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SCIENTIFIC INVESTIGATIONS

Medical Complaints Are More Common in Young School-Aged Children with Parent Reported Insomnia Symptoms

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Objective: Studies in adults have found significant association between sleep disturbances and various medical symptoms/disorders. However, in children, few studies have explored this complex association in clinical samples. In this study, we examined prevalence of medical complaints in children with insomnia symptoms in a large general population of school aged children.

Methods: We conducted a cross sectional study of 700 children, ages 5–12 years, from the Penn State Children's Cohort. All children underwent a medical and psychiatric history, physical examination, 9-h overnight polysomnography, and neuropsychological testing. Comprehensive sleep and development questionnaires were completed by a parent. We compared 135 (19.3%) children with parent-reported sleep disturbances to 565 (80.7%) children with no parent-reported sleep disturbances.

Results: Insomnia symptoms were significantly associated with gastrointestinal regurgitation and headaches after controlling for demographic variables, apnea hypopnea index, ADHD, learning disorder or other psychiatric/behavioral disorder, socioeconomic status, and minority status. Children with gastrointestinal regurgitation and headaches compared to children without these symptoms were 3.3 times and 2.3 times as likely to suffer from sleep disturbances, respectively. Objectively, sleep latency increased in the sleep disturbance group, and there were significant differences between groups in REM latency, slow wave, and stage 2 sleep.

Discussion: These results underscore the importance of inquiring about insomnia symptoms when children present with medical complaints particularly gastrointestinal regurgitation or headaches and taking a comprehensive medical history when children present with sleep complaints. Future studies are needed to replicate these findings and explore the possible underlying pathophysiological abnormalities of such comorbidity between insomnia symptoms and medical symptoms in children.

Keywords: Insomnia, insomnia symptoms, medical complaints, gastrointestinal regurgitation, headaches, pediatric sleep disorders

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In the past, sleep was considered a passive process; however, recent research has shown that it is an active process with physiological changes in several vital organs and organ systems in the body, particularly the brain and central nervous system. It is known that respiratory, cardiovascular, and gastrointestinal systems undergo significant physiological changes during sleep.[1] Sleep loss increases the risk of impaired glucose tolerance/diabetes and hypertension and alters immune function.[2-5] Sleep disorders may lead to disturbances in functioning of various organs or organ systems and organ specific diseases may lead to disturbances in sleep. Moreover, the association between common medical symptoms/disorders (pain, infectious diseases) and sleep disturbances has been well documented.[6-8] However, most of these findings came from investigations pertaining to adults.

In children, sleep disturbances in certain medical disorders have been reported. Children with asthma have been found to have increased nocturnal awakenings with increased wake time and decreased mean sleep time.[9] Infants and children with pathological reflux have difficulty initiating sleep, increased nocturnal awakenings, and increased daytime sleepiness.[10] Children with obesity, scoliosis, progressive neuromuscular disease, and craniofacial abnormalities (Pierre Robin, Goldenhar syndrome, Treacher-Collins syndrome) are at increased risk for sleep related breathing disturbances and/or nocturnal hypoventilation.[1] However, most of the published studies in children are limited to sleep disturbances in specific medical disorder in a clinical setting.

Sleep disturbances are common in children with prevalence of parent reported sleep disturbances ranging from 20% to 30%.[11-15] Even though there is substantial published literature examining sleep and medical disorders/symptoms in adults, there is a lack of studies exploring this complex association in children, particularly young school-aged children from the

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general population. In this study, we examined the prevalence of medical complaints in children with and without insomnia symptoms in a large general population sample of school aged children (5–12 years of age).

