

### SCIENTIFIC INVESTIGATIONS

# A Community-Based Study of Sleep and Cognitive Development in Infants and Toddlers

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Study Objectives: To examine the prevalence and correlates of nighttime awakenings and to explore the association between sleep and cognitive development in a community sample of infants and toddlers.

**Methods:** A total of 590 healthy infants (aged 2–11 months) and 512 toddlers (aged 12–30 months) from 8 provinces of China were assessed for their sleep and cognitive development. Data on sleep duration and nighttime awakenings were collected through the Brief Infant Sleep Questionnaire. Cognitive development was assessed by trained pediatricians using the Bayley Scales of Infant Development.

**Results:** Prevalence of no nighttime awakening, and nighttime awakening(s) for 1×/night, 2×/night, and  $\ge$  3×/night was 6.8%, 20.2%, 33.2%, and 39.3% in infants, and was 25.8%, 34.6%, 23.8%, and 15.8% in toddlers, respectively. Nighttime awakenings were generally associated with younger age, lower maternal education level, and being currently breastfed. In addition, nighttime awakenings were associated with being boys in toddlers. After controlling for potential confounders, infants with nighttime awakenings for 2×/night were found to have significantly higher Mental Development Index (MDI) score, as compared to those without and those with more frequent nighttime awakenings. However, toddlers with nighttime awakenings for  $\ge$  3×/night had significantly lower MDI, as compared to those with fewer nighttime awakenings. Total sleep duration was not associated with any developmental indices in both infants and toddlers.

**Conclusions:** Frequent nighttime awakenings are associated with poor cognitive functions in toddlers. Meanwhile, a nonlinear association between nighttime awakenings and cognitive performance was found among infants. The findings provide a developmental context for the effect of sleep on cognitive abilities in young children. Further longitudinal studies and interventional studies on the effects of parent-based sleep-focused intervention on cognitive abilities among young children are warranted.

Keywords: cognition, infant, psychomotor performance, sleep, toddler

**Citation:** Sun W, Li SX, Jiang Y, Xu X, Spruyt K, Zhu Q, Tseng C, Jiang F. A community-based study of sleep and cognitive development in infants and toddlers. *J Clin Sleep Med.* 2018;14(6):977–984.

### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** There is some evidence on the effects of sleep in early development, yet the existing studies are limited by a relatively small sample size and selected clinical populations (eg, preterm babies, infants with snoring). Data on sleep and cognitive abilities in physically healthy young children remain scanty. Therefore, we conducted an epidemiological study to investigate different aspects of sleep in relation to cognitive abilities in a large representative community sample of infants and toddlers.

Study Impact: A distinct pattern of association between sleep quality (ie, frequency of nighttime awakenings) and cognitive abilities in young children at different developmental stages was found. The findings provide a developmental context for the implications of nighttime awakenings in early years and underscore the need to address frequent nighttime awakenings particularly in toddlers. Future research is warranted to develop parent-based, sleep-focused educational intervention in the community and to examine the effects of such intervention on children's early development.

### INTRODUCTION

Inadequate sleep may have disruptive effects on the cognitive functions and learning capacity in children and adolescents.<sup>1-4</sup> A meta-analytic review has reported a positive relationship between sleep duration and cognitive performance among 5- to 12-year-old children.<sup>5</sup> Although the effects of sleep duration on cognition and behavioral problems have been clearly demonstrated in older children,<sup>5</sup> the evidence of this association is less consistent in young children. For example, some studies found that short sleep duration during toddlerhood is associated with preschoolers' verbal and nonverbal performance,<sup>6,7</sup> whereas others did not find an association between sleep duration and executive function from infancy to preschool age.<sup>8,9</sup>

Sleep problems are common in infants and toddlers (eg, 75.9% in mainland China, 24.4% in the United States).<sup>10-12</sup> Specifically, the prevalence of nighttime awakenings among children 0 to 3 years of age ranges from 20% to 66%,

depending on the defining criteria and age.13-18 Apart from insufficient sleep, behavioral sleep problems may potentially have a negative effect on several aspects of child development, including cognitive functioning.<sup>19,20</sup> Frequent nighttime awakenings could lead to fragmented sleep and compromise the quality of sleep in young children. However, few studies have explored nighttime awakenings in relation to cognitive development in infants and toddlers.<sup>21</sup> A previous study conducted in 10-month-old infants found that those with more fragmented sleep showed poorer performance on the Bayley Scales of Infant Development. Nonetheless, this study was limited by a small sample size (n = 50) and a narrow age range of the study participants.<sup>22</sup> Meanwhile, other existing studies only focused on the clinical samples (eg, infants with frequent snoring),<sup>23,24</sup> or high-risk young children (eg, those with autism).<sup>25</sup> There has been a paucity of data to explore the relationship between nighttime awakenings and cognitive abilities in the healthy full-term developing children.

