ORIGINAL RESEARCH Associations Between Self-Reported Sleep Disturbances and Cognitive Impairment: A Population-Based Cross-Sectional Study

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Objective: Cognitive impairment is a rapidly growing global public health problem in China and worldwide. In the recent decades, emerging studies have explored the associations between sleep disturbances and cognitive impairment. However, the variety of the results imply us that further studies should be conducted for the associations.

Methods: This is a cross-sectional study conducted between August and October 2018 in five cities in Hebei province, China. Subjects were 21,376 community residents. Cognitive impairment was screened by the Chinese version of the Mini-Mental State Examination (MMSE). Scales of Athens Insomnia Scale (AIS), Berlin Questionnaire (BQ), REM (rapid eye movement) Sleep Behavior Disorder Questionnaire (RBDQ-HK), Ullanlinna Narcolepsy Scale (CUNS), and Cambridge-Hopkins Restless Legs Syndrome Questionnaire (CH-RLSq) were used to access insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, and restless leg syndrome.

Results: The mean \pm SD (standard error) of MMSE, AIS, RBDQ-HK, and CUNS were 27.95 ± 4.79 , 2.16 ± 3.39 , 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , and $3.76 \pm 2.16 \pm 3.39$, 5.55 ± 7.75 , 5.52.31, respectively. Among the participants, 10.6% and 1.5% of the participants were identified as having a high risk of sleep apnea and restless leg syndrome, respectively. The results of multiple linear regression showed that cognitive impairment was associated with insomnia ($\beta = -0.037$, p < 0.001) and narcolepsy ($\beta = -0.023$, p < 0.001). The association between sleep apnea ($\beta = -0.002$, p > 0.05), REM sleep behavior disorder ($\beta = 0.006$, p > 0.05), restless leg syndrome ($\beta = -0.007$, p > 0.05), and cognitive impairment were not supported. Other factors associated with cognitive impairment were gender, age, education level, married status, and region.

Conclusion: This study provides some epidemiological evidence for the association between sleep disturbances and cognitive impairment among community residents in central China. In this study, the associations between insomnia, narcolepsy, and cognitive impairment were identified, but the associations between sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome, and cognitive impairment were not supported among community residents.

Keywords: insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome, cognitive impairment

Introduction

In recent decades, cognitive impairment has been a rapidly growing global public health problem. Globally, around 50 million people could be diagnosed with dementia, and approximately 60% of them lived in low- and middle-income countries (LMIC), including China.¹ In China, cognitive impairment was also an urgent public health issue with high prevalence because of the rapid aging process.^{2,3} Until now, many lifestyle-related risk factors and certain medical conditions have been identified to be associated with the development of cognitive impairment, which were also recommended by the World Health Organization (WHO).⁴

Although the associations between sleep problems and cognitive impairment were identified in many studies, ⁵⁻⁹ improving sleep quality was not recommended to prevent cognitive impairment by WHO. A recent specialist consensus

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also mentioned that the mechanisms by which sleep disturbances might affect cognitive impairment remained unclear.¹⁰ Both of these remind us that the associations between sleep problems and cognitive impairment need to be further explored.

In the recent decades, emerging studies have explored the associations between sleep disturbances and cognitive impairment, and some kinds of sleep disturbances were identified to be associated with cognitive impairment, such as insomnia and¹¹ sleep disordered breathing.^{12,13} However, the results about the associations between some other kinds of sleep disturbances and cognitive impairment are varied. For example, the associations between REM (rapid eye movement) sleep behavior disorder and cognitive impairment were conflicted,^{14–17} the associations between narcolepsy and cognitive impairment were lack of evidence in the population,¹⁸ and the associations between restless leg syndrome and cognitive impairment were less reported. All of these remind us that more studies should be conducted to clarify the associations between specific sleep disturbances and cognitive impairment.

To fill the gaps, a cross-sectional study was conducted in Chinese Hebei province to examine the associations between five kinds of common sleep disturbances (insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome)¹⁹ and cognitive impairment among community residents. This study not only can provide more epidemiological evidence for the association between sleep disturbances and cognitive impairment but also can help us to further understand the association between insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome, and cognitive impairment.