METHODS

Subjects for this study were participants in the Penn State Children's Cohort, a population-based study of sleep related breathing disorder. Detailed description of the study design and methods of data collection have been previously reported.[2,16] The study was designed in 2 phases. In the first phase, general information from the parents about their child's sleep and behavioral patterns was collected using a screening questionnaire based on the survey published by Ali et al.,[17] validated to identify children at high risk for sleep related breathing disorder. This questionnaire was sent home to parents of every elementary school student in 3 local school districts (n = 7,312) with a 78.5% response rate. In the second phase of this study, each year 200 children were selected from the questionnaires that were returned that year. Using a stratification of grade, sex, and risk for sleep related breathing disorder, we randomly selected children from each stratum to maintain representativeness of the original sample. Seven hundred children completed phase 2, for a response rate of 70%. We contrasted the subjects who completed the PSG recording with those who completed the phase 1 questionnaire but were not selected for phase 2. There were no significant differences in age, gender, and race between the 2 groups. This study was approved by the Institutional Review Board at Penn State College of Medicine. Informed consent from parents of all participants and assent from all children was obtained prior to participation.

Seven hundred children who had complete data on sleep related questions were considered for this study. Detailed history was obtained from the parent who accompanied the child to the sleep laboratory including demographic information and detailed medical history including complaints pertaining to all major systems (allergies or drug hypersensitivity, cardiovascular, endocrine, ENT, gastrointestinal, genitourinary, neurological, respiratory, and musculoskeletal), psychiatric history, and medication history. Specific medical symptoms were assessed with close-ended questions. For example, to assess gastrointestinal regurgitation the parent was asked "Does food or liquid come back up into your child's mouth or does your child complain of tasting food or liquid back up in his mouth?" Parents also completed several questionnaires pertaining to sleep and behavior. All children were administered a comprehensive battery of neuropsychological test prior to their overnight polysomnogram to screen for attention deficit hyperactivity disorder (ADHD) by a trained psychometrist. Each child also underwent a comprehensive physical examination, including a standardized ENT and pulmonary examination.

Socioeconomic status (SES) was assessed based upon the professional status of the parent.[18] Parent occupation was defined as professional if the parent had either a professional or managerial occupation and as non-professional if the parent was unemployed, disabled, retired, a student, or had a secretarial or non-managerial occupation. Children with at least one parent defined as professional were considered to be of relatively high SES; children with neither parent being defined as professional were considered to be of low SES.

Questions about sleep completed by the parent of the child as a part of pediatric behavioral scale included the following 2 items: (1) "Has trouble falling asleep." (2) "Wakes up often in the night." The parent was asked to rate these items based on the child's sleep over the past *2 months*, on a 4-point Likert scale from 0 to 3, with 0 "Almost never or not at all," 1 "Sometimes or just a little," 2 "Often or pretty much," and 3 "Very often or very much."

All children underwent a 9-h PSG with a parent present in a sound-attenuated, light and temperature controlled room in our General Clinical Research Center. Childrens' bedtime and waketime approximated their typical sleep times. Each child was monitored with an infrared video and a computerized system (24 analog channel and 10 dc channel TS amplifier using Gamma software, Grass Telefactor, Inc.) including 4 channels of electroencephalogram (EEG), 2-channel bilateral electrooculogram (EOG), and chin and anterior tibial electromyogram (EMG). Respiration was assessed throughout the night by use of a thermocouple at nose and mouth (model TCT R, Grass Telefactor, Inc), nasal pressure transducer (MP 45-871 ± 2 cm H_2O, Validyne Engineering Cort), and piezoelectric thoracic and abdominal respiratory effort belts (model 1312, Sleepmate). A subjective estimate of snoring was obtained from parental report. In addition, we obtained an objective estimate of snoring during the PSG by monitoring breathing sounds with a microphone attached to the throat (model 1250, Sleepmate Technologies), as well as a separate room microphone. All-night hemoglobin oxygen saturation was obtained by pulse oximeter (model 8800, Nonin Medical) attached to the finger. A single-channel electrocardiogram (ECG) was also recorded. All PSG records were scored in accordance with The American Thoracic Society standards for cardiopulmonary sleep studies in children.[19] Apneas and hypopneas were scored by 2 different trained scorers, and discrepancies were resolved by the senior author (EOB). Obstructive apnea was defined as a cessation of airflow ≥ 5 sec and an out-of-phase strain gauge movement. A hypopneic event was defined as a reduction of airflow of approximately 50% with an associated decrease in oxygen saturation (SpO2) ≥ 3% or an associated breathing related arousal. Based on these data an apnea/hypopnea index (AHI) was calculated ([apnea + hypopnea]/hours of sleep). Central apneas were not included in the AHI calculation.