Sleep during early childhood is often affected by a constellation of biological, behavioral, psychosocial, and cultural factors.<sup>26</sup> Increased nighttime awakenings in young children have been found to be related to the practice of co-sleeping with parents, receiving breastfeeding, and maternal mental health problems such as anxiety and depression.<sup>27–29</sup> In a cross-cultural survey, young Asian children were found to have shorter sleep duration, and to be more likely to have frequent nighttime awakenings and to co-sleep with their parents, as compared to their white counterparts.<sup>10</sup> Although sleep may be implicated in a child's cognitive development, whether such sleep characteristics, commonly observed in young Asian children, are linked to the development of cognitive abilities remains unclear.

To address the limitations in the existing literature, we aimed to conduct a large-scale epidemiological study to examine the prevalence and associated factors of nighttime awakenings in Chinese infants and toddlers, and to investigate the association of sleep quantity and sleep quality as reflected by nighttime awakenings with cognitive abilities in these young children.

### **METHODS**

### **Study Procedure and Participants**

The current study was conducted from October 2012 to March 2013, in collaboration with 16 hospitals from 8 provinces in mainland China. A multistage, stratified random sampling technique was applied to obtain a nationally representative sample of young children. The eight representative provinces (Inner Mongolia, Guangxi and Yunan in the western region, Hunan in the central region, Hebei, Shangdong, Zhejiang, and Jiangsu in the eastern region) were selected according to the geographical distribution of health-system coverage in China.<sup>30</sup> One downtown hospital and one suburban hospital from each selected province were randomly selected to cover the populations in both urban and rural regions. All the participating hospitals have a clinic to provide maternal and child health care services to the community. All healthy full-term infants and toddlers within the target age (2 to 30 months) visiting the

clinic for their regular health examination during the research period were invited to take part in the study. Children were excluded from the study if they were twins or triplets, or if they had any congenital diseases or experienced any complication at birth.

The study protocol was approved by the Shanghai Children's Medical Centre Human Ethics Committee (SCMCIRB-2012047). Written informed consent was obtained from the caregiver of each child. Participants did not receive any incentives for taking part in the study.

### **Sleep Measure**

The Chinese version of the Brief Infant Sleep Questionnaire (BISQ),<sup>31,32</sup> adopted from a previous cross-cultural study,<sup>10</sup> was used to measure a child's sleep quantity and quality. This widely used questionnaire has been validated against actigraphy and sleep logs, and includes specific questions about a child's daytime and nighttime sleep patterns. The child's primary caregiver was asked to complete BISQ based on the child's sleep characteristics during the previous 2 weeks before visiting the clinic, such as sleep duration, nighttime awakenings, and sleep practices (eg, bedroom sharing). Total sleep duration was calculated by summing daytime and nighttime sleep duration. Nighttime awakenings were assessed by the following two questions: (1) How often does your child awaken during the night? (2) On average, how long in total was your child awake during the night?

### **Developmental Assessment**

General development of the young children between the age of 2 to 30 months was assessed with the Chinese version of the Bayley Scales of Infant Development (BSID-I). It is a standardized diagnostic test of cognitive and motor development used in children aged 2 to 30 months, which has been validated in mainland China in 1993.33 The Mental Development Index (MDI) derived from the BSID-I is an indicator of the level of a child's cognitive and language development. The Psychomotor Development Index (PDI) provides an estimate of a child's fine and gross motor abilities. A higher score on BSID-I suggests better performance. The mean and standard deviation of BSID-I Chinese-adjusted norms are 100 and 16, respectively. The original psychometric reliability calculated by the Spearman-Brown prediction formula was 0.73-0.97 for MDI and was 0.67-0.97 for PDI. All assessments were conducted by well-trained pediatricians and the approximate duration of the assessment was 45 to 60 minutes. Interrater reliability as measured by kappa analysis had to reach 80% for all the pediatricians in the training phase before proceeding to the assessment phase of this study. Pediatricians conducted the BSID-I as part of a comprehensive assessment with the children in the study, which also included a physical examination and laboratory tests. To avoid assessor bias, they were not informed of specific study hypotheses at the time of conducting the assessments with the participating families.

