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SCIENTIFIC INVESTIGATIONS

Associations of frequent pain symptoms with excessive daytime sleepiness in adolescents: a longitudinal study

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Study Objectives: Pain symptoms, sleep disturbance, and daytime sleepiness are common in adolescents. This study examined the cross-sectional and prospective associations between pain symptoms and excessive daytime sleepiness (EDS) in a large sample of adolescents.

Methods: Participants were 7,072 adolescents (mean age = 14.58 years) in a follow-up study of behavior and health in Shandong, China. A self-administered structured questionnaire was used to assess pain symptoms (headache, stomachache, and other general pain), body weight and height, sleep, anxiety/depression, substance use, and family environment in November–December in 2015 and 1 year later. The Chinese adolescent daytime sleepiness scale was used to measure daytime sleepiness.

Results: Of the sample, 19.8% and 23.2% had moderate or severe EDS at baseline and at 1-year follow-up, respectively. The prevalence and 1-year incidence rates of EDS significantly increased with the frequencies of pain symptoms. Frequent pain was significantly associated with increased risk of EDS at baseline (odds ratio = 2.01, 95% confidence interval = 1.56–2.59), incident EDS (odds ratio = 1.41, 95% confidence interval = 1.03–1.93), and persistent EDS (odds ratio = 2.17, 95% confidence interval = 1.52–3.09) while adjusting for adolescent and family covariates, including anxiety/depression, nocturnal sleep duration, insomnia symptoms, frequent snoring, body mass index, and hypnotic use. Similar associations were observed across headache, stomachache, and other pain.

Conclusions: Frequent pain is significantly and independently associated with increased risk of EDS. Our findings suggest that assessing and treating pain symptoms is important to improve healthy sleep and reduce risk of EDS in adolescents. Further research is needed to understand the underlying psychological and neurobiological mechanisms between pain and daytime sleepiness in adolescents.

Keywords: chronic pain, headache, daytime sleepiness, sleep disturbance, stomachache, adolescents

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Chronic pain, sleep disturbance, and daytime sleepiness are prevalent in adolescents. Data on the prospective association between pain and excessive daytime sleepiness in the general population of adolescents are scarce.

Study Impact: This longitudinal study of 7,072 Chinese adolescents found that frequent pain was significantly associated with increased risk of incident and persistent excessive daytime sleepiness over 1-year follow-up. The associations remained significant even after adjustment for sleep duration, insomnia, and anxiety/depression. These findings underscore the importance of assessing and treating pain to improve healthy sleep and reduce risk of excessive daytime sleepiness in adolescents.

INTRODUCTION

Epidemiological studies have demonstrated that most adolescents sleep less than 8 hours per night on weekdays,[1] 10–20% have difficulty initiating sleep,[2,3] and 20–40% report excessive daytime sleepiness (EDS).[4] Insufficient sleep, sleep disturbance, and EDS in adolescents have a range of adverse health and psychosocial outcomes, including but not limited to obesity, substance use, self-harm, accidents, behavioral and emotional problems, impaired daily functioning, and poor school performance.[1,5–9]

Sleep regulation and disturbance during adolescence is related to developmental, biological, psychosocial, school, and family factors.[1,10,11] EDS is the tendency to fall asleep during normal waking hours. While insufficient sleep is the most common cause of EDS, there are a number of extrinsic factors (eg, digital media use, watching television, video games, homework, extracurricular activities, social interaction, jobs, caffeinated beverage use before bedtime, irregular sleep schedules, early school start) and intrinsic/biological factors (eg, puberty development, insomnia, circadian rhythm sleep disorder, sleep-related breathing disorders, narcolepsy) that may lead to EDS among adolescents.[1,12] Identifying modifiable risk factors is crucial to provide information on potential targets for intervention to promote healthy sleep and prevent EDS in adolescents. One of the potentially manageable risk factors is chronic/recurrent pain.[13–15]

Pain is one of the most common somatic complaints in children and adolescents.[16–19] The median prevalence rate of chronic pain

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in pediatric populations is estimated to range from 11% to 38%, with headache, abdominal pain, and musculoskeletal pain being the most common types of pain.[18] Chronic pain caused by unidentified medical conditions begins to increase from age 12 years and is more prevalent in girls than in boys.[13,17,18,20] Growing evidence suggests that chronic pain is associated with sleep disturbances, short sleep duration, and daytime sleepiness in the pediatric population and that more than half of pediatric patients with chronic pain report disturbed sleep.[13–15,21,22] However, the majority of epidemiological studies of chronic pain and sleep disturbance in pediatric populations are cross-sectional or case-control design.[15,21,23] Furthermore, existing prospective studies on the impact of chronic pain on sleep are mostly conducted in specific pediatric pain populations and their findings are mixed.[13,22,24] Although some clinical studies have reported that daytime sleepiness is more prevalent in adolescents with chronic pain vs healthy controls,[25,26] to our knowledge, no prospective population-based studies have specifically investigated the associations between pain symptoms and EDS in adolescents.