Methods

Sampling and Participants

Data analyzed in this study were obtained from the Hebei Epidemiological Survey of Sleep Disturbance (HBESSD). Hebei is a province located in the middle of China, and its Gross Domestic Product (GDP) per capital ranked 21st in all the 31 provinces of Chinese mainland. In this study, a multistage stratified cluster sampling was used to collect the data according to the following 4 steps. In each step, simple random sampling was used to select the regions to conduct this study. Firstly, five cities (Shijiazhuang, Baoding, Xingtai, Zhangjiakou, Qinhuangdao) were randomly selected from all the 11 cities in Hebei province. Secondly, we randomly selected three counties and one district in each selected city (Xinhua, Jinzhou, Yuanshi, Lingshou, Jingxiu, Zhuozhou, Yixian, Shunping, Qiaodong, Shahe, Weixian, Pingxiang, Qiaoxi, Zhuolu, Chicheng, Yangyuan, Shanhaiguan, Changli, Lulong, Qinglong). Thirdly, one township or sub-district was randomly selected from each county or district, respectively. Fourthly, we randomly selected one village (neighborhood) in each township (sub-district). In total, we selected 15 villages and 5 neighborhoods to conduct this study. In all of the selected villages and neighborhoods, community residents aged 18 years and above were employed in the interview. In this study, subjects with severe cognitive disorders or major depression disorders were excluded from this study. Finally, 21,376 valid questionnaires were collected in this study.

The interview was conducted from June to August 2018. Before the survey, all the interviewers should be well trained to fully understand the research and questionnaire. The questionnaires should be checked on each interview day to ensure the accuracy of the answers. The interviewers should revisit or call the participants to solve the missing data problem.

Patient and Public Involvement Statement

For each participant, the local general practitioner or the village administration firstly approached them with a personal visit. Upon their agreement on the written informed consent, the interview was scheduled by one interviewer.

Measures

Cognitive Impairment

Cognitive impairment was screened by the Chinese version of the Mini-mental State Examination (MMSE).²⁰ It contains 30 items with a maximum score of 30 points.²¹ Previous studies have identified it as a good screening tool for cognitive impairment.^{22,23} Lower scores referred to a higher risk of cognitive impairment. In this study, cognitive impairment was

the dependent variable in the data analyses, and the scores of MMSE were analyzed to explore the association between sleep disturbances and cognitive impairment.

Insomnia

We used the Athens Insomnia Scale (AIS) to evaluate participants' insomnia status in this study.²⁴ The Chinese version of this scale was also proved to be a reliable and valid instrument.²⁵ The higher score indicated a higher risk of insomnia. It was also translated into different languages worldwide.^{26,27} In this study, the scores of AIS were analyzed to identify the association between insomnia and cognitive impairment.

Sleep Apnea

Sleep apnea was estimated by the Chinese version of the Berlin Questionnaire.^{28,29} It contained 10 items, which can be divided into three categories, snoring behavior, daytime sleepiness, and high blood pressure/BMI. Participants with two or more positive responses in the three categories were at risk of sleep apnea.³⁰ The diagnostic accuracy of this scale was also evaluated in previous Chinese studies.³¹ In this study, the participants at risk of sleep apnea or not were analyzed to identify the association between sleep apnea and cognitive impairment.

REM Sleep Behavior Disorder

The Chinese version of the REM (Rapid Eye Movement) Sleep Behavior Disorder Questionnaire (RBDQ-HK) was used to assess sleep behavior disorder in this study.³² In this scale, there were 17 items about dream-related and behavioral manifestation, and the scores ranged from 0 to 100. The higher scores indicated a higher risk of REM sleep behavior disorder. This scale was also used in some other studies with nice reliability and validity.^{33,34} The scores of RBDQ-HK were analyzed in this study.