### Sociodemographic Information

Shanghai Children's Medical Center Socio-Demographic Questionnaire was used to collect demographic information,

Table 1—Characteristics of infants (aged 2 to 11 months) with different frequency of nighttime awakenings.

		Frequency of Nighttime Awakenings				Statistic	
	Overall	None	1×/night	2×/night	≥ 3×/night	Value	Ρ
Infant, n (%)	590	40 (6.8)	119 (20.2)	196 (33.2)	232 (39.3)		
Age, months, mean (SD)	5.23 (2.51)	5.55 (2.41)	5.69 (2.73)	4.83 (2.37)	5.29 (2.48)	3.32	.02
Male, n (%)	321 (54.7)	18 (45.0)	62 (52.1)	108 (55.1)	133 (57.3)	2.27	.13 <sup>b</sup>
Birth weight, grams, mean (SD)	3407 (609)	3326 (381)	3462 (567)	3434 (719)	3372 (561)	0.94	.42
Maternal education level, n (%)						3.84	.05 <sup>b</sup>
Secondary school or lower <sup>a</sup>	164 (28.3)	6 (15.4)	30 (25.4)	63 (32.3)	65 (28.6)		
High school	170 (29.4)	11 (28.2)	37 (31.4)	46 (23.6)	76 (33.5)		
College or above	245 (42.3)	22 (56.4)	51 (43.2)	86 (44.1)	86 (37.9)		
Being currently breastfed, n (%)	429 (77.9)	30 (78.9)	69 (63.9)	141 (77.9)	189 (84.4)	10.02	.002 <sup>b</sup>
Bedroom sharing, n (%)	472 (80.5)	32 (80.0)	86 (72.3)	162 (83.1)	192 (82.8)	2.98	.09 <sup>b</sup>
Nighttime sleep duration, hours, mean (SD)	9.35 (1.47)	9.43 (1.26)	9.49 (1.42)	9.27 (1.43)	9.35 (1.55)	0.58	.63
Daytime sleep duration, hours, mean (SD)	3.56 (1.70)	3.51 (1.70)	3.51 (1.70)	3.66 (1.75)	3.49 (1.66)	0.40	.75
Total sleep duration, hours, mean (SD)	12.90 (2.03)	12.94 (1.74)	12.91 (1.98)	12.94 (2.02)	12.85 (2.13)	0.08	.97
Duration of nighttime awakening(s), hours, mean (SD)	0.63 (0.72)	0.05 (0.32)	0.35 (0.39)	0.64 (0.78)	0.86 (0.76)	48.70	< .001

Superscript letters indicate: a = secondary school is equivalent to 9th grade level in the United States, b = linear-by-linear association. SD = standard deviation.

such as parental age, parental education level, birth condition, and feeding patterns.

### **Statistical Analyses**

An initial examination of the data was performed to test for normality and outliers. Independent t tests and Mann-Whitney Utests were conducted to compare sleep duration and frequency of nighttime awakenings between infants (aged 2 to 11 months) and toddlers (aged 12 to 30 months). In light of the substantial changes of the sleep development in early years,<sup>34,35</sup> further analyses were subsequently conducted separately for the two age groups: infants aged 2 to 11 months (n = 590), and toddlers aged 12 to 30 months (n = 512). Infants and toddlers were further divided into four groups for analyses according to their frequency of nighttime awakenings: no awakening, once per night  $(1\times/night)$ , twice per night  $(2\times/night)$ , and at least three times per night ( $\geq 3 \times$ /night). Comparisons of the sociodemographic characteristics, sleep-related parenting practices (eg, bedroom sharing), and sleep duration across different frequency of nighttime awakening groups were performed using the  $\chi^2$  test for discrete variables, and one-way analysis of variance (ANOVA) for continuous variables. The frequency of nighttime awakenings and the duration of nighttime awakenings were highly correlated with each other ( $r_s = .65, P < .001$ ); as such, nighttime awakening frequency was used as the main indicator of sleep quality and was included in the major analyses.

