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SCIENTIFIC INVESTIGATIONS

Association between sleep structure and amnesic mild cognitive impairment in patients with insomnia disorder: a case-control study

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Study Objectives: To examine the association between sleep structure and amnesic mild cognitive impairment (aMCI) in patients with insomnia disorder.

Methods: A total of 256 patients with insomnia disorder were diagnosed by neurologists, 45 of whom were diagnosed with aMCI according to the Petersen criteria, and 45 participants with intact cognition were chosen as controls matched for age and education. A case-control study was conducted to compare sleep structure between aMCI and control patients with insomnia disorder. We evaluated self-reported sleep problems by the Insomnia Severity Index and objective sleep features by polysomnography. Logistic regression models were used to estimate the associations between sleep parameters and aMCI in patients with insomnia disorder.

Results: There was no significant difference in Insomnia Severity Index scores between the aMCI and control groups. In the logistic regression after adjustment for covariates, people with a longer sleep duration (adjusted odds ratio [aOR] = 0.56, 95% confidence interval [CI]: 0.36–0.89), greater sleep efficiency (aOR = 0.50, 95% CI: 0.32–0.77), and a higher percentage of total sleep time in stage 3 of non–rapid eye movement sleep (N3%) (aOR = 0.02, 95% CI: 0.01–0.15) have a lower relative probability of having aMCI. By contrast, higher N1% (aOR = 2.28, 95% CI: 1.36–3.82) and wake after sleep onset (aOR = 1.31, 95% CI: 1.11–1.55) may be risk factors for aMCI in patients with insomnia.

Conclusions: In patients with insomnia disorder, sleep duration, sleep fragmentation, sleep efficiency, N1% and N3% were independently associated with the presence of aMCI. In the clinical setting, if patients with insomnia show much more serious abnormalities in these sleep indices, clinicians should pay attention to their cognitive function. In-depth research would also be worthwhile to elaborate the causality between sleep and cognitive decline.

Keywords: insomnia disorder, amnesic mild cognitive impairment, polysomnography, case-control study.

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BRIEF SUMMARY

Current Knowledge/Study Rationale: In clinical practice we found that patients with insomnia disorder who had certain characteristic sleep structure abnormalities were more likely to have complaints about their memory. A case-control study was conducted to test this hypothesis by comparing sleep structure between amnesic mild cognitive impairment and control patients with insomnia disorder.

Study Impact: If the association between sleep features and amnesic mild cognitive impairment in patients with insomnia disorder can be clarified, clinicians may examine more closely their patients' cognitive function. The implementation of targeted treatments, such as cognitive behavioral therapy for insomnia and medication, may not only improve sleep disturbances but also reduce the risk of cognitive decline at the earliest possible stage, a goal worthy of attention and in-depth research.

INTRODUCTION

According to the *World Alzheimer Report 2018*,[1] 50 million people worldwide were living with dementia in 2018, and this group will grow exponentially because of the rapidly aging population. Mild cognitive impairment (MCI), affecting 10–20% of people older than 65 years, is regarded as a transitional stage between normal aging and dementia,[2] and approximately 14.9% of these instances of MCI will convert to dementia within 2 years.[3] Alzheimer disease (AD) is the most common type of dementia.[4] MCI associated with memory deficits, called amnesic mild cognitive impairment (aMCI), has a higher risk of progression to AD.[5] In view of the lack of effective treatment for AD,[6] successful implementation of early detection and prevention strategies in the aMCI stage is of great importance.

Over the past decade, the association between insomnia and cognitive deficits has attracted increasing attention.[7–12] Insomnia is a sleep disorder characterized by nonrestorative sleep or difficulty in initiating or maintaining sleep, both with daytime consequences.[13] A wide range of "insomnia" definitions exist in published studies, spanning from self-reported insomnia to insomnia diagnosed with the fifth edition of *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5), and the main differences from this study is that they did not exclude patients

with insomnia symptoms caused by sleep disorders. Over half of adults above 60-years-old have self-reported insomnia complaints,[14] whereas the prevalence of insomnia disorder ranges from 12% to 20%.[15] Some previous studies, by using polysomnography (PSG) in the general population, have demonstrated differences in sleep characteristics (eg, reduced rapid eye movement sleep [REM] and increased fragmentation of slow-wave sleep [SWS][16] or more severe sleep-disordered breathing indices[17]) between participants with MCI and those with intact cognition. However, in patients with clinically diagnosed insomnia disorder, studies on the difference in sleep architectures between those with MCI and intact cognition are sparse.

In clinical practice, we found that patients with insomnia disorder who had certain characteristic sleep structure abnormalities were more likely to have complaints about their memory. Thus, we aimed to compare subjective sleep characteristics, assessed by questionnaires, and objective sleep features, measured by PSG, in insomnia disorder patients with aMCI to those with normal cognition. If the association between sleep features and aMCI in patients with insomnia disorder could be clarified, clinicians would examine more closely their patients' cognitive function. And the implementation of targeted treatments, such as cognitive behavioral therapy for insomnia and medication,[18] may not only improve sleep disturbances but also reduce the risk of cognitive decline at the earliest stage possible, which is a goal worthy of attention and in-depth research.