Data Analysis

The children were divided into 2 groups (SDis [sleep disturbance] group & No-SDis [no sleep disturbance] group) based on the response of parents on sleep related questions. Children who were rated by the parent as "Almost never or not at all" or "Sometimes or just a little" on both probes were included in the "No-SDis" group and the children who were rated as "Often or pretty much" or "Very often or very much" on either one or both sleep related probes were included in the "SDis" group.

All statistical analyses were performed with SPSS software for Windows (version 17.0; SPSS, Chicago, IL). Data are reported as mean ± SD or proportions (percentages). The 2 groups were compared by χ^2 or analysis of variance (ANOVA) for sig-

Table 1—Polysomnographic Measures in the Two Groups

	SDis (n = 135)	No-SDis (n = 565)	p
SL (min)	33.1 ± 26	28.1 ± 23.5	0.041
REML	148.1 ± 59.6	164.2 ± 86.6	0.041
TST (min)	453.3 ± 44.6	453.7 ± 49.8	NS
SE (%)	85.8 ± 8	85.9 ± 8.6	NS
Stage1 (%)	3.3 ± 3	3.5 ± 3.3	NS
Stage2 (%)	48.7 ± 9.7	45.6 ± 11.6	0.002
SWS (%)	27.5 ± 8.8	31.1 ± 11.1	≤ 0.001
REM (%)	20.6 ± 5.4	19.9 ± 5.7	NS
AHI	0.72 ± 1.1	0.85 ± 1.7	NS
Arousal Index	3.4 ± 2.6	3.3 ± 2.6	NS

SDis, Sleep disturbance; No-SDis, No sleep disturbance; SL, Sleep latency; REML, REM latency; TST, Total sleep time; SE, Sleep efficiency; Stage 1, Stage 1 sleep; Stage 2, Stage 2 sleep; SWS, Slow wave sleep; REM, REM sleep; AHI, Apnea hypopnea index.

Table 2—Medical Complaints and Disorder in Children with Sleep Disturbances

	SDis (n = 135)	No-SDis (n = 565)	χ^2	p
Allergies	40%	38.1%	0.165	NS
Chronic cough	6.7%	5.4%	0.377	NS
GI pain/colic	14.2%	5.9%	10.7	0.001
GI vomiting	3.7%	1.8%	1.885	0.171
Joint pains	8.2%	5.9%	0.987	NS
Headaches	24.4%	13.2%	10.5	0.001
GI heartburn	8.2%	3.4%	6.1	0.014
GI regurgitation	7.5%	2%	11.2	0.001
Chronic sinusitis	14.8%	11.1%	1.5	NS
Bedwetting	17%	10.9%	3.9	0.049
Wheezing	12.7%	10.7%	0.426	NS
Chest pain	4.5%	1.8%	3.5	0.062
Palpitations	0.8%	1.6%	0.558	NS

SDis, Sleep disturbance; No-SDis, No sleep disturbance; GI, Gastrointestinal.

nificant differences in demographic and clinical features. Binary logistic regression analysis with 95% confidence intervals (CIs) was used to assess for the relative association between the presence of sleep disturbance and the associated medical complaints. To control other factors likely to affect sleep, we statistically controlled for age, gender, and BMI percentile adjusted for age and gender in model 1; with model 2 controlling also for apnea hypopnea index; model 3 additionally controlling for current ADHD, learning disorder, or other psychiatric/behavioral disorder; and model 4 further controlling for SES and minority status. Of note, among the 700 subjects, we had SES data for only 518 subjects; thus in model 4, we allowed only the 3 medical complaints that were significant in the 1st and 2nd model. $P < 0.05$ was used as the criterion for statistical significance.