The associations between the frequency of nighttime awakenings and BSID-I scores (MDI and PDI) were tested by the analysis of covariance (ANCOVA) in which recruited provinces and the child's age and sex were adjusted. In addition, linear regression models were established separately for each age group (ie, infants and toddlers) to examine the associations between sleep parameters (eg, total sleep duration, frequency of nighttime awakenings) and MDI. In fully-adjusted models, total sleep duration and nighttime awakening frequency were entered as independent variables, and recruited provinces, child's age and sex, birth weight, maternal education level, bedroom sharing, and current feeding pattern (breastfeeding) were entered as covariates. Covariates were selected on the basis of preliminary univariate statistical results and the previous reports of the factors associated with cognitive development in young children (see **Table S1** in the supplemental material).<sup>36,37</sup>

All analyses were performed using the Statistical Package for Social Sciences (SPSS) for Windows 22.0 (SPSS Inc., Chicago, Illinois, United States). The effect sizes of significant results were calculated and reported with the followings: Cohen *d* for *t* test, *r* for Pearson correlation, Cramér *V* for chi-square analysis, partial  $\eta^2$  for ANOVA and ANCOVA analysis, and  $\Delta R^2$  for the linear regression analysis. The statistical significance level was set at .05.

### RESULTS

### **Sample Characteristics**

A total of 1,102 young children (590 infants and 512 toddlers) were recruited and assessed (mean age: 12.40 [standard deviation 8.13] months, 53.8% male). Sample characteristics of the recruited infants and toddlers are presented in **Table 1** and **Table 2**. Approximately 69% of the infants obtained the recommended amount of daily sleep (12 to 16 h/d), and 80% of the toddlers slept for 11 to 14 h/d as recommended by the American Academy of Sleep Medicine.<sup>34</sup> On average, infants slept longer during the day than toddlers ( $3.56 \pm 1.70$  versus  $2.15 \pm 0.77$  hours, t = 17.97, d = 1.08, P < .001), but infants slept shorter during the night ( $9.35 \pm 1.47$  versus  $9.67 \pm 1.06$  hours, t = -4.17, d = -0.25, P < .001). Infants had a longer total sleep duration as compared to toddlers ( $12.90 \pm 2.03$  versus  $11.83 \pm 1.26$  hours, t = 10.49, d = 0.63, P < .001). Infants had more frequent nighttime awakenings than toddlers ( $2.19 \pm 1.22$ 

Table 2—Characteristics of toddlers (aged 12 to 30 months) with different frequency of nighttime awakenings.

		Fre	Statistic				
	Overall	None	1×/night	2×/night	≥ 3×/night	Value	Р
Toddler, n (%)	512	132 (25.8)	177 (34.6)	122 (23.8)	81 (15.8)		
Age, months, mean (SD)	19.14 (5.17)	20.68 (5.23)	19.62 (5.12)	18.57 (5.05)	18.17 (4.83)	5.53	.001
Male, n (%)	241 (47.1)	62 (47.0)	89 (50.3)	69 (56.6)	51 (63.0)	6.13	.01 <sup>b</sup>
Birth weight, grams, mean (SD)	3395 (581)	3452 (615)	3413 (531)	3385 (651)	3278 (508)	1.58	.19
Maternal education level, n (%)						4.23	.04 <sup>b</sup>
Secondary school or lower <sup>a</sup>	131 (26.0)	34 (26.2)	34 (19.7)	36 (29.8)	27 (34.2)		
High school	133 (26.4)	31 (23.8)	47 (27.2)	34 (28.1)	21 (26.6)		
College or above	239 (47.5)	65 (50.0)	92 (53.2)	51 (42.1)	31 (39.2)		
Being currently breastfed, n (%)	52 (11.0)	4 (3.3)	11 (6.7)	13 (11.5)	24 (33.3)	37.49	< .001 <sup>b</sup>
Bedroom sharing, n (%)	426 (83.2)	110 (83.3)	139 (78.5)	103 (84.4)	74 (91.4)	2.83	.09 <sup>b</sup>
Nighttime sleep duration, hours, mean (SD)	9.67 (1.06)	9.79 (1.02)	9.65 (1.03)	9.61 (1.17)	9.62 (1.03)	0.80	.50
Daytime sleep duration, hours, mean (SD)	2.15 (0.77)	2.17 (0.64)	2.16 (0.71)	2.19 (0.96)	2.06 (0.78)	0.50	.68
Total sleep duration, hours, mean (SD)	11.84 (1.26)	11.96 (1.08)	11.83 (1.26)	11.81 (1.38)	11.69 (1.32)	0.81	.49
Duration of nighttime awakening(s), hours, mean (SD)	0.34 (0.68)	0.003 (0.02)	0.33 (0.65)	0.52 (0.90)	0.67 (0.67)	58.03	< .001