Narcolepsy

The Chinese version of the Ullanlinna Narcolepsy Scale (CUNS) was used to evaluate the participants' risk of narcolepsy.³⁵ There are 11 items with total scores ranging from 0 to 44.³⁶ A higher score means a higher risk of narcolepsy. This scale was evaluated with good reliability and validity in many previous studies.^{37–39} In this study, we analyzed the scores of CUNS to explore the association between narcolepsy and cognitive impairment.

Restless Leg Syndrome

Cambridge-Hopkins Restless Legs Syndrome Questionnaire (CH-RLSq) was used to assess restless legs syndrome, and its validity and sensitivity for diagnosing restless legs syndrome were also proved in previous studies.⁴⁰ It was also used and translated into other languages.^{41,42} In this study, we analyzed it as a categorical variable with yes or no basing on the standard of CH-RLSq.

Social-Demographic Variables

Gender was measured by male (1) and female (0). Age was calculated by the participants' date of birth, we recoded it into 18–34 years (1), 35–49 years (2), 50–64 years (3) and 65 years or above (4). Education level was assessed by the academic degree with answers that illiteracy/semiliterate, elementary school, junior school, high school, college, or bachelor and above. As a small percentage of college and bachelor's degrees, we recoded it into illiteracy/semiliterate (1), elementary school (2), junior school (3), and high school or above (4). Married status was evaluated by one question about the participants' married status. The answers were never married, married, divorced, widowed, deuterogamist, and others. As a small percentage of the last 4 answers, we recoded it into never married (1), married (2), and others (3). Region was assessed by the region where the participants lived, and the answers were urban (0) and rural (1).

Statistical Analyses

Stata for Windows (version 12.0) was used for data analysis. Student's *t*-test and one-way ANOVA (Analysis of Variance) were used to compare the statistical differences of cognitive impairment on the categorical variables.

Bivariate correlation was conducted to test the correlations between cognitive impairment and continuous variables. Multiple linear regression was further performed to examine the association between insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome, and cognitive impairment, and the standardized coefficients (β) and their 95% confidence interval were used to show the results. The associations between the five kinds of sleep disturbances (insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome) and cognitive impairment were analyzed one by one, after controlling the social-demographic variables. We also added all five types of sleep disturbances in one model to analyze the association between the five kinds of sleep disturbances and cognitive impairment. For each categorical independent variable, one category was used as the reference group, and the remaining categories were included in the model as dummy variables. All significance tests were two-tailed and a p-value of 0.05 or lower was considered to be statistically significant.

Results

In this study, we collected 21,376 valid questionnaires. The social-demographic characteristics and estimated sleep disturbances based on standard scales are illustrated in Table 1. Among these participants, there were more participants, who were females (54.0%), married (86.5%), with junior school degrees (38.7%), and living in the rural region (71.9%). More details about the social-demographic characteristics of our sample could be found in the second column of Table 1. The mean \pm SD (standard error) of MMSE, AIS, RBDQ-HK, and CUNS were 27.95 \pm 4.79, 2.16 \pm 3.39, 5.55 \pm 7.75, and 3.76 \pm 2.31, respectively. Among the participants, 10.6% and 1.5% of the participants were identified as having a high risk of sleep apnea and restless leg syndrome, respectively. The results of univariate analyses found that gender (t = 11.53, p < 0.001), age (F = 9303.47, p < 0.001), education level (F = 2061.04, p < 0.001), married status (F = 1091.41, p < 0.001), region (t = -9.25, p < 0.001), insomnia (r = 0.28, p < 0.001), REM sleep behavior disorder (r = -0.24, p < 0.001), narcolepsy (r = -0.18, p < 0.001), restless leg syndrome (t = -7.67, p < 0.001) were associated with cognitive impairment.