The current longitudinal study of a large sample of Chinese adolescents (n = 7,072) was conducted to address the following questions. First, is frequent pain significantly associated with increased risk of EDS by cross-sectional baseline data analysis? Second, does frequent pain predict incident and persistent EDS over 1-year follow-up? Third, is the association between frequent pain and EDS independent of nocturnal sleep duration and insomnia, although pain often interferes with sleep initiation and restorative sleep and makes a person prone to drowsiness? Finally, does EDS vary across pain conditions (ie, headaches, stomachache or abdominal pain, or other nonspecific pain)?

METHODS

Participants and procedure

Participants were 7,072 adolescents who were resurveyed 1 year later in the Shandong Adolescent Behavior & Health Cohort study in Shandong, China. Detailed sampling and data collection methods have been described elsewhere.[27–29] In brief, participants were sampled from 5 middle and 3 high schools in 3 counties of Shandong, with consideration of the representativeness of adolescent students in the region, prior study collaboration, convenience, and budget.

Baseline survey was conducted in 7–11th graders in November–December 2015 (n = 11,831). All 7th, 8th, and 10th graders at baseline were invited to participate in a follow-up survey 1 year later in 2016.[7,30] A self-administered, structured questionnaire was used to assess pain symptoms, sleep, mental health, psychosocial factors, and family environment. After getting permission from the target schools, trained public health workers administered the questionnaire to participants in their classrooms during regular school hours. Before filling out the questionnaire, participants were asked to read the instruction carefully, including the purpose of the survey and how to answer the questions. They were also informed that the survey was anonymous, and their participation was voluntary. We obtained permission to conduct the study from the principals in the target schools and informed consent from participants before the survey. The study was approved by the research ethics committee of Shandong University School of Public Health and target schools.

Measures

The following measures included in the questionnaire were used to assess dependent and independent variables and covariates for the current study,

Excessive daytime sleepiness

The Chinese Adolescent Daytime Sleepiness Scale (CADSS)[31] was used to assess EDS at baseline and 1-year later. The CADSS consists of 7 questions that ask about adolescents' general feeling of drowsiness and dozing off at different situations during the daytime in the past month. Example items are "During the past month, how often would you say you feel sleepy during the day?" "During the past month, how often would you say you have dozed off in the morning classes?", and "During the past month, how often would you say you have dozed off while reading or doing homework?" All the 7 items can be found in Liu et al.[31] Each item is rated on a Likert scale from 1 = never to 5 = almost every day. Summing up the scores of the 7 items yields a total CADSS score, ranging from 7 to 35. A total score of 23 has been suggested as a cutoff of moderate or severe daytime sleepiness or EDS during the past month.[10,31] Incident EDS was defined as the occurrence of new EDS (ie, CADSS score ≥ 23) at 1-year follow-up among adolescents without EDS at baseline. Persistent EDS was defined as the prevalence of EDS (ie, CADSS score ≥ 23) at both baseline and 1 year later. The CADSS has satisfactory psychometric properties.[7,10,31] Cronbach's alpha with the current sample was 0.89 at baseline and 0.91 at 1-year follow-up.

Pain symptoms at baseline

Pain symptoms without known medical causes were assessed by 3 items in the Youth Self-Report somatic complaints subscale: headache, stomachache/abdominal pain, and other nonspecific pain (aches or pains except for stomachache or headache).[32,33] Each pain item is rated on a 3-point scale: "0" = not true, "1" = somewhat or sometimes true, and "2" = very true or often true during the past 6 months. Frequent pain was defined by the presence of any of the 3 pain symptoms as "very true" or "often true" during the past 6 months.[19,34] The Chinese Youth Self-Report has been reported to have satisfactory psychometric properties.[33]

Sleep duration and sleep problems at baseline

Nocturnal sleep duration on weekdays was assessed by the question: During the past month, on a typical school day, how many hours of actual sleep did you get at night? Frequent snoring was evaluated by the question with an answer of at least 3 times/week: During the past month, how often did you snore loudly? Hypnotic use was assessed by the question: During the past month, how often did you take medicine to help sleep?

