Insomnia and Psychopathological Features Associated With Restless Legs Syndrome in Chinese Adolescents

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ABSTRACT

Objective: Little is known about psychopathological features associated with restless legs syndrome (RLS) in pediatric populations. This study examined sleep duration, insomnia, and psychopathological profile associated with RLS in a large community sample of adolescents.

Methods: Participants included 11,831 adolescents from 3 counties of Shandong, China. Mean age of the participants was 15.0 (SD = 1.5) years, and 51% were boys. In November and December 2015, participants completed a structured questionnaire to assess sleep duration, sleep problems, behavioral/emotional problems, and hopelessness. RLS was assessed by the 2003 National Institutes of Health (NIH) Restless Legs Syndrome Diagnosis and Epidemiology Workshop criteria.

Results: Of the sample, 9.5% met the 2003 NIH workshop criteria for RLS, and 2.2% had RLS at least 3 times per week. Compared with adolescents without RLS, adolescents with RLS < 3 times per week and those with RLS ≥ 3 times per week demonstrated significantly higher rates of insomnia symptoms (13.8%, 20.0%, and 36.4%, respectively; $\chi^2 = 117.84$, $P < .0001$), internalizing (9.1%, 18.5%, and 34.1%; $\chi^2 = 238.84$, $P < .001$) and externalizing (9.8%, 17.4%, and 34.1%; $\chi^2 = 193.87$, $P < .001$) problems, and hopelessness (13.0%, 16.9%, and 27.8%; $\chi^2 = 54.10$, $P < .001$). After adjusting for demographics and internalizing and externalizing problems, RLS ≥ 3 times per week was associated with a doubled risk of insomnia (OR = 2.05; 95% CI, 1.53–2.75). After adjusting for demographics, sleep duration, and insomnia, RLS ≥ 3 times per week was associated with a more than doubled risk of internalizing (OR = 2.65; 95% CI, 1.94–3.62) and externalizing problems (OR = 2.75; 95% CI, 2.02–3.74).

Conclusions: RLS is associated with increased risk of insomnia, hopelessness, and both internalizing and externalizing problems. Our findings suggest that clinicians need to assess RLS in adolescents with sleep and mental health problems.

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Restless legs syndrome (RLS) is a neurologic sensorimotor disorder. Individuals with RLS have an overwhelming urge to move their legs to relieve unpleasant sensations of tingling, pulling, creeping, or nervousness. The urge is worsened during rest or inactivity and in the evening or night. RLS is prevalent in the general population, with prevalence rates of 5% to 10% in adults and 2% to 4% in pediatric populations.[1] RLS is more prevalent in female than in male adults.[1,2] The etiology of RLS is unclear, but multiple psychosocial, biological (dopamine system and iron), and genetic factors are associated with RLS.[3] RLS has significant impact on an individual's rest, sleep, mood, cognition, and well-being and is associated with multiple somatic and neuropsychiatric diseases in pediatric and adult populations.[1,3–7]

Depression, anxiety, and attention-deficit/hyperactivity disorder (ADHD) are common psychiatric disorders in individuals with RLS.[1,5,8–10] For example, in a retrospective study of 374 patients with childhood-onset RLS, the authors found that 64% patients had 1 or more comorbid psychiatric disorders, 29.1% had mood disturbances, 25% had ADHD, 11.5% had anxiety disorders, and 10.9% had behavioral disturbances.[8] In a review of literature, the authors reported that up to 44% of subjects with ADHD had RLS or RLS symptoms, and up to 26% of subjects with RLS had ADHD or ADHD symptoms.[10] However, little is known if these psychiatric disorders/symptoms in patients with RLS are independent from short sleep duration, sleep disturbance, and/or medications because of RLS.[11]

Although epidemiologic and clinical studies of RLS have markedly increased over the last 2 decades,[1] RLS has been underinvestigated, underdiagnosed, and undertreated, especially in the pediatric population.[12] Epidemiologic data and psychopathologic characteristics associated with RLS in children and adolescents are scarce. Several epidemiologic studies in Western countries show that 2% to 4% of adolescents suffer from RLS, with 0.5% to 1% reporting moderate-to-severe symptoms.[1] However, in a recent study of Caucasian and Hispanic adolescents and young adults in the United States, Silva et al[6] reported a prevalence of RLS as high as 8.4%. No sex difference was observed in Western children and adolescents. RLS in children has been demonstrated to be associated with ADHD, growing pains, behavioral disorders, and low ferritin levels.[5,6]