METHODS

Participants

This study was conducted in the Department of Neurology (Encephalopathy Department) of Hubei Integrated Chinese and Western Medicine Hospital. The study was approved by the Medical Ethics Committee of Hubei Integrated Chinese and Western Medicine Hospital. Written informed consent was obtained from all participants.

From December 2016 to August 2019, 256 patients were diagnosed with insomnia disorder by physicians among the patients who visited the outpatient department of neurology for sleep problems. The 256 patients were the source population for this case-control study. A diagnosis of insomnia disorder was based on DSM-5 criteria: (1) difficulty initiating or maintaining sleep, with sleep onset latency or wake time after sleep onset (WASO) greater than 30 minutes, or early morning awakening after sleeping less than 6.5 hours, or a sleep efficiency (SE) below 85%; (2) insomnia symptoms occurring at least 3 nights per week for at least 3 months; (3) significant distress or altered functioning in social, occupational, or other significant domains; (4) insomnia symptoms that could not be better explained by other types of sleep disorders, for example, the average number of apnea/hypopnea events per hour of sleep (apnea-hypopnea index, AHI) was calculated and the patient was diagnosed with sleep apnea hypopnea syndrome if AHI > 5 events/h; (5) insomnia not attributable to the physiological effects of a substance (eg, a drug of abuse or a medication); (6) coexisting mental disorders and medical conditions that did not adequately explain the predominant complaint of insomnia (eg, severe depression or severe anxiety).

Our study subjects were patients diagnosed with aMCI according to the Petersen criteria[19,20]: (1) the chief complaint of memory disorder confirmed by families or caregivers, or objective evidence of memory impairment (memory test scores were less than 1.5 standard deviations from the intact controls with matching age and education); (2) cognitive concern expressed by a physician, informant, participant, or nurse; (3) mild abnormalities on an overall cognitive rating scale, such as a Montreal Cognitive Assessment Scale (MoCA)[21] score < 26; (4) normal functional activities; and (5) no diagnosis of dementia and no physical and mental disorders that could cause brain dysfunction. The participants with intact cognition (IC) were defined by having MoCA scale scores of 26 points or higher (adjusted according to education level) and normal functional activities. Control patients with IC were recruited from the source population. All controls were selected and matched for education and age (± 3 years) with the study participants. Patients with severe visual or hearing impairment, severe aphasia or physical disability, or who were unable to cooperate in completing the neuropsychological assessment due to other reasons were excluded.

Sleep evaluation

Each participant was equipped with an overnight PSG monitor between 5 PM and 8 PM at the neurological department by medical technicians (Q.L., Y.Y.) using standard techniques. PSG sleep recording consisted of continuous recordings from 6 electroencephalographic leads (international 10–20 system: F3-A2, F4-C1, C3-A2, C4-A1, O1-A2, O2-A1), 2 electro-oculographic leads (ROC-A1, LOC-A2), 4 electromyography leads (2 submental and 2 bilateral tibialis anterior), thermistors for nasal and oral airflow, strain gauges for thoracic and abdominal excursion, finger pulse oximetry, and electrocardiography.

Sleep data were collected and manually scored via the Alice 6 LDxN Diagnostic Sleep System (Philips Respironics, Bend, OR) by 2 trained sleep technicians (L.Z., Y.Y.) who were blind to the study purpose. Reported sleep indices included sleep scoring data (eg, time in bed, total sleep time [TST], sleep latency, WASO, percent SE, time in each stage), arousal events (eg, arousal index), cardiac events (eg, average heart rate during sleep), movement events (eg, number of periodic limb movements during sleep), and respiratory events (eg, AHI) according to Version 2.3 of *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications*.[22]

We evaluated the degree of insomnia with the Insomnia Severity Index[23] in the morning after overnight PSG monitoring. The dimensions evaluated were severity of sleep onset, sleep maintenance and early morning awakening problems, sleep dissatisfaction, interference in daytime functioning from sleep difficulties, noticeability of sleep problems by others, and distress caused by sleep difficulties. The total score was interpreted as follows: absence of insomnia (0–7), subthreshold insomnia (8–14), moderate insomnia (15–21), and severe insomnia (22–28).

Neuropsychological assessment

The morning after the PSG recording, the patients were referred for a comprehensive neuropsychological assessment including the MoCA (Beijing edition),[21] Zung self-rating anxiety/depression scales,[24,25] and the activities of daily living scale.[26] All neurological examinations took approximately 1 hour and were conducted by neurologists (L.Z., Q.L.) and diagnosed by neurologists (L.S., H.Y.) who were blind to the sleep outcomes. Two neurologists (Z.G., L.S.) were responsible for the administration and supervision of these neuropsychological examinations. The patients diagnosed with aMCI were informed after the examinations to prevent the progression of cognitive decline.