Insomnia was assessed by the Youth Self-Rating Insomnia Scale (YSIS).[28] The YSIS consists of 8 items that assess insomnia symptoms and waking symptoms or daytime consequences within the past month. The symptoms assessed include difficulty initiating sleep, difficulty maintaining sleep, early morning awakening, unrefreshing sleep, poor sleep quality, sleep

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insufficiency, sleep dissatisfaction, and interference of sleep disturbance with daytime functioning. Example items are "During the past month, how often would you say you feel difficulty falling asleep?" "During the past month, how often would you say you have insufficient sleep?" All the 8 items can be found in Liu et al.[28] Each item is rated on a 5-point scale from 1 (never) to 5 (almost every day). Summing the scores on the 8 items yields a total YSIS score ranging from 8 to 40. A higher total score of the YSIS indicates a greater insomnia severity during the past month. A total score of 26 has been suggested as a cutoff of moderate or severe insomnia.[28] The YSIS has been demonstrated to have acceptable psychometric properties in Chinese adolescents.[28] Cronbach's alpha for the sample was 0.80.

Anxious/depressive symptoms at baseline

The Chinese Youth Self-Report of Achenbach's Child Behavior Checklist was used to measure anxious/depressive symptoms.[32,33] The Youth Self-Report anxious/depressed subscale consists of 16 items that can be found in the *Manual for the Youth Self-Report*.[32] Each item is rated on a 3-point scale: "0" = not true, "1" = somewhat or sometimes true, and "2" = very true or often true. Summing up the scores of the 16 items yields a total depressive score. A total score > 14 has been suggested as cutoff to define clinically relevant anxious/depressive symptoms in Chinese adolescents.[35] Cronbach's alpha with the present sample was 0.88 for the subscale.

Other adolescent and family covariates at baseline

Other adolescent factors included in the study as covariates were age, sex, body mass index calculated based on self-reported body weight and height, chronic diseases (yes or no), ever cigarette smoking (yes or no), ever alcohol drinking (yes or no), and the school that participants were attending (7 dummy variables for 8 schools). Family covariates were father's education and occupation, self-reported family economic status, and interparental relationship (**Table 1**). Mother's education and occupation were not included because family social economic status is more likely to be determined by father's education and occupation in traditional Chinese culture.

Statistical analysis

Sample characteristics at baseline were described by proportion (%) for categorical variables and mean (standard deviation) for continuous variables. Chi-square tests were performed to examine the differences in the rates of EDS across the 3 pain symptoms (ie, headache, stomachache/abdominal pain, and other pain) and any pain (ie, presence of any of the 3 pain symptoms). A series of logistic regression analyses were performed to examine the associations of pain symptoms with EDS at baseline and at 1-year follow-up, respectively. Model 1 was performed to examine the bivariate associations between pain symptoms and EDS. Model 2 was performed to examine the adjusted associations between pain symptoms and EDS while controlling for adolescent and family covariates except for sleep duration and insomnia in **Table 1**. Model 3 was performed to examine the adjusted associations between pain symptoms and EDS while controlling for adolescent and family covariates in Model 2 plus sleep duration and insomnia. Same analyses were performed for adolescents with persistent EDS (ie, CADSS score ≥ 23 at both baseline and 1 year later). In addition, interactions of pain symptoms by sex on EDS were examined with logistic regression analyses. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 24.0 (Armonk, NY: IBM Corp.).

RESULTS

Among 8,629 7th–8th graders and 10th graders at baseline, 7,072 were resurveyed, with a follow-up rate of 82.0%. Mean age of the sample at baseline was 14.58 (standard deviation = 1.45) and about half were female. **Table 1** presents detailed adolescent and family characteristics of the sample at baseline.

Prevalence of pain symptoms and EDS

As shown in **Table 1**, approximately 45% and 8% adolescents reported having pain symptoms sometimes and often over the past 6 months, respectively. Headache was most prevalent, with 36.6% and 4.6% being sometimes and often, respectively.

Of the sample, 19.8% and 23.2% had EDS at baseline and at 1-year follow-up, respectively. Among 5,670 adolescents without EDS at baseline, 927 (16.3%) developed EDS at 1-year follow-up. Among 1,402 adolescents who had EDS at baseline, 715 (51.0%) still had EDS at 1-year follow-up, and 687 (49.0%) did not have EDS.