Only 2 epidemiologic studies have been conducted in Chinese children and adolescents.[13,14] In a study of 1,549 Chinese adolescents, Zhang et al[14] used a single question (Did you have uncomfortable feelings in your legs while

Clinical Points

- Little is known about psychopathological features associated with restless legs syndrome (RLS) in pediatric populations.
- RLS was associated with increased risk of insomnia, internalizing/externalizing problems, and hopelessness.
- In pediatric patients with sleep disturbance and behavioral/emotional problems, RLS should be assessed and treated. Likewise, in pediatric patients with RLS, sleep and mental health problems should be assessed and treated.

resting at night?) to identify RLS and reported that 2.8% of the sample had RLS symptoms at least once a week. Female adolescents at late puberty stage reported more RLS symptoms than male adolescents. The authors also found that RLS symptoms were significantly associated with sleep problems, impaired daytime functions, poor general health, and frequent temper outbursts. In another study of 6,792 Chinese children and adolescents aged 8 to 17 years, Xue and colleagues[13] reported that the overall prevalence of clinical RLS was 2.2%, significantly increasing with age and more prevalent in females than in males (2.7% vs 1.7%). Sleep disturbance, including difficulty falling asleep/interrupted sleep/poor quality of sleep, insufficient hours of sleep, and negative mood were commonly reported by those with RLS.

To our knowledge, no studies have been conducted to comprehensively examine sleep duration, insomnia, and psychopathological characteristics associated with RLS in the general population of adolescents. The objectives of the current study with standardized sleep and mental health measures were to examine the prevalence of and the associated sleep and internalizing and externalizing psychopathological characteristics of RLS in a large sample of Chinese adolescents. On the basis of the literature,[2,5,10,14] we hypothesized that adolescents with RLS have more insomnia symptoms and behavioral/emotional problems compared with individuals without RLS and that insomnia and behavioral/emotional problems increase with frequency/severity of RLS symptoms. We also hypothesized that the associations of RLS with insomnia and psychopathology are independent from each other and from demographic characteristics.

METHODS

Participants and Procedure

Shandong Adolescent Behavior & Health Cohort is an ongoing longitudinal study of adolescent health in Shandong, China. Detailed sampling and data collection has been described elsewhere.[15,16] In brief, participants included 11,836 adolescents from 5 middle and 3 high schools in 3 counties (Lijin, Yanggu, and Zoucheng) of Shandong Province, China. Shandong, located in the middle eastern coast of China, is a typical province in terms of population structure and social and cultural life. Shandong had a total population of 95.8 million in 2010, and about half of its population are rural residents. Three counties and 8 schools in Shandong were selected for the study, with consideration of their social demographics, the representativeness of adolescent students in the region, prior study collaboration, convenience, and budget to conduct the study.

After permission was obtained from the 8 target schools, all 7th graders (freshmen in middle schools) and 10th graders (freshmen in high schools) were selected to participate in the study for 2-year follow-up. Half of the students from the 8th, 9th, and 11th grades were randomly selected using the school classes as sampling units for 1-year follow-up.

In November and December 2015, the baseline survey was conducted. Participants completed a self-administered, structured adolescent health questionnaire (AHQ) to assess behavioral and mental health problems and to collect demographic information. After getting permission from the class teachers for the sampled classes, trained master's-level public health workers administered the AHQ to participants in their classrooms during regular school hours. All sampled students attending school on the day of the survey gave their consent even though they were given the option of not participating. Before filling out the questionnaire, participants were instructed to read the instructions carefully and informed that the survey was anonymous and their participation was voluntary with no penalties for nonparticipation. Informed consent was obtained from participants, and permission was obtained from parents before the survey. This is the most commonly used procedure to conduct school-based health surveys in China, and a high response rate is usually obtained from students.[17,18] The study was approved by the research ethics committee of Shandong University School of Public Health and target schools.

