), 405-414 (2016).
 22. Mulraney M, Giallo R, Lycett K. The bidirectional relationship between sleep problems and internalizing and externalizing problems in children with ADHD: a prospective cohort study. *Sleep. Med* 17(1), 45-51 (2016).
 23. Yen CF, King BH, Tang TZ. The association between short and long nocturnal sleep duration and risky behaviors and the moderating factors in Taiwanese adolescents. *Psychiatry. Res* 179(1), 69-74 (2010).
 24. Wang CC, Liu TL, Hsiao RC, *et al.* The relationships of insomnia and short and long nocturnal sleep durations with quality of life and the moderating effects of sex and age in Taiwanese adolescents. *Neuropsychiatry* 7(2), 640-641 (2017).
 25. Morash-Conway J, Gendron M, Corkum P. The role of sleep quality and quantity in moderating the effectiveness of medication in the treatment of children with ADHD. *Atten. Defic. Hyperact. Disord* 9(1), 31-38 (2017).
 26. Bogdan AR, Reeves KW. Sleep duration in relation to attention deficit hyperactivity disorder in American adults. *Behav. Sleep. Med* 20(1), 1-11 (2016).
 27. Scott N, Blair PS, Emond AM, *et al.* Sleep patterns in children with ADHD: a population-based cohort study from birth to 11 years. *J. Sleep. Res* 22(2), 121-128 (2013).
 28. Matamura M, Tochigi M, Usami S, *et al.* Associations between sleep habits and mental health status and suicidality in a longitudinal survey of monozygotic twin adolescents. *J. Sleep. Res* 23(3), 290-294 (2014).
 29. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (4th ed. text revision). American Psychiatric Association, Washington, DC, USA (2000).
 30. Gau SS, Shang CY, Liu SK. Psychometric properties of the Chinese version of the Swanson, Nolan, and Pelham, version IV scale- parent form. *Int. J. Methods Psychiatr. Res* 17(1), 35-44 (2008).
 31. Swanson JM, Kraemer HC, Hinshaw SP, *et al.* Clinical relevance of the primary findings of the MTA: success rates based on severity of ADHD and ODD symptoms at the end of treatment. *J. Am. Acad. Child. Adolesc. Psychiatry* 40(2), 168-179 (2001).
 32. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. *J. Psychosom. Res* 48(6), 555-60 (2000).
 33. Yen CF, Ko CH, Yen JY, *et al.* The multidimensional correlates associated with short nocturnal sleep duration and subjective insomnia among Taiwanese adolescents. *Sleep* 31(11), 1515-1525 (2008).
 34. Chen SH. Children's Depression Inventory-Taiwan Version. Psychological Publishing Co, Taipei (2008).
 35. Kovacs M. Children's Depression Inventory. Multi-Health Systems Inc, North Tonawanda, NY, USA (1992).
 36. March JS. Multidimensional Anxiety Scale for Children. Multi-Health Systems Inc, North Tonawanda, NY, USA (1997).
 37. Yen CF, Yang P, Wu YY. Factor structure, reliability and validity of the Taiwanese version of the Multidimensional Anxiety Scale for children. *Child. Psychiatry. Hum. Dev* 41(3), 342-52 (2010).
 38. Liu X, Buysse DJ. Sleep and youth suicidal behavior: a neglected field. *Curr. Opin. Psychiatry* 19(3), 288-293 (2006).
 39. Mann JJ. Neurobiology of suicidal behavior. *Nat. Rev. Neurosci* 4(1), 819-828 (2003).
 40. Gau SF, Soong WT. Sleep problems of Junior High School students in Taipei. *Sleep* 18(8), 667-673 (1995).
 41. Shin C, Kim J, Lee S. Sleep habits, excessive daytime sleepiness and school performance in high school students. *Psychiatry. Clin. Neurosci* 57(4), 451-453 (2003).
 42. Shinkoda H, Matsumoto K, Park YM, *et al.* Sleep-wake habits of schoolchildren according to grade. *Psychiatry. Clin. Neurosci* 54(3), 287-289 (2000).
 43. Mann JJ, Brent DA, Arango V. The neurobiology and genetics of suicide and attempted suicide: a focus on the serotonergic system. *Neuropsychopharmacology* 24(5), 467-77 (2001).
 44. Atzori M, Cuevas-Olguin R, Esquivel-Rendon E, *et al.* Locus ceruleus norepinephrine release: a central regulator of CNS spatio-temporal activation? *Front. Synaptic. Neurosci* 8(1), 25 (2016).
 45. Charrier A, Olliac B, Roubertoux P, *et al.* Clock genes and altered sleep-wake rhythms: their role in the development of psychiatric disorders. *Int. J. Mol. Sci* 18(5), E938 (2017).
 46. Dahl RE, Lewin DS. Pathways to adolescent health: sleep regulation and behavior. *J. Adolesc. Health* 31(6), 175-184 (2002).
 47. Corkum P, Lingley-Pottier P, Davidson F, *et al.* Better nights/better days-distance intervention for insomnia in school-aged children with/without ADHD: a randomized controlled trial. *J. Pediatr. Psychol* 41(6), 701-713 (2016).
 48. Hiscock H, Sciberras E, Mensah F, *et al.* Impact of a behavioural sleep intervention on symptoms and sleep in children with attention deficit hyperactivity disorder, and parental mental health: randomized controlled trial. *BMJ* 350(1), h68 (2015).