Multiple linear regressions were further performed to analyse the associations between the five kinds of sleep disturbances (insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome) and cognitive impairment, and the standardized coefficients (β) were used to show the results for these analyzed variables. In the first five models (Model 1 to Model 5), the associations between insomnia, sleep apnea, REM sleep behavior disorder, narcolepsy, restless leg syndrome, and cognitive impairment were analyzed one by one, after controlling the socialdemographic variables. The results supported that cognitive impairment was respectively associated with insomnia (β = -0.031, p < 0.001), narcolepsy ($\beta = -0.015$, p < 0.001), and restless leg syndrome ($\beta = -0.007$, p < 0.05) after controlling gender, age, education level, married status, and region in Model 1, 4, and 5. However, the association between sleep apnea ($\beta = -0.002$, p > 0.05), REM sleep behavior disorder ($\beta = -0.005$, p > 0.05), and cognitive impairment were not statistically significant in Model 2 and 3. In Model 6, we added all five types of sleep disturbances to one model, and we found that insomnia ($\beta = -0.037$, p < 0.001) and narcolepsy ($\beta = -0.023$, p < 0.001) were still associated with a higher risk of cognitive impairment. However, the association between restless leg syndrome ($\beta = -0.007$, p > 0.05), sleep apnea $(\beta = -0.002, p > 0.05)$, REM sleep behavior disorder ($\beta = 0.006, p > 0.05$), and cognitive impairment was not statistically significant. In all of the six models, the social-demographic variables controlled in the regressions (gender, age, education level, married status, and region) were supported to be associated with cognitive impairment (all p < 0.05). The Variance Inflation Factor (VIF) values in these models ranged from 1.0 to 2.5 in these regressions, which reminded us that the multicollinearity problem in the regressions was at a lower level. The detailed results of multiple linear regressions are shown in Table 2.

Discussion

Using a large-scale, representative survey in central China, we found that insomnia and narcolepsy were associated with cognitive impairment, but the associations between sleep apnea, REM sleep behavior disorder, restless leg syndrome, and cognitive impairment were not supported among the community residents.

The first finding in this study was that insomnia and narcolepsy were associated with cognitive impairment, after controlling for some social-demographic variables. In fact, the revealed results are not new and have been identified in

Variable	n (%)	MMSE (Mean±SD)	t/F/r
Total	21,376 (100.0)	27.95±4.79	-
Gender			t=11.53 [‡]
Male	9839 (46.0)	28.36±4.03	
Female	11,537 (54.0)	27.60±5.32	
Age			F=9303.47 [‡]
18–34 years	4424 (20.7)	29.98±0.48	
35–49 years	4970 (23.3)	29.99±0.34	
50–64 years	7282 (34.1)	29.70±1.92	
≥ 65years	4700 (22.0)	21.17±6.26	
Education level			F=2061.04 [‡]
Illiteracy/ semiliterate	2691 (12.6)	22.62±7.97	
Elementary school	5264 (24.6)	26.98±5.18	
Junior school	8274 (38.7)	29.29±2.48	
High school or above	5147 (24.1)	29.59±1.79	
Married status			F=1091.41
Unmarried	1548 (7.2)	29.52±2.61	
Married	18,487 (86.5)	28.22±4.40	
Others	34 (6.3)	22.47±7.53	
Region			t=-9.25 [‡]
Urban	5100 (23.9)	28.49±3.67	
Rural	16,276 (76.1)	27.78±5.07	
Insomnia	2.16±3.39	-	r=0.28 [‡]
Sleep apnea			t=-1.45
High risk	2264 (10.6)	27.81±4.91	
Low risk	19,112 (89.4)	27.97±4.77	
REM sleep behavior disorder	5.55±7.75	-	r=-0.24 [‡]
Narcolepsy	3.76±2.31	-	r=-0.18 [‡]
Restless leg syndrome			t=-7.67 [‡]
High risk	328 (1.5)	25.95±6.11	
Low risk	21,078 (98.5)	27.98±4.76	

 Table I
 Social-Demographic Description and Single Analyses About Factors Associated with Cognitive Impairment (MMSE Scores) in the Sample

Note: [‡]p<0.001.