Measures in the Adolescent Health Questionnaire

Restless legs syndrome. The following 4 questions developed by the 2003 National Institutes of Health (NIH) Restless Legs Syndrome Diagnosis and Epidemiology Workshop were used to assess RLS and its severity[19]: (1) Do you have strange or uncomfortable sensations in your legs combined with an urge or need to move your legs? (2) Do these feelings occur mainly or only at rest and do they improve with movement? (3) Are these feelings worse in the evening or night than in the morning? and (4) How often do these feelings occur? If the participant answered "yes" to all of the first 3 questions, he/she was considered to have RLS symptoms. If the participant had RLS symptoms and answered the fourth question as at least 3 times per week, he/she was considered to have clinical RLS.

Sleep duration and insomnia. Night sleep duration and insomnia symptoms were assessed by 4 items adapted from the Pittsburgh Sleep Quality Index (PSQI).[20] Sleep duration was assessed with the question "During the past month, on an average school day, how many hours of actual sleep did you get at night?" Insomnia symptoms were assessed with questions about difficulty falling asleep, difficulty maintaining sleep, and early morning awakening. The

Table 1. Prevalence (%) of RLS Symptoms and Clinical RLS by Age and Sex

	RLS Symptoms (< 3 times/wk)			Clinical RLS (≥ 3 times/wk)		
Age (y)	Male (n = 6,018)	Female (n = 5,813)	Total (N = 11,831)	Male (n = 6,018)	Female (n = 5,813)	Total (N = 11,831)
12	7.6	6.1	6.9	2.1	2.0	2.0
13	6.2	6.5	6.3	1.5	0.7	1.1
14	8.0	9.7	8.9	2.6	1.8	2.2
15	8.6	8.9	8.7	2.3	1.4	1.8
16	10.0	12.7	11.4	2.9	2.3	2.6
17	10.8	13.0	11.9	3.8	2.7	3.2
18	13.9	12.2	13.0	2.6	4.3	3.5
Total	8.8	10.2	9.5	2.5	1.8	2.2
χ^2	20.78	38.87	56.79	10.94	17.18	23.97
P	.002	.002	.000	.090	.009	.001

Abbreviation: RLS = restless legs syndrome.

participants answered each question about insomnia with a response option of rarely or never (< 1 time per week), sometimes (1 or 2 times per week), often (3–5 times per week), or almost every day (6 or 7 times per week). If the response was often or almost every day, the symptom was considered clinically significant (ie, at least 3 times per week). The Chinese PSQI has satisfactory psychometric properties.[21] The 4 items have been used in multiple studies of Chinese adolescents.[17,22]

Behavioral/emotional problems. The Youth Self-Report (YSR) of Child Behavior Checklist was used to measure behavioral problems.[23,24] The YSR comprises 103 problem items to which the respondent can answer "0" if the problem is not true of himself or herself, "1" if the item is somewhat or sometimes true, or "2" if it is very true or often true within the past 6 months. By summing answers of "1" and "2" on all problem items, 8 syndromes and 2 second-order factors (internalizing and externalizing) can be assessed. The externalizing factor is made up of aggressive behavior and delinquent behavior; the internalizing factor is made up of anxious/depressed, withdrawn, and somatic complaints. Scores > 90th percentile of the entire sample on each scale were used as cutoff points to define a clinically significant behavioral problem.[25,26] Cronbach α was 0.93 for internalizing problems and 0.91 for externalizing problems with the current sample.

Hopelessness. The Beck Hopelessness Scale (BHS) is a 20-item, true-or-false, self-report scale designed to assess negative expectancies about the future.[27] It is scored by summing the keyed responses of pessimism for each of the 20 items. The Chinese BHS has acceptable psychometric properties in Chinese populations.[28] Cronbach α was 0.75 with the current sample.