As can be seen from **Figure 1**, the rates of EDS at baseline and 1-year follow-up significantly increased with the frequency of all the 3 pain symptoms at baseline (all $P < .05$). For example, the prevalence of EDS at baseline increased from 16.5% in adolescents who did not report headache at baseline to 42.7% in those who reported frequent headache (**Figure 1A**), the incidence rate of EDS at 1-year follow-up increased from 15.1 to 28.9% (**Figure 1B**), and the rate of persistent EDS increased from 10.5 to 38.5% (**Figure 1C**). Similar tendency was observed between boys and girls (ie, the rates of EDS increased with pain symptoms for both boys and girls).

Cross-sectional associations of EDS with pain symptoms at baseline

Table 2 presents the odds ratios (ORs) of EDS in relation to pain symptoms at baseline. Univariate logistic regressions (Model 1) showed that adolescents who reported any of the 3 pain symptoms sometimes and often were 1.38–1.69 and 3.61–3.80 times more likely to have EDS, respectively (all $P < .001$). After adjusting for adolescent and family covariates (Model 2), all ORs were reduced to a limited degree and were still significant except for any pain sometimes. With additional adjustment of sleep duration and insomnia (Model 3), the ORs were further reduced but still tended to increase with advancing frequency of pain symptoms, and the ORs for frequent pain symptoms all remained statistically significant. Illustratively, frequent pain was significantly associated with about 2-fold risk increase of EDS (OR = 2.17 [95% confidence interval (CI)] = 1.57–2.99 for headache, OR = 1.87 [95%

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Table 1—Sample characteristics and pain symptoms at baseline.

	N*	n or mean	% or SD
Female sex	7,072	3,536	50.0
Age, mean (SD)	7,072	14.58	(1.45)
Ever smoking	7,072	1,339	18.9
Ever drinking	7,072	2,417	34.2
Chronic disease	7,071	271	3.8
BMI, mean (SD)	7,019	20.10	(3.47)
Frequent snoring	6,750	237	3.5
Insomnia symptoms	7,072	1,075	15.2
Sleep duration (hour), mean (SD)	6,926	6.80	(1.27)
Hypnotic use	6,731	111	1.6
Anxiety/depressive symptoms	7,072	801	11.3
Family economic status	7,005		
Excellent or good		1,444	20.6
Fair		4,719	67.4
Poor or very poor		842	12.0
Father's education	6,995		
Primary school		966	13.8
Middle school		3,784	54.1
High school		1,303	18.6
College or above		942	13.5
Father's occupation: nonfarm	7,072	4,380	62.0
Parental relationship	6,995		
Excellent		2,997	42.8
Good		1,838	26.3
Fair		1,732	24.8
Poor/separated/divorced		428	6.1
Headache	6,560		
No		3,857	58.8
Sometimes		2,401	36.6
Often		302	4.6
Stomachache	6,515		
No		4,989	76.6
Sometimes		1,284	19.7
Often		242	3.7
Other nonspecific pain	6,424		
No		4,923	76.6
Sometimes		1,356	21.1
Often		145	2.3
Any pain	6,631		
No		3,101	46.8
Sometimes		2,973	44.8
Often		557	8.4

*Total N varied due to missing data. SD = standard deviation.

CI = 1.33–2.62] for stomachache, OR = 1.91 [95% CI = 1.15–2.84] for other pain, and OR = 2.01 [95% CI = 1.56–2.59] for any pain) (all $P < .01$).

Associations between baseline pain symptoms and incident EDS at follow-up

The analysis was limited to those adolescents who did not have EDS at baseline to determine the predicting role of pain symptoms in the incidence of EDS at 1-year follow-up. **Table 3** presents the ORs of incident EDS with pain symptoms at baseline. Model 1 showed that adolescents who reported any of the 3 pain symptoms sometimes and often were 1.11–1.29 and 1.82–2.28 times more likely to develop EDS at 1-year follow-up, respectively. After adjusting for adolescent and family covariates (Model 2), frequent headache (OR = 1.85, 95% CI = 1.26–2.72), stomachache (OR = 1.73, 95% CI = 1.13–2.64), and any pain (OR = 1.59, 95% CI = 1.17–2.16) were still significantly associated with incident EDS at 1-year follow-up. With additional adjustment of sleep duration and insomnia (Model 3), frequent headache (OR = 1.64, 95% CI = 1.10–2.45), stomachache (OR = 1.54, 95% CI = 1.00–2.37), and any pain (OR = 1.41, 95% CI = 1.03–1.93) remained significantly associated with increased risk of incident EDS at 1-year follow-up.