Superscript letters indicate: a = secondary school is equivalent to 9th grade level in the United States, b = linear-by-linear association. SD = standard deviation.

versus  $1.28 \pm 1.09 \times$ /night, t = 13.10, d = 0.79, P < .001), and the total duration of nighttime awakenings was longer in infants as compared to toddlers ( $0.63 \pm 0.72$  versus  $0.34 \pm 0.68$  hours, log-transformed: t = 9.71, d = 0.59, P < .001).

The average MDI and PDI were  $103.13 \pm 17.12$  and  $101.97 \pm 15.91$ , respectively. In the overall sample, lower MDI was associated with younger age (r = .23, P < .001), lower birth weight (r = .12, P < .001), lower maternal education level (F = 34.57,  $\eta^2 = 0.19$ , P < .001), and being currently breastfed (t = 6.78, d = 0.42, P < .001); lower PDI was associated with lower birth weight (r = .10, P = .001) and lower maternal education level (F = 10.74,  $\eta^2 = 0.19$ , P < .001). There were differences in MDI (F = 47.85,  $\eta^2 = 0.23$ , P < .001) and PDI scores (F = 33.03,  $\eta^2 = 0.17$ , P < .001) in the children recruited from different provinces (**Table S1**).

# Prevalence and Correlates of Frequent Nighttime Awakenings

Prevalence of no nighttime awakening, and nighttime awakening(s) for 1×/night, 2×/night, and  $\ge$  3×/night was 6.8%, 20.2%, 33.2%, and 39.3% in infants, respectively. **Table 1** shows the characteristics of sociodemographic features, current feeding pattern, sleep practice, and sleep duration among infants with different frequency of nighttime awakenings. Frequency of nighttime awakenings was significantly associated with younger age ( $\eta^2 = 0.02$ , P = .02), lower maternal education level (V = 0.10, P = .05), and being currently breastfed (V = 0.18, P = .002) in infants.

Prevalence of no nighttime awakening, and nighttime awakening(s) for 1×/night, 2×/night and  $\ge$  3×/night was 25.8%, 34.6%, 23.8%, and 15.8% in toddlers, respectively. **Table 2** shows the characteristics of sociodemographic features, current feeding pattern, sleep practice, and sleep duration among toddlers with different frequency of nighttime awakenings. Frequency of nighttime awakenings was significantly associated

with younger age ( $\eta^2 = 0.03$ , P = .001), being boys (V = 0.11, P = .01), lower maternal educational level (V = 0.10, P = .04), and being currently breastfed (V = 0.32, P < .001) in toddlers.

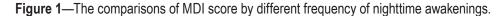
### **Association Between Sleep and Cognitive Functions**