Negative life events. A modified version of the Chinese Adolescent Self-Rating Life Events Checklist (ASLEC)[29] was used to measure the frequency and severity of life stress experienced during the past year. It lists 50 negative life events, covering multiple social stress domains from family, school, interpersonal relationships, and health problems. Respondents rate the perceived stressfulness of each experienced event (ie, the extent to which the event affected respondent's life) on a 4-point Likert scale ranging from 1 "not at all" to 4 "extremely severe." The ASLEC has been reported to have satisfactory 2-week test-retest reliability ($r = 0.70$) and construct validity.[29]

Child and family demographic factors. Child factors included age, sex, grade, and chronic physical diseases/disabilities (yes or no). Family factors included paternal education and family economic status.

Statistical Analysis

Age and sex differences in the prevalence of RLS were examined by χ^2 tests. Participants were categorized into 3 groups: non-RLS, RLS < 3 times per week, and RLS ≥ 3 times per week. Generalized linear model was used to examine the difference in sleep duration across the 3 groups. Univariate logistic regression analyses were performed to examine the associations between RLS and insomnia symptoms, behavioral/emotional problems, and hopelessness. Multivariate logistic regressions were performed to examine the independent associations of RLS with insomnia symptoms, adjusting for the effects of child and family factors (age, sex, chronic disease, life events, father's education, and family economic status), internalizing problems, and externalizing problems. Multivariate logistic regressions were performed to examine the independent associations of RLS with behavioral/emotional problems and hopelessness, adjusting for the effects of child and family factors, sleep duration, and insomnia. Statistical tests of the regression estimates or odds ratios were based on Wald statistics. All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY; IBM Corp).

RESULTS

All sampled students attending school on the day of the baseline data collection (n = 11,836) were requested to participate in the survey and returned their questionnaires. Five students returned their questionnaires blank and were excluded from statistical analysis. The mean age of the sample was 15.0 (SD = 1.5) years, and 51% were boys.

Prevalence of RLS

Table 1 presents the prevalence rates of RLS by age and sex. Of the sample, 9.5% met the 2003 NIH workshop diagnostic criteria[19] for RLS, and 2.2% had clinically significant RLS

Table 2. Sleep Duration and Insomnia Symptoms by RLS

	No RLS (n = 10,710)	RLS < 3 times/wk (n = 863)	RLS ≥ 3 times/wk (n = 258)	F/χ^2	*P*
Sleep duration					
Mean (SD)	7.12 (1.43)	6.93 (1.40)	6.70 (1.46)	17.28	.000
Adj mean (SE)	7.10 (0.01)	7.13 (0.04)	7.04 (0.08)	0.49	.613
Insomnia					
DIS, %	8.2	12.4	25.2	100.32	.000
OR (95% CI)	1.00	1.58 (1.27–1.97)	3.76 (2.80–5.04)		
Adj OR (95% CI)	1.00	1.15 (0.92–1.45)	2.00 (1.45–2.78)		
DMS, %	4.3	5.3	12.6	38.76	.000
OR (95% CI)	1.00	1.24 (0.90–1.70)	3.19 (2.16–4.70)		
Adj OR (95% CI)	1.00	1.00 (0.72–1.39)	1.74 (1.14–2.65)		
EMA, %	4.3	7.0	12.1	43.36	.000
OR (95% CI)	1.00	1.66 (1.25–2.20)	3.05 (2.06–4.53)		
Adj OR (95% CI)	1.00	1.36 (1.01–1.83)	1.70 (1.11–2.61)		
Any insomnia, %	13.8	20.0	36.4	117.84	.000
OR (95% CI)	1.00	1.56 (1.30–1.87)	3.58 (2.75–4.67)		
Adj OR (95% CI)	1.00	1.21 (1.01–1.47)	2.05 (1.53–2.75)		

Abbreviations: Adj = adjusting for age, gender, chronic disease, life events, internalizing problems, externalizing problems, father education, and family economic status; DIS = difficulty falling asleep; DMS = difficulty maintaining sleep; EMA = early morning awakening; OR = odds ratio; RLS = restless legs syndrome.

(≥ 3 times per week). The prevalence of RLS significantly increased with age, from < 7% at ages 12 to 13 to 13.0% at age 18 ($\chi^2 = 56.79$, $P < .001$). RLS was more prevalent in female than in male adolescents (10.2% vs 8.8%, $\chi^2 = 7.03$, $P = .008$), whereas clinical RLS was more prevalent in male than in female adolescents (2.5% vs 1.8%, $\chi^2 = 6.19$, $P = .013$).