Associations of persistent EDS with baseline pain symptoms

The analysis was limited to adolescents who had EDS at baseline and 1-year follow-up compared with those adolescents without EDS at either baseline or follow-up. **Table 4** presents the ORs of persistent EDS with pain symptoms at baseline. Model 1 showed that adolescents who reported headache, stomachache, or other pain sometimes (OR = 1.40–1.91) and frequent (OR = 5.31–5.42) were significantly at increased risk of persistent EDS. After adjusting for adolescent and family covariates (Model 2), all ORs became smaller, but they were still significant except for headache sometimes. With additional adjustment of sleep duration and insomnia (Model 3), albeit all ORs were further reduced, frequent headache (OR = 2.24, 95% CI = 1.42–3.51), stomachache (OR = 2.48, 95% CI = 1.57–3.94), other pain (OR = 2.30, 95% CI=1.25–4.25), and any pain (OR = 2.17, 95% CI = 1.52–3.09) were still significantly associated with increased risk of persistent EDS.

There were no significant interactions of pain symptoms by sex on EDS in the cross-sectional and longitudinal analyses.

DISCUSSION

Pain symptoms and daytime sleepiness are both common in adolescents. Little is known about the prospective association between pain symptoms and EDS in the general adolescent population. To our knowledge, this is the first longitudinal study of pain symptoms and EDS in a large sample of Chinese adolescent students (n = 7,072). Our major findings are summarized and discussed below.

Regardless of the type of pain symptoms, the prevalence and subsequent incidence rates of EDS significantly increased with the frequency of pain symptoms at baseline (**Figure 1**). Multivariate logistic regression analyses showed that frequent pain at baseline was significantly associated approximately 40% increased risk of incident EDS (OR = 1.41, 95% CI =

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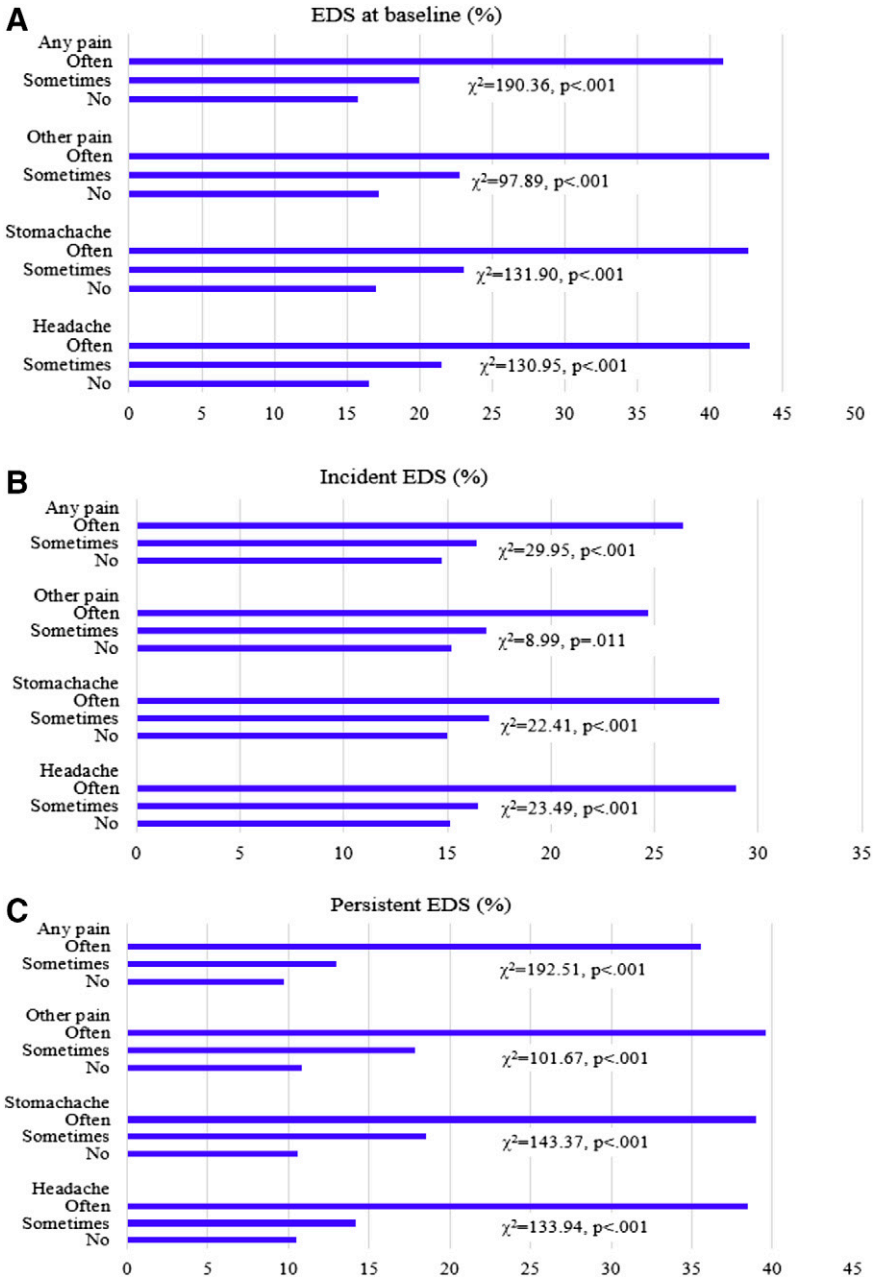
Figure 1—Rates of EDS increased with pain symptoms at baseline.