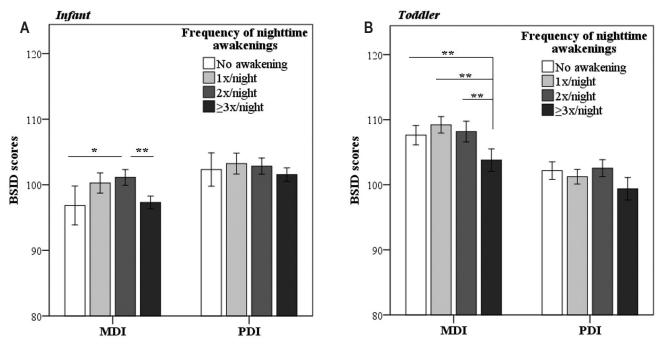
As shown in **Figure 1A**, the results of ANCOVA suggested that the frequency of nighttime awakenings was associated with MDI score (F = 3.00, partial  $\eta^2 = 0.02$ , P = .03) but not PDI score (P > .05) among infants. *Post hoc* analysis indicated that infants with nighttime awakenings for 2×/night had higher MDI scores than those without nighttime awakening (P < .05) and those with more frequent nighttime awakenings ( $\geq 3\times/$  night) (P < .05). **Figure 1B** shows the comparison of BSID scores among toddlers with different frequency of nighttime awakenings. Higher frequency of nighttime awakenings ( $\geq 3\times/$  night) was related to lower MDI (F = 3.84, partial  $\eta^2 = 0.02$ , P = .01) but not PDI (P > .05) in toddlers.

Results from linear regression analyses on the association between sleep characteristics and MDI are presented in **Table 3**. In the fully-adjusted model, nighttime awakenings for 2×/night were significantly associated with higher MDI in infants (P = .01,  $\Delta R^2_{sleep} = 0.016$ ), although this association was not observed for nighttime awakenings for  $\geq 3\times/night$  (P > .05). However, the analyses in the toddler group showed that nighttime awakenings for  $\geq 3\times/night$  were significantly associated with lower MDI (P = .03,  $\Delta R^2_{sleep} = 0.014$ ). Total sleep duration was not found to be associated with MDI in both infant and toddler samples.

### DISCUSSION

The current study provided community-based data on the prevalence and associated factors of reported nighttime awakenings in Chinese infants and toddlers. The findings





The comparisons of MDI score by different frequency of nighttime awakenings among infants (A) and toddlers (B). Error bars are standard error. Analysis of covariance (adjusted for recruited province, age and sex) and least significant difference *post hoc* analysis were conducted. Asterisks indicate statistical significance: \* = P < .05, \*\* = P < .01. BSID = Bayley Scales of Infant Development, MDI = Mental Development Index, PDI = Psychomotor Development Index.

Table 3—R	Results of linear	regression analys	ses on the	association between	sleep	characteristics and MDI.

	$B_{adj} \pm SE$	β	Р	$\Delta R^2$
Infant				0.016
Total sleep duration	-0.08 ± 0.29	-0.01	.78	
Frequency of nighttime awakenings				
No awakening	Ref.			
1×/night	1.45 ± 2.56	0.04	.57	
2×/night	$6.03 \pm 2.43$	0.18	.01	
≥ 3×/night	$2.30 \pm 2.38$	0.07	.34	
Toddler				0.014
Total sleep duration	0.81 ± 0.56	0.06	.15	
Frequency of nighttime awakenings				
No awakening	Ref.			
1×/night	-0.09 ± 1.79	-0.002	.96	
2×/night	0.20 ± 1.99	0.01	.92	
≥ 3×/night	-5.15 ± 2.39	-0.11	.03	

Adjusted for recruited province, child's age and sex, birth weight, maternal education level, bedroom sharing and being currently breastfed.  $\beta$  = standardized coefficients, B = unstandardized coefficients, MDI = Mental Development Index, SE = standard error of B.

showed an association between sleep quality as reflected by the frequency of nighttime awakenings and cognitive abilities in young children, with a distinct pattern found at different developmental stages. In particular, poorer cognitive performance was observed in toddlers with more frequent nighttime awakenings, whereas infants with modest frequency of night awakenings (about twice per night) showed better cognitive performance. In line with the findings of a previous cross-cultural survey,<sup>10</sup> our study showed that the average frequency of nighttime awakenings in Chinese young children ( $1.8\times/night$ ) was higher as compared to the figure ( $0.8\times/night$ ) reported by a recent review that included the studies conducted predominantly in white populations.<sup>38</sup> The observed cultural difference in the reported frequency of nighttime awakenings might be due to some distinct sleep-related parenting practices, such as bedroom sharing, that are more common in Asian culture.<sup>10</sup> Similar to other studies,<sup>28</sup> we found that a marginally significant association between bedroom sharing and the frequency of reported nighttime awakenings in infants and toddlers. Although the exact causes of increased nighttime awakenings in young children in association with bedroom sharing remain unclear, there are several possible explanations that may account for this observation. It is possible that improper sleeprelated parenting practices may have contributed to night waking problems in these young children. Meanwhile, sleep proximity could potentially affect the parental report of nighttime awakenings. Co-sleeping parents might be more likely to notice the movements of their child during sleep that were not necessarily suggestive of a waking state. It is also possible that co-sleeping parents might have more mental health difficulties or sleep problems themselves, which could potentially affect their child's sleep<sup>29</sup> or might result in a biased evaluation of their child's sleep.39