Sleep Duration and Insomnia Associated With RLS

Table 2 shows the mean sleep duration and insomnia symptoms among participants without RLS, with RLS < 3 times per week, and with RLS ≥ 3 times per week. Mean sleep duration was significantly reduced from 7.12 hours for adolescents without RLS to 6.70 hours for those with RLS ≥ 3 times per week ($F = 17.28$, $P < .001$). However, the difference in sleep duration became nonsignificant after adjusting for child and family characteristics and internalizing and externalizing problems ($F = 0.49$, $P = .613$).

Figure 1 shows the prevalence of insomnia symptoms among adolescents who had no RLS, RLS < 3 times per week, or RLS ≥ 3 times per week. More than one-third of adolescents with RLS ≥ 3 times per week (36.4%) and one-fifth of adolescents with RLS < 3 times per week (20.0%) had insomnia symptoms, compared with 13.8% of adolescents without RLS ($\chi^2 = 117.84$, $P < .0001$).

Table 2 shows the associations of RLS with individual insomnia symptoms. RLS was significantly associated with increased risk of all insomnia symptoms. After adjusting for child and family characteristics and internalizing and externalizing problems, the associations remained significant. The risk of insomnia associated with RLS increased by 21% (OR = 1.21; 95% CI, 1.01–1.47) for those with RLS < 3 times per week and increased 2-fold for those with RLS ≥ 3 times per week (OR = 2.05; 95% CI, 1.53–2.75).

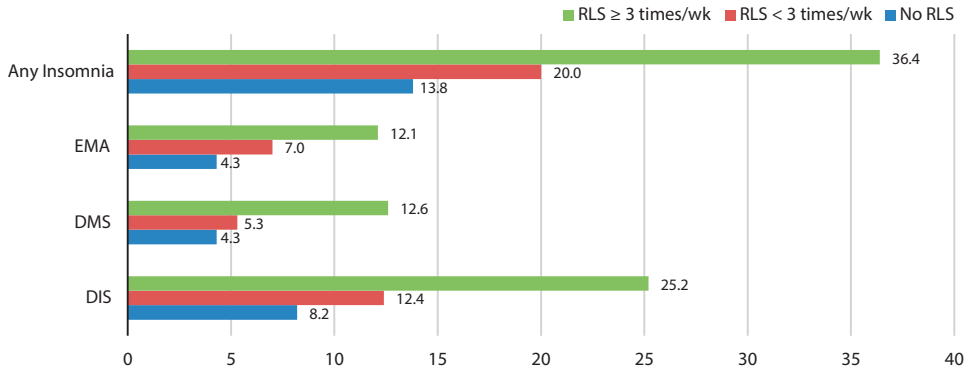
Psychopathological Profile Associated With RLS

Figure 2 shows the prevalence rates of psychopathological problems among adolescents who had no RLS, RLS < 3 times per week, or RLS ≥ 3 times per week. The prevalence rates of all problems were highest in adolescents (27%–35%) with RLS ≥ 3 times per week, followed by adolescents with RLS < 3 times per week (15%–19%), and were lowest in adolescents without RLS (8%–13%) (all $P < .0001$).

Table 3 shows the associations of RLS with various psychopathological problems before and after adjusting for the potential confounding effects of child and family characteristics, sleep duration, and insomnia. In the univariate analyses, RLS < 3 times per week and RLS ≥ 3 times per week were both significantly associated with increased odds of all behavioral and emotional problems and hopelessness. Although the adjusted odds ratios became smaller, they were still above 1 and were 1.16 to 1.91 for RLS < 3 times per week and 1.85 to 3.30 for RLS ≥ 3 times per week.