(A) EDS at baseline = CADSS score ≥ 23 at baseline. **(B)** Incident EDS = the occurrence of new EDS (ie, CADSS score ≥ 23) over the 1-year follow-up. **(C)** Persistent EDS = CADSS score ≥ 23 at both baseline and 1 year later. CADSS = Chinese Adolescent Daytime Sleepiness Scale, EDS = excessive daytime sleepiness.

1.03–1.93) and 2-fold risk of persistent EDS (OR = 2.17, 95% CI = 1.52–3.09), independent of sex, age, substance use, anxiety/depression, body mass index, frequent snoring, sleep duration, insomnia symptoms, and sleep medication use. Our findings support previous clinical studies that show that adolescents with persistent pain are more likely to have daytime sleepiness.[13,15,26]

The mechanisms between pain symptoms and EDS during adolescence are not clear but can be understood within a biopsychosocial and developmental framework. Adolescence is a period from puberty to adulthood, along with marked physical and psychosocial developmental changes and increased risk of behavioral, emotional, and sleep problems. Developmental changes in sleep-wake regulation and sleep patterns are characterized as reduced time in slow-wave sleep and latency to rapid eye movement sleep and a preference for a delayed sleep phase during adolescence.[1,36] These sleep changes are attributed to the misalignment of endogenous circadian rhythms, puberty-related phase delay, and psychosocial developmental needs (such as, heavy homework, night social activities, and early

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Table 2—Cross-sectional associations of pain symptoms with excessive daytime sleepiness at baseline (n = 7,072).

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Headache						
No	1.00		1.00		1.00	
Sometimes	1.38***	1.21–1.57	1.18*	1.02–.37	1.10	0.94–1.29
Often	3.76***	2.95–4.80	2.61***	1.95–3.51	2.17***	1.57–2.99
Stomachache						
No	1.00		1.00		1.00	
Sometimes	1.69***	1.46–1.95	1.27**	1.08-1.50	1.11	0.93–1.34
Often	3.61***	2.77–4.71	2.31***	1.69–3.17	1.87***	1.33–2.62
Other pain						
No	1.00		1.00		1.00	
Sometimes	1.60***	1.38–1.84	1.30**	1.10–1.53	1.23*	1.03–1.47
Often	3.80***	2.71–5.31	2.46***	1.63–3.70	1.91**	1.15–2.84
Any pain						
No	1.00		1.00		1.00	
Sometimes	1.35***	1.18–1.54	1.12	0.96–1.30	1.03	0.88–1.21
Often	3.73***	3.07–4.53	2.55***	2.02-3.23	2.01***	1.56–2.59

*$P < .05$, **$P < .01$, ***$P < .001$. Model 1 = univariate logistic regression, Model 2 = multivariate logistic regression with participating schools and covariates except for sleep duration and insomnia symptoms in **Table 1**, Model 3 = Multivariate logistic regression with covariates in Model 2 plus sleep duration and insomnia symptoms. CI = confidence interval, OR = odds ratio.

Table 3—Associations of pain symptoms with incident EDS at 1-year follow-up in adolescents without EDS at baseline (n = 5,670).