We accounted for the sampling probability from phase 1 to phase 2 enrollments in all of the analyses to generate population level estimates and to make inference back to population from which the phase 2 study participants were selected. BMI percentiles adjusted for age and gender were based on Centers for Disease Control and Prevention criteria.[20]

RESULTS

Among the seven hundred children, 135 (19.3%) children met the criteria for sleep disturbance (SDis group) and 565 children (80.7%) did not have sleep disturbances (No-SDis group). Subjects in the two groups did not differ in age (SDis: 8.8 ± 1.8; Non-SDis: 8.8 ± 1.7), gender (females [%]: SDis: 54.5%; No-SDis: 51.7%) or BMI percentile (SDis: 60.9 ± 30.6; No-SDis: 61.2 ± 28.7).

Polysomnographic results in the 2 groups are shown in Table 1. The sleep disturbance group had significantly increased sleep latency and stage 2 sleep, and decreased REM latency and slow wave sleep (SWS). No differences were found between groups in total sleep time, sleep efficiency, percentage of stage 1 sleep, and percentage of REM sleep. The 2 groups did not differ in apnea hypopnea index or arousal index.

Significantly more children in the SDis group had parent reported complaints of gastrointestinal pain/colic, gastrointestinal heartburn, gastrointestinal regurgitation, headaches, and bedwetting (Table 2). The two groups did not differ in parent-reported complaints of allergies, chronic cough, chronic sinusitis, wheezing, chest pain, palpitations, vomiting, or joint pains.

In order to assess for the relative association between the presence of sleep disturbance and associated medical complaints, we employed a binary logistic regression analysis. We included all the medical complaints with significance level of ≤ 0.2 (P value in the descriptive χ^2 analysis) in this regression analysis (Table 3). In the first model while controlling for age, gender, and percentile for BMI for age and gender, we allowed all the associated medical complaints into the equation. The strongest variable was gastrointestinal regurgitation, followed by gastrointestinal pain/colic, and headaches. In the second model, we controlled for AHI in addition to the demographic variables. Again, the same 3 medical complaints were significantly associated with sleep disturbance. In the third model, we controlled for current ADHD, learning disorders, or other psychiatric/behavioral disorders in addition to the demographic variables and AHI. Gastrointestinal regurgitation, gastrointestinal pain/colic and headaches remained significant in this model. In the final model (model 4), we controlled for SES and minority status in addition to other variables controlled in the previous models. In this model only gastrointestinal regurgitation and headaches continued to be significantly associated with sleep disturbance with gastrointestinal regurgitation being the stronger of the two.

DISCUSSION

The overall prevalence of 19.3% of sleep disturbances by parent report in this community sample of young school aged children is consistent with previous reports.[11-15] One of the key determinants of insomnia in children as defined by International Classification of Sleep Disorders is either difficulty in falling asleep, staying asleep or both as reported by the parent.[21] In this study we defined sleep disturbance in a similar manner and therefore could be considered as insomnia symptoms.

To our knowledge, this is the first study exploring the comorbidity of medical complaints and the insomnia symptoms in a

Table 3—Multivariate Regression Analysis of Medical Complaints/Disorders as a Predictor of Sleep Disturbance

Sleep disturbance	Model 1		Model 2		Model 3		Model 4	
	OR	p	OR	p	OR	p	OR	p
GI regurgitation	3.4	0.011	3.4	0.011	3	0.031	3.3	0.026
GI pain/colic	2.1	0.026	2.1	0.023	2	0.05	-	-
Headaches	2	0.004	2	0.005	2	0.007	2.3	0.004
Age	1	0.84	1	0.90	1	0.66	0.94	0.35
Gender	0.9	0.60	0.9	0.53	0.8	0.3	0.63	0.06
pctBMI	1	0.85	1	0.9	1	0.80	1	0.74
AHI			0.9	0.37	0.9	0.34	1	0.9
Psych/Behav					3.7	≤ 0.0001	4	≤ 0.0001
SES*							1	0.92
Minority status							1	0.95

*Among the 700 subjects, we had SES data in only 518 subjects; thus in model 4, we allowed only the 3 medical complaints that were significant in the 1st and 2nd model. GI, Gastrointestinal; pctBMI, BMI percentile adjusted for age & gender; Psych/Behav, current ADHD and/or learning disorder and/or other psychiatric/behavioral disorders; AHI, apnea hypopnea index; SES, Socioeconomic status.

community sample of young school-aged children. Significantly more children with sleep disturbances reported medical complaints. Specifically, gastrointestinal symptoms (heartburn, pain/colic and regurgitation), headaches, and bedwetting were significantly more common in children with sleep disturbances.