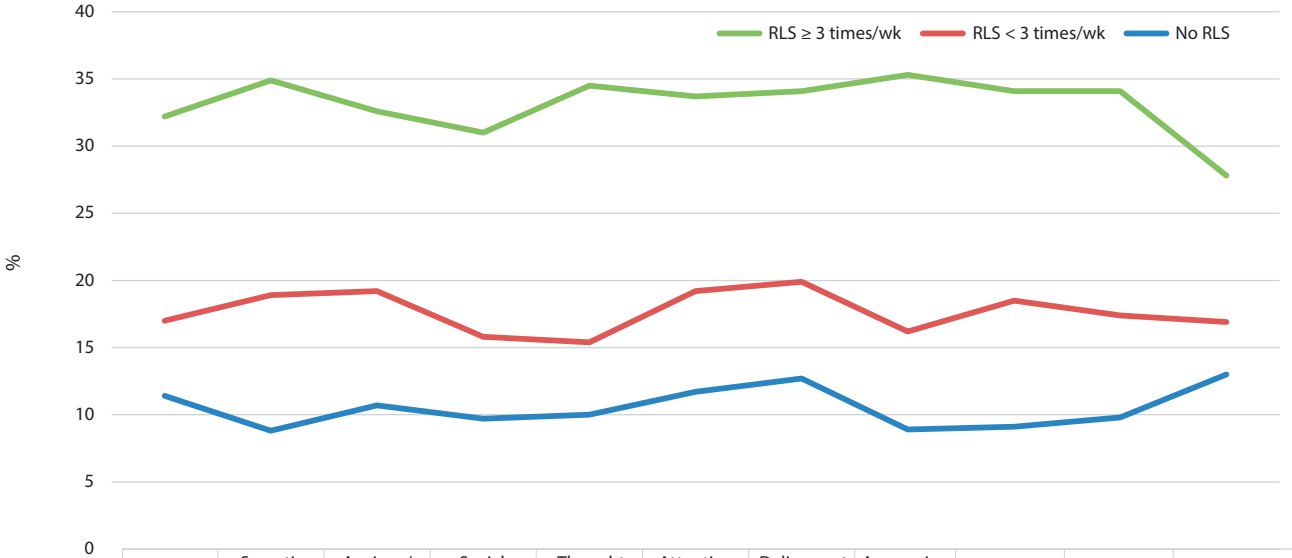
There were no significant interactions between insomnia and RLS for internalizing

Figure 1. Insomnia Symptoms in Adolescents With and Without RLS



Abbreviations: DIS = difficulty falling asleep, DMS = difficulty maintaining sleep, EMA = early morning awakening, RLS = restless legs syndrome.

Figure 2. Psychopathological Profiles in Adolescents With and Without RLS



	Withdrawn	Somatic Complaints	Anxious/ Depressed	Social Problems	Thought Problems	Attention Problems	Delinquent Behavior	Aggressive Behavior	Internalizing	Externalizing	Hopelessness
No RLS	11.4	8.8	10.7	9.7	10.0	11.7	12.7	8.9	9.1	9.8	13.0
RLS < 3 times/wk	17.0	18.9	19.2	15.8	15.4	19.2	19.9	16.2	18.5	17.4	16.9
RLS ≥ 3 times/wk	32.2	34.9	32.6	31.0	34.5	33.7	34.1	35.3	34.1	34.1	27.8

Abbreviation: RLS = restless legs syndrome.

(P = .313) and externalizing problems (P = .288), attention problems (P = .884), or hopelessness (P = .323).

DISCUSSION

To our knowledge, this represents the first and largest study to describe insomnia symptoms and psychopathological characteristics associated with RLS in adolescents (N = 11,831). Our major findings are summarized and discussed, as follows.

First, RLS is prevalent in Chinese adolescents, with 9.5% meeting the 2003 NIH epidemiologic research diagnostic criteria for RLS and 2.2% experiencing RLS at least 3 times a week (ie, clinical RLS). The prevalence of clinical RLS is consistent with several epidemiologic studies of RLS using clinical diagnostic criteria in Western populations[1] and 1 study in Chinese adolescents.[13] The prevalence of RLS symptoms (9.5%) in our sample is similar to that in a US study of Caucasian and Hispanic adolescents and young adults (8.4%).[6] The variance of prevalence reported in previous studies may be mainly due to differences in the assessment and criteria used to define RLS. The variance of prevalence may also be explained by the fact that comorbid mental disorders, such as ADHD, are very common[5,10] and have been diagnosed as complementary diagnoses or missed owing to invalid or unstandardized measures. Although clinical RLS was associated with higher risk of insomnia and behavioral/emotional problems, RLS < 3 times per week was more prevalent and was significantly associated with increased risk of these problems as well. Pediatric RLS is a common spectrum and should be paid clinical attention, and further studies are needed to investigate the clinical and developmental changes and their long-term effects on adolescents' mental and physical health.