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Headache						
No	1.00		1.00		1.00	
Sometimes	1.11	0.95–1.30	1.01	0.85–1.19	0.99	0.83–1.18
Often	2.28***	1.62–3.21	1.85**	1.26–2.72	1.64*	1.10–2.45
Stomachache						
No	1.00		1.00		1.00	
Sometimes	1.29**	1.07–1.55	1.13	0.92–1.38	1.05	0.86–1.29
Often	2.20***	1.51–3.22	1.73*	1.13–2.64	1.54*	1.00–2.37
Other pain						
No	1.00		1.00		1.00	
Sometimes	1.21*	1.01–1.45	1.08	0.89–1.32	1.07	0.87–1.31
Often	1.82**	1.09–3.04	1.24	0.70–2.22	1.08	0.67–1.97
Any pain						
No	1.00		1.00		1.00	
Sometimes	1.14	0.98–1.33	1.02	0.86–1.20	1.00	0.84–1.18
Often	2.09***	1.60–2.73	1.59**	1.17–2.16	1.41*	1.03–1.93

*$P < .05$, **$P < .01$, ***$P < .001$. Model 1 = univariate logistic regression, Model 2 = multivariate logistic regression with participating schools and covariates except for sleep duration and insomnia symptoms in **Table 1**, Model 3 = multivariate logistic regression with covariates in Model 2 plus sleep duration and insomnia symptoms. CADSS = Chinese Adolescent Daytime Sleepiness Scale, CI = confidence interval, EDS = excessive daytime sleepiness, incident EDS = the occurrence of new EDS (ie, CADSS score ≥ 23) over the 1-year follow-up, OR = odds ratio.

school starting).[1,3,9,11] These psychosocial needs and developmental changes are a source of stress, and stress results in mood dysregulation, pain, impaired sleep, and daytime sleepiness.

There are several potential pathways to explain the pain-EDS link during adolescence. First, pain itself often interferes with sleep initiation and restorative sleep,[13,22] which can cause sleep

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Table 4—Associations of pain symptoms with persistent EDS in adolescents with EDS at baseline and follow-up vs those adolescents without EDS at either baseline or follow-up (n = 5,458).

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Headache						
No	1.00		1.00		1.00	
Sometimes	1.40***	1.18–1.67	1.13	0.92–1.38	0.99	0.79–1.24
Often	5.31***	3.91–7.22	3.04***	2.05–4.51	2.24***	1.42–3.51
Stomachache						
No	1.00		1.00		1.00	
Sometimes	1.91***	1.58–2.32	1.46***	1.16–1.82	1.21	0.94–1.56
Often	5.40***	3.88–7.51	2.98***	1.98–4.49	2.48***	1.57–3.94
Other pain						
No	1.00		1.00		1.00	
Sometimes	1.79***	1.48–2.16	1.41**	1.13–1.76	1.20	0.93–1.54
Often	5.42***	3.59–8.18	3.28***	1.92–5.60	2.30**	1.25–4.25
Any pain						
No	1.00		1.00		1.00	
Sometimes	1.38***	1.15–1.65	1.08	0.88–1.33	0.92	0.73–1.16
Often	5.13***	3.99–8.56	2.98***	2.18–4.07	2.17***	1.52–3.09

P < .01, ***P < .001. Model 1 = univariate logistic regression, Model 2 = multivariate logistic regression with participating schools and covariates except for sleep duration and insomnia symptoms in **Table 1, Model 3 = multivariate logistic regression with covariates in Model 2 plus sleep duration and insomnia symptoms. CADSS = Chinese Adolescent Daytime Sleepiness Scale, CI = confidence interval, EDS = excessive daytime sleepiness, OR = odds ratio, persistent EDS = CADSS score ≥ 23 at both baseline and 1 year later.

loss and use of sleep pills and then results in EDS. Second, pain can cause anxiety/depression,[14,24] which in turn results in sleep disturbance and EDS. However, the associations observed in the study cannot be fully explained by sleep problems and anxiety/depression because these associations were only reduced to a moderate extent after controlling for sleep duration, insomnia symptoms, use of sleep pills, and anxiety/depression. Third, pain can cause circadian misalignment and disrupted sleep–wake cycles[37] and then lead to EDS. Furthermore, although use of pain medications for pain relief was not surveyed in the study, some medications such as aspirin and ibuprofen could impact sleep quantity and sleep efficiency, possibly leading to sleep loss and EDS. On the other hand, some pain medications such as anticonvulsants (eg, gabapentin, carbamazepine, lamotrigine) and tricyclic antidepressants (eg, imipramine, amitriptyline) often have a sedating effect and increase risk of EDS.[13]