In addition to co-sleeping, we found that young children who were currently breastfed were more likely to have more frequent nighttime awakenings. Nighttime awakenings in infants may naturally serve the adaptive functions for the child's need of feeding and seeking comfort during the night. However, the association between current breastfeeding and frequent nighttime awakenings might be modulated by other factors, such as improper parenting practices during nighttime breastfeeding (eg, nursing to sleep) that could hinder the development of the abilities required for the young children to fall asleep independently.<sup>40</sup> In addition, some parents may assume breastfeeding to be a comforting behavior to facilitate their child's sleep.<sup>41</sup> Although such a strategy is effective in reducing sleep latency in the short term, it may prevent young children from learning self-soothing skills to maintain self-regulated sleep at night.

Our study showed a distinct pattern of association between the frequency of nighttime awakenings and cognitive abilities in young children at different developmental stages. Interestingly, infants with modest frequency of nighttime awakenings were found to show better cognitive abilities than those rarely waking up during the night (ie, no nighttime awakening). This finding was in line with that of previous studies showing that neonates and young infants with reduced arousals or longer noninterrupted sleep period have slower brain development in their first year.<sup>42,43</sup> Meanwhile, the association between frequent nighttime awakenings and poorer cognitive development was found in infants and toddlers after controlling for potential confounding influence of maternal education level on both cognitive performance and nighttime awakenings. Sleep consolidation is an age-dependent process that develops throughout the first few years of life.44-46 When children grow older, they are expected to gradually develop the ability to maintain self-regulated sleep throughout the night, along with the well-established attachment and mature selfsoothing skills.<sup>47</sup> As a result, the frequency of nighttime awakenings is expected to decrease significantly with increasing age.<sup>31,48</sup> A previous study conducted in Chinese preschoolers has also found that preschoolers with behavioral sleep problems (eg, difficulty maintaining sleep, bedtime resistance) had lower total IQ scores.<sup>49</sup> In this regard, it is possible that sleep

fragmentation and poor sleep quality as reflected by frequent nighttime awakenings might lead to a neurocognitive decrement. Experimental studies using animal models have shown that chronic sleep fragmentation impairs hippocampal-dependent cognitive functions by reducing neurogenesis.<sup>50</sup> From a clinical perspective, frequent nighttime awakenings are often found in young children with developmental concerns, such as autism and intellectual disability, which might potentially explain the findings in some toddlers.<sup>51,52</sup> Nonetheless, there is a need for prospective follow-up studies to delineate the association between these developmental outcomes and frequent nighttime awakenings.

The current study did not find an association between total sleep duration and cognitive performance in infants and toddlers. This result was in line with that of previous studies conducted among young children, emphasizing the importance of other aspects of sleep in relation to cognitive development during this developmental stage. A previous study has shown that infants with better ultradian sleep regulation (eg, lower sleep fragmentation) had higher MDI scores.<sup>22</sup> In addition, infants with better circadian sleep regulation (ie, higher proportion of nighttime sleep) have been found to perform better on executive function tasks.<sup>53</sup> Another speculation of the insignificant association observed between sleep duration and cognitive performance might be because most of the young children in the current sample obtained the recommended amount of sleep.

The findings of this study provide a developmental context for the implications of nighttime awakenings in early years and underscore the need to address frequent nighttime awakenings particularly in toddlers. Although poor sleep may not be the only factor contributing to impaired cognitive functioning in young children, sleep problem is a potentially modifiable risk factor that can be the target for clinical intervention and prevention. In this regard, there has been some evidence to support the efficacy of behavioral treatment in improving nighttime awakenings in young children.<sup>54</sup> Future longitudinal studies are needed to investigate the effects of age-appropriate sleep-focused intervention on the cognitive development in young children.