Among all the medical complaints only gastrointestinal regurgitation, gastrointestinal pain/colic, and headaches were significantly associated with insomnia symptoms after controlling for demographic variables and apnea hypopnea index with gastrointestinal regurgitation having the strongest association. These medical complaints remained significantly associated with sleep disturbance on controlling further for current ADHD/learning disorder or other current psychiatric and behavioral disorder. As it is likely that both sleep and medical disturbances could be affected by the SES and minority status we reassessed the relative association by further controlling for SES and minority status. After controlling for SES and minority status only 2 medical complaints (gastrointestinal regurgitation and headaches) remained significantly associated. Gastrointestinal regurgitation emerged as the strongest variable. Children with gastrointestinal regurgitation were 3.3 times as likely to suffer from insomnia symptoms, and children with headaches were 2.3 times as likely to suffer from insomnia symptoms.

Even though we cannot assess the cause and effect relationship because of the cross-sectional nature of the study, it is possible that the association is bidirectional in nature or that the medical disturbances may have caused the insomnia symptoms or insomnia symptoms might have resulted in medical complaints. However, these results underscore the importance of inquiring about insomnia symptoms when children present to their pediatrician or family physician with medical complaints, particularly with complaints of gastrointestinal regurgitation or headaches. Pediatricians and family physicians often do not inquire about sleep related complaints and these results emphasize the importance of obtaining such a history. It is also possible that children with sleep disturbances are more likely to suffer from insomnia symptoms. Therefore, when children present with complaints of insomnia symptoms, a comprehensive medical history, specifically various medical complaints should be obtained. Future studies should explore whether treatment of sleep complaints improve the associated medical complaints and vice versa.

Objective PSG measures of sleep initiation (sleep latency) increased in sleep disturbed group, however, PSG measures of sleep maintenance or sleep fragmentation (sleep efficiency, total sleep time, percent stage 1 sleep, or arousal index) did not differ between the Sleep Disturbance and No-Sleep Disturbance group. Insomnia is diagnosed based entirely on subjective symptoms as reported by the subject in adults and adolescents and as reported by the parent in children. In adults objective sleep data as measured by PSG indicate significant differences between insomniacs and controls, however of not enough specificity or sensitivity to be useful in clinical practice. In these children we did note slight decrease in SWS and increase in stage 2 sleep. The role of SWS in general is not well known but there is speculation that SWS may play a role in cognitive and somatic functions including memory related functions.[22,23] In any event the observed differences are small and probably not physiologically significant.

Insomnia in adults is considered to be a disorder of hyperarousal associated with autonomic hyperarousal with activation of the stress system; abnormalities, especially the activation of stress response system could lead to the medical symptoms and disorders, (particularly disorders related to gastrointestinal and neurological systems).[24,25] Therefore, it is possible that activation of the stress response system could be responsible for both the sleep disturbances as well as comorbid medical complaints in these children. Future studies should address these questions.

There are several limitations that should be considered in interpreting the results of this study. Insomnia symptoms and medical complaints/symptoms history was obtained from parents. Thus there is a possibility of rater biases. The validity of parent report for sleep disturbances and medical history is not known. Nonetheless, it is a common clinical practice to obtain history and other pertinent information from the parent for young school aged children and thus parent report may be valid to some extent. Finally in some of the disorders that are of low prevalence in the general population of young school-aged children, such as diabetes or thyroid disorder, such an association may not be detected.

In conclusion, these data indicate significant association between parent reported insomnia symptoms and medical complaints of gastrointestinal regurgitation and headaches in

young school aged children independent of other factors affecting sleep. Prospective studies exploring this association and therapeutic trials may help further in terms of clarifying cause and effect relationship. In addition, future studies are needed to explore the possible underlying pathophysiological causes of such comorbidity between insomnia symptoms and medical symptoms in children.

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