Abbreviation: SD, standard error.

many previous studies.^{43–45} However, due to the limitation of the small sample size and special patients in some previous studies,^{46,47} our study further supported these associations among community residents. These associations may be explained by problems with sleep duration, which have been identified to be associated with cognitive impairment in previous studies.^{48,49} The mechanism may be caused by the effect of increasing cerebral β -amyloid burden, which was found in previous studies.^{50–52}

In this study, the association between sleep apnea and cognitive impairment was not supported after controlling the social-demographic variables. In fact, associations between sleep apnea and cognitive impairment were found in previous studies.^{53,54} The mechanism may be explained by the neurocognitive decline in individuals with sleep apnea. Patients with sleep apnea may lead to recurrent intermittent hypoxia, and it may further gradually lead to the brain neurodegenerative processes.⁵⁵ However, the association was also influenced by sleep apnea diagnostic methods and recruitment, which was identified in the previous study.⁵⁶ The inconsistent results for this study may be caused by the scale of Berlin Questionnaire and the sample of community residents.

The associations between REM sleep behavior disorder and cognitive impairment were not found in this study. Many previous clinical studies supported the association,^{57,58} but a longitudinal prospective study also did not support the

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Variable	Model I	Model 2	Model 3	Model 4	Model 5	Model 6
Male	0.017 (0.009, 0.026)‡	0.021 (0.012, 0.029)‡	0.020 (0.012, 0.029) [‡]	0.022 (0.013, 0.030)‡	0.021 (0.012, 0.029) [‡]	0.018 (0.010, 0.027) [‡]
Age (Ref.= ≥65 years)						
18–34 years	0.634 (0.622, 0.647) [‡]	0.640 (0.628, 0.653) [‡]	0.640 (0.628, 0.652) [‡]	0.640 (0.628, 0.653) [‡]	0.640 (0.628, 0.652) [‡]	0.633 (0.620, 0.645) [‡]
35-49 years	0.673 (0.662, 0.685) [‡]	0.678 (0.667, 0.689) [‡]	0.678 (0.666, 0.689) [‡]	0.678 (0.667, 0.690) [‡]	0.678 (0.666, 0.689) [‡]	0.672 (0.661, 0.684) [‡]
50-64 years	0.768 (0.757, 0.779) [‡]	0.769 (0.758, 0.780) [‡]	0.767 (0.756, 0.779) [‡]			
Education level (Ref.= High school or above)						
Illiterate/Semiliterate	-0.213 (-0.224, -0.202) [‡]	-0.215 (-0.226, -0.204) [‡]	-0.215 (-0.226, -0.204) [‡]	-0.216 (-0.227, -0.205) [‡]	-0.215 (-0.226, -0.204) [‡]	-0.213 (-0.224, -0.202) [‡]
Elementary school	-0.031 (-0.042, -0.019) [‡]	-0.033 (-0.044, -0.021) [‡]	-0.033 (-0.044, -0.021) [‡]	-0.033 (-0.045, -0.022) [‡]	-0.033 (-0.044, -0.021) [‡]	-0.031 (-0.043, -0.020) [‡]
Junior school	0.011 (0.000, 0.022) [†]	0.011 (0.000, 0.022)	0.011 (0.000, 0.022)	0.010 (-0.001, 0.022)	0.011 (0.000, 0.022)	0.011 (0.000, 0.022)
Married status (Ref.=Others)						
Unmarried	0.067 (0.054, 0.080) [‡]	0.068 (0.055, 0.081) [‡]	0.068 (0.055, 0.081) [‡]	0.069 (0.056, 0.081) [‡]	0.068 (0.055, 0.081) [‡]	0.068 (0.055, 0.081) [‡]
Married	0.092 (0.079, 0.104) [‡]	0.093 (0.081, 0.105) [‡]	0.093 (0.081, 0.105) [‡]	0.093 (0.081, 0.106) [‡]	0.093 (0.081, 0.105) [‡]	0.092 (0.080, 0.104) [‡]
Rural region	-0.052 (-0.061, -0.043) [‡]	-0.054 (-0.063, -0.045) [‡]	-0.054 (-0.063, -0.045) [‡]	-0.055 (-0.064, -0.046) [‡]	-0.054 (-0.062, -0.045) [‡]	-0.053 (-0.062, -0.044) [‡]
Insomnia	-0.031 (-0.039, -0.022) [‡]	-	-	-	-	-0.037 (-0.046, -0.028) [‡]
Sleep apnea	-	-0.002 (-0.010, 0.007)	-	-	-	-0.002 (-0.010, 0.007)
REM sleep behavior disorder	-	-	-0.005 (-0.013, 0.004)	-	-	0.006 (-0.003, 0.014)
Narcolepsy	-	-	-	-0.015 (-0.023, -0.007)‡	-	-0.023 (-0.031, -0.014) [‡]
Restless leg syndrome	-	-	-	-	-0.010 (-0.018, -0.001) [†]	-0.007 (-0.015, 0.002)
Adjusted R^2	0.622	0.621	0.621	0.622	0.622	0.623