Second, while RLS was more prevalent in female adolescents, clinical RLS was more prevalent in male adolescents. The sex difference in previous studies is inconsistent. However, most previous studies demonstrate that clinical RLS is more prevalent in females than in males and the sex difference appears to begin in late puberty.[1,14] Little is known about sex difference in RLS symptoms. Further studies need to examine the developmental changes and sex difference of RLS in children and adolescents.

Third, RLS was significantly associated with increased risk of insomnia after adjusting for demographics and mental health problems, suggesting that the association is unlikely explained by demographic factors and present mental health status. We also found that the prevalence of insomnia increased with the frequency of RLS. Furthermore, RLS was associated with all 3 of the most common insomnia symptoms (difficulty falling asleep, difficulty maintaining sleep, and early morning awakening). Previous studies reported that RLS was associated with difficulty falling asleep.[6,14] RLS can affect an individual's sleep and cause difficulty falling asleep, difficulty maintaining sleep, and early morning awakening because symptoms of RLS often occur and may be more severe during the night. However, little is known as to whether insomnia can lead to or worsen RLS symptoms. Further epidemiologic and clinical studies are warranted.

Table 3. Psychopathological Profile (% scale score ≥ 90th percentile) by RLS

	No RLS (n = 10,710)	RLS < 3 times/wk (n = 863)	RLS ≥ 3 times/wk (n = 258)	χ^2	*P*
Behavioral/emotional problems					
Withdrawn, %	11.4	17.0	32.2	120.22	.000
OR (95% CI)	1.00	1.59 (1.32–1.92)	3.68 (2.81–4.81)		
Adj OR (95% CI)	1.00	1.16 (0.94–1.44)	1.85 (1.36–2.52)		
Somatic complaints, %	8.8	18.9	34.9	267.98	.000
OR (95% CI)	1.00	2.42 (2.01–2.90)	5.55 (4.26–7.24)		
Adj OR (95% CI)	1.00	1.91 (1.56–2.33)	3.20 (2.37–4.30)		
Anxious/depressed, %	10.7	19.2	32.6	164.48	.000
OR (95% CI)	1.00	1.98 (1.66–2.38)	4.02 (3.08–5.25)		
Adj OR (95% CI)	1.00	1.48 (1.21–1.81)	2.02 (1.49–2.76)		
Social problems, %	9.7	15.8	31.0	154.49	.000
OR (95% CI)	1.00	1.73 (1.43–2.11)	4.17 (3.18–5.47)		
Adj OR (95% CI)	1.00	1.32 (1.06–1.64)	2.23 (1.63–3.04)		
Thought problems, %	10.0	15.4	34.5	175.13	.000
OR (95% CI)	1.00	1.64 (1.35–2.00)	4.75 (3.65–6.19)		
Adj OR (95% CI)	1.00	1.32 (1.07–1.64)	2.48 (1.82–3.36)		
Attention problems, %	11.7	19.2	33.7	144.11	.000
OR (95% CI)	1.00	1.79 (1.50–2.14)	3.82 (2.93–4.98)		
Adj OR (95% CI)	1.00	1.26 (1.03–1.55)	1.91 (1.40–2.59)		
Delinquent behavior, %	12.7	19.9	34.1	127.90	.000
OR (95% CI)	1.00	1.71 (1.43–2.04)	3.55 (2.73–4.62)		
Adj OR (95% CI)	1.00	1.51 (1.23–1.84)	2.09 (1.54–2.83)		
Aggressive behavior, %	8.9	16.2	35.3	234.91	.000
OR (95% CI)	1.00	1.99 (1.64–2.41)	5.59 (4.29–7.27)		
Adj OR (95% CI)	1.00	1.60 (1.29–1.99)	3.30 (2.43–4.48)		
Internalizing, %	9.1	18.5	34.1	238.84	.000
OR (95% CI)	1.00	2.28 (1.90–2.74)	5.19 (3.98–6.76)		
Adj OR (95% CI)	1.00	1.73 (1.41–2.13)	2.65 (1.94–3.62)		
Externalizing, %	9.8	17.4	34.1	193.87	.000
OR (95% CI)	1.00	1.94 (1.61–2.33)	4.76 (3.65–6.21)		
Adj OR (95% CI)	1.00	1.62 (1.31–2.00)	2.75 (2.02–3.74)		
Hopelessness, %	13.0	16.9	27.8	54.10	.000
OR (95% CI)	1.00	1.37 (1.13–1.65)	2.59 (1.95–3.44)		
Adj OR (95% CI)	1.00	1.27 (1.04–1.56)	1.81 (1.33–2.45)		