Biologically, neurobiological mechanisms may play a role in the relationship between pain and EDS. For example, both chronic pain conditions and daytime sleepiness are linked to reduced concentrations or hypoactivities of serotonin and blunted hypothalamic-pituitary-adrenal axis activities.[38–41] Growing studies have also shown thta melatonin plays important roles in sleep-wake regulation and pain modulation through multiple mechanisms.[42,43] Furthermore, orexin, a neuropeptide involved in the regulation of arousal, wake–sleep cycle, has recently been demonstrated to be involved in neuropathic and visceral nociception, headache, orofacial pain, rheumatoid arthritis, and stress induced analgesia.[44]

According to a recent literature review, self-reported sleep disturbances, including shorter sleep duration, insomnia symptoms, and poor sleep quality, are more likely to occur in youth with headache or migraine than healthy peers.[13] In the current study, we did not find the risk of EDS being specific to any pain symptoms (ie, headache, stomachache/abdominal pain, and other pain), although the ORs of EDS somewhat differed across the 3 types of pain. Further research is warranted to examine the prospective associations and biological mechanisms between different types of pain and sleep problems in adolescents.

The study has several strengths. First, the longitudinal study of a large sample of adolescents (n = 7,072) allows us to look at the associations of the 3 common pain symptoms with EDS over time. Second, EDS was assessed by a valid scale, with satisfactory psychometric properties in Chinese adolescents.[31] Third, large sample size allows us to adjust for multiple potential adolescent and family confounders such as anxiety/depression, snoring, sleep duration, and insomnia to examine the independent associations between pain symptoms and EDS.

The findings need to be interpreted considering the following limitations. First, all data were assessed by self-report, which may have led to biased reporting of pain and EDS. Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Self-report is the most common method to assess self-reported pain frequency and intensity. Objective measures of sleep duration and sleep problems such as actigraphy and electroencephalography are desirable, but self-reports

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remain as the typical method in large-scale epidemiological studies. Second, although CADSS has demonstrated satisfactory reliability and validity in Chinese adolescents,[31] further validation with objective assessment like multiple sleep latency test is needed. Third, EDS was assessed at baseline and 1 year later. It is unknown if EDS had any changes during the period from baseline survey to 1-year follow-up survey. Persistent EDS and recurrent EDS could not be differentiated. Third, we did not have information about pain history, pain characteristics (eg, intensity and duration), pain tolerance, and pain medications used, all of which may have different impacts on sleep and daytime sleepiness.[13,15,22,45] Fourth, although the sample size is large, participants were sampled from 8 schools in 1 province of China, the findings from the sample may not be generalized to other adolescent populations because both pain[46] and sleep[47,48] in pediatric populations are influenced by psychosocial, cultural, and environmental factors. For example, nearly 40% of participants in the current study were drawn from families where fathers were farmers. Adolescent students in China have a busy school schedule, heavy homework load, have to go to school in the early morning, stay up late, and study on the weekend to enter top universities.[49,50] All these factors may have influence on the pain-sleep/daytime sleepiness link. Future longitudinal research considering pain intensity and location, clinical/objective assessments of sleep, and cultural and school factors in diverse adolescent populations is warranted.

In summary, our study of a large sample of adolescents provides evidence that EDS is more prevalent in adolescents with pain symptoms and that pain symptoms appear to be a significant and independent predictor of EDS. Although further research is needed to clarify the exact nature of the relationship between pain and EDS, these findings underscore the importance of assessing and treating pain in the prevention and intervention of sleep disturbance/EDS because pain, sleep disturbance, and EDS are common in adolescents. Comprehensive assessments and management of pain symptoms, sleep disturbances, and EDS should be incorporated into routine health care of adolescents. Further research is needed to investigate the underlying psychosocial, developmental, pathophysiological, and neurobiological mechanisms between pain, sleep, and daytime sleepiness in adolescents. Further research is also needed to understand the reciprocal influence of inadequate sleep on the pain experience.

ABBREVIATIONS

CADSS, Chinese Adolescent Daytime Sleepiness Scale
CI, confidence interval
EDS, excessive daytime sleepiness
OR, odds ratio
YSIS, Youth Self-Rating Insomnia Scale

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