Table 2 Multiple Linear Regression for the Association Between Sleep Disturbances and Cognitive Impairment (n = 21,376)

Notes: β and its 95% confidence interval were shown in this table, and the β means the standardized coefficient in the regressions. REM refers rapid eye movement. The dependent variable cognitive impairment was analyzed by the scores of MMSE. Insomnia was analyzed by the scores of AIS (Athens Insomnia Scale). Sleep apnea was analyzed by the high risk of sleep apnea or not basing on the standard of Berlin Questionnaire. REM sleep behavior disorder was analyzed by the scores of RBDQ-HK (REM Sleep Behavior Disorder Questionnaire). Narcolepsy was analyzed by the scores of CUNS (Ullanlinna Narcolepsy Scale). Restless leg syndrome was analyzed by the high risk of restless leg syndrome or not basing on the standard of CH-RLSq (Cambridge-Hopkins Restless Legs Syndrome Questionnaire). [†]p<0.05; [‡]p<0.001.

association.¹⁷ Studies supporting this association mainly explain it as an effect of amyloid- β deposition,⁵⁹ but the recent studies have found that amyloid accumulation does not always begin at the early stage of cognitive impairment with Lewy Bodies.⁶⁰ The other reason may be that lack of REM sleep is not necessarily related to REM sleep behavior disorder,⁶¹ and REM sleep deprivation does not seem to be the whole explanation for impaired cognition in REM sleep behavior disorder.

In this study, the association between restless leg syndrome and cognitive impairment was significant in 0.05 level, when we controlled social-demographic variables. However, the association was disappeared when we further controlled other 4 types of sleep disturbances. The results remind us that the association between restless leg syndrome and cognitive impairment could be absorbed into insomnia or narcolepsy, which can be discussed in the further studies. Actually, there were few studies, which reported this association before. A study in France reported an absent association between restless leg syndrome and amyloid burden. Since amyloid burden is an important biomarker for cognitive impairment,⁶² it can imply us the absence of association between restless leg syndrome and cognitive impairment.

Some limitations should be considered when we interpret the findings. First and most important, because of the crosssection design, we cannot infer any causal relationships for the results. Secondly, due to the numerous varieties of sleep disturbances, although we analyzed 5 kinds of relatively common and important sleep disturbances, some other kinds of sleep disturbances also need to be considered in future studies. Thirdly, sleep disturbances and cognitive impairment were evaluated using standard scales. Although the sensitivity and specificity of these scales have been identified in previous studies, the accuracy of the scales was also lower than the clinical diagnoses. It may cause some bias to the findings in this study. Fourthly, a variety of cognitive impairment was not considered because of the limitation of the scale of MMSE.

Conclusions

Despite these limitations, this is one of the few studies conducted among community residents to explore the associations between sleep disturbances and cognitive impairment using a large-scale, representative survey in central China. The associations between insomnia, narcolepsy, and cognitive impairment are supported in the study, but we did not find an association between sleep apnea, REM sleep behavior disorder, restless leg syndrome, and cognitive impairment. These findings provide some epidemiological evidence for the association between sleep disturbances and cognitive impairment among community residents in central China, and are helpful for us to further understand the associations between sleep disturbances and cognitive impairment.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

The Institutional Review Board (IRB) of Hebei Provincial Mental Health Center approved the study protocol before the data collection (Ref. No. 201813). This study was performed in compliance with the 1964 Declaration of Helsinki and its later amendments. Written informed consent was obtained from all the participants in the current study.

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Disclosure

The authors report no conflicts of interest in this work.

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