Abbreviations: Adj = adjusting for age, gender, chronic disease, life events, sleep duration, insomnia, father education, and family economic status; OR = odds ratio; RLS = restless legs syndrome.

Fourth, RLS was significantly associated with hopelessness and multiple domains of behavioral/emotional problems, including internalizing, externalizing, social, thought, and attention problems. Although the associations became partially attenuated after adjusting for demographics, sleep duration, and insomnia, these associations remain significant. This means that short sleep duration and insomnia may only partially mediate the association between RLS and psychopathological problems.[11] The associations of RLS with multiple internalizing and externalizing problems and attention problems in adolescents are consistent with the findings of recent literature reviews.[5,10] The relationship between RLS and psychopathology may be complex: bidirectional or coexisting because of sharing similar biological and genetic mechanisms.[9,10] For example, RLS may lead to psychopathology via sleep disturbance, which can cause depression, anxiety, and attention problems.[30,31] Psychopathology such as depression may cause or exacerbate RLS symptoms.[5] RLS and psychopathology such as ADHD may share a common dopamine dysfunction.[10] Large-scale longitudinal studies are needed to examine the causal relationship between RLS and psychopathology.

In interpreting the findings from the current study, the following limitations need to be kept in mind. First, clinical interviews for RLS diagnosis and mental health problems were not conducted in the study. It is unknown to what extent RLS diagnosed on the basis of the 2003 NIH workshop criteria[19] is consistent with the clinical diagnosis of RLS. It is also unknown to what extent the behavioral/emotional problems, such as attention problems, reported here in the questionnaire survey are consistent with clinical diagnoses. Second, because all measures used in this study were self-reported and some questions used to ask adolescent and family demographics were not test-retested, it is possible that some of the effects may have been due to shared method variance. Objective measures of sleep duration and sleep problems, such as overnight polysomnography,[32] are desirable, but self-reports and interviews remain the measures of choice in large-scale epidemiologic sleep studies.[17,33,34] Third, as is true for all cross-sectional research, we could not establish the causal relationships between RLS and insomnia and psychopathological problems. Prospective studies with clinical interviews and diagnosis are needed to examine whether the association is causal or not. Furthermore, this is a school-based epidemiologic survey of adolescent students. Teachers in China are traditionally believed to play the role of parents at school, and students are instructed to absolutely follow teachers' instructions as influenced by Confucianism.[35] Although the survey was anonymous and students' participation was

voluntary, some students might feel obligated to participate in the survey. Further research including test-retest is warranted to confirm if the findings can be replicated and if the findings can be generalized to other adolescent populations.

In summary, although the prevalence of clinical RLS is about 2% in adolescents, RLS symptoms are prevalent (9.5%). RLS symptoms are associated not only with increased risk of insomnia but also with a wide range of internalizing and externalizing problems, attention problems, and hopelessness. These mental health problems and hopelessness may result in serious clinical and psychosocial problems and even suicide attempt and suicide death.[36,37] These findings suggest the importance of early screening adolescents for RLS and including RLS assessment in the routine pediatric and psychiatric clinical practice. On the other hand, adolescents with RLS should be psychiatrically assessed and treated for comorbid psychiatric problems for effective treatment of RLS and for prevention of serious mental consequences.

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