The main strengths of our study included the recruitment of a large number of low-risk young children from the community, and the formal assessment of a child's cognitive abilities by clinicians using a standardized test, instead of the parentreported questionnaires. Meanwhile, the findings of this study should be considered in light of several limitations. First, the sleep assessment in this study was based on the parental report. Future studies should incorporate objective measures (eg, actigraphy, video or polysomnographic recordings) to corroborate subjective reports. In a previous study conducted in 10-month-old infants, although the parental report of nighttime awakenings was not related to lower MDI, nighttime awakenings as measured by actigraphy were shown to be negatively associated with cognitive function.<sup>22</sup> Second, the current study was limited by its cross-sectional design, which precluded the inference of causal relationship. Further studies are warranted to delineate the causal factors associated with frequent nighttime awakenings in young children and to further explore the potential mechanisms underlying the association between

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frequent nighttime awakenings and poor cognitive development. Third, some of the factors that might confound the association between sleep and cognitive abilities were not measured in this study, such as parent-child interactions, maternal mental health, parental knowledge of children's sleep patterns, and parental smoking, as well as other environmental factors. Finally, the objective assessment of a child's cognitive abilities was based on an older version of the BSID, which was the only version with well-established norms available in the Chinese population. Future studies should adopt other validated, standardized assessment tools to further explore specific cognitive functions that may be affected by sleep during early child development.

In conclusion, our study showed a distinct pattern of association between nighttime awakenings and cognitive performance in young children. During the first year of life, nighttime awakenings with varied frequency are common as reported across different studies.<sup>55,56</sup> However, to the authors' knowledge, this is the first study, albeit with a cross-sectional design, to show the developmental implication of nighttime awakenings, particularly on cognitive abilities, in young children. Future longitudinal studies are warranted to further examine the developmental outcomes in relation to nighttime awakenings in young children. Further research is also needed to explore the effects of parent-based, sleep-focused educational intervention in the community on children's early development.

## ABBREVIATIONS

BSID-I, Bayley Scales of Infant Development MDI, Mental Development Index PDI, Psychomotor Development Index

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### ACKNOWLEDGMENTS

The authors thank the children and their families for their participation and the 16 hospitals in the eight provinces for facilitating the recruitment of this study. We appreciate Dr. Chingfan Sheu from the Institute of Education, National Cheng Kung University, Taiwan for his advice on data analysis.

### SUBMISSION & CORRESPONDENCE INFORMATION

#### Submitted for publication September 10, 2017 Submitted in final revised form February 3, 2018 Accepted for publication March 6, 2018

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### DISCLOSURE STATEMENT

The work was performed in Shanghai Children's Medical Center in collaboration with Shijiazhuang City Maternal and Child Health Hospital (Hebei), Shijiazhuang Qiaodong Maternal and Child Health Station (Hebei), Yiwu City Maternal and Child Health Hospital (Zhejiang), Yiwu Choucheng Health Center (Zhejiang), Rizhao Juxian People's Hospital (Shandong), Rizhao City People's Hospital (Shandong), Hongze County Maternal and Child Health Hospital (Jiangsu), Huai'an City Maternal and Child Health Hospital (Jiangsu), Kunming Children's Hospital (Yunnan), Inner Mongolia Maternal and Child Health Hospital (Inner Mongolia), Liuyang City Maternal and Child Health Hospital (Hunan), Liuyang Gugang Health Center (Hunan), Nandan County Maternal and Child Health Hospital (Guangxi), and Guangxi Autonomous Region Maternal and Child Health Hospital (Guangxi). All the authors have seen and approved the manuscript. The authors report no conflicts of interest. The study was supported by the Chinese National Natural Science Foundation (81422040, 81172685); MOE New Century Excellent Talents (NCET-13-0362); Ministry of Science and Technology (2010CB535000); Shanghai Science and Technology Commission (12411950405, 14441904004, 13QH1401800, 2016YFC1305203); Shanghai Municipal Committee of Education (D1502); The fourth round of Three-Year Public Health Action Plan (2015-2017) (GWIV-36). All funding was awarded to Dr. Fan Jiang. The funding body had no role in the conception, design, conduct, interpretation, or analysis of the study or in the approval of the publication.