The MoCA[21] is a brief cognitive screening tool for MCI and covers a wide range of cognitive functions, including spatial/executive ability, naming, language fluency, attention, memory, abstract thinking, and orientation. The MoCA score is derived by adding the points of each successfully completed task, and 1 additional point added if the individual had 12 or fewer years of formal education, for a possible maximum of 30 points. Higher scores indicate better global cognition. A final total score of 26 and above is considered normal. The self-rating depression scale[24] and self-rating anxiety scale[25] each contain 20 items scored based on frequency (1, rarely; 2, some of the time; 3, very often/often; 4, almost/always). The total score for the 20 questions was multiplied by 1.25, with the integer score as a standard score. A standard score below 50 was considered to indicate the absence of depression and anxiety. The activities of daily living scale[26] included a physical self-maintenance scale (6 items) and an instrumental activities of daily living scale (8 items). For each item, the scoring was determined by a 4-point coding system, so the total score could range from 14 to 56. Scores greater than 22 points (the cutoff score) were defined as demonstrating impairment in activities of daily living.[27]

Statistical analysis

EpiData 3.1 software was used to establish the database. The continuous variables were expressed as the mean ± SD ($\bar{X} \pm SD$). The Kolmogorov-Smirnov and Levene tests were used as normality and equal variance tests, respectively. Univariate analysis was conducted using χ^2 or Fisher's exact test for dichotomized and categorical variables, Student's *t* test for normally distributed continuous variables, and Mann-Whitney *U* test for non–normally distributed continuous variables. For PSG-derived variables, we constructed a multivariable logistic regression model to determine independent associations. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs) for every 1-hour increase in TST, every 10% increase in percentage of TST in stage 1 of non–rapid eye movement sleep (N1%) and in N3%, and every 15-minute increase in WASO. For each variable model 1 was adjusted for age, sex, education, smoking, and alcohol intake, and model 2 was adjusted for model 1 + BMI, depression, and anxiety symptoms. All statistical analyses were performed using SPSS version 24.0, and a 2-tailed *P*-value below.05 indicated statistical significance.

Table 1—Demographic and clinical characteristics in the intact cognition (IC) group and amnesic mild cognitive impairment (aMCI) group.

	Mean (SD) or n (%)		*P*-Value
	aMCI (n = 45)	IC (n = 45)	
Age, years	64.07 (6.99)	63.24 (6.97)	.578
Female sex, n (%)	23.00 (51.11)	27.00 (60.00)	.396#
BMI, kg/m^2	23.77 (3.02)	23.98 (2.74)	.730
Smoker, n (%)	12.00 (26.67)	8.00 (17.78)	.310#
Drinker, n (%)	6.00 (13.33)	5.00 (11.11)	.748#
Education, y	10.78 (3.21)	11.16 (3.38)	.588
Retiree, n (%)	41.00 (91.11)	37.00 (82.22)	.215#
SDS score	36.28 (5.49)	34.26 (4.88)	.076
SAS score	36.22 (5.95)	34.32 (4.71)	.105
ADL score	14.04 (0.30)	14.22 (1.06)	.283

All test statistics are Student's *t* tests unless otherwise specified. Values are the mean (SD) or n (%). ADL = activities of daily living scale, BMI = body mass index, SAS = self-rating anxiety scale, SD = standard deviation, SDS = self-rating depression scale. #Chi-squared analyses were used.

RESULTS

Comparison of demographic profiles

A total of 90 eligible insomnia disorder patients were included in the study: 45 patients with aMCI (mean: 64.1 years, SD: 6.99) and 45 participants with IC (mean: 63.2 years, SD: 6.97). The insomnia disorder patients with aMCI and IC showed similar demographic profiles (**Table 1**). There were no differences in age, sex, BMI, education level, smoking, alcohol intake, retirement status, or depression or anxiety symptoms between the aMCI group and IC group. Compared to the IC patients, the patients with aMCI had significantly lower scores in memory, spatial/executive ability, language fluency, and abstract thinking (**Table 2**).

Sleep characteristics

There were no significant differences in self-reported sleep from either the total score or items on the Insomnia Severity Index between the aMCI group and IC group (**Table 2**). Sleep indices in the IC group and aMCI group are shown in **Table 3**, and reduced TST, worse SE, increased WASO, higher N1%, and lower N3% were observed. Compared with normal PSG parameters in healthy adults pooled in a recent meta-analysis,[28] some PSG indices showed marked differences. TST in aMCI group was shorter than that in IC group and normal reference (334.5 min vs 360.0 min vs 372.0 min). SE in aMCI group was worse than that in IC group and normal reference (72.4% vs 84.3% vs 83.2%). WASO in aMCI group was much higher than that in IC group and the normal reference (102.0 vs 56.00 vs 64.0 minutes). N1% in aMCI group was higher than that in IC group and normal reference (32.0% vs 21.0% vs 8.7%). N3% in aMCI group was much lower than that in IC group and normal reference (3.1% vs 8.0% vs 18.1%).

Table 2—Comparisons of the Montreal Cognitive Assessment (MoCA) and Insomnia Severity Index (ISI) between the IC group and aMCI group.

	Mean (SD)		*P*-Value
	aMCI (n = 45)	IC (n = 45)	
MoCA score	23.60 (1.538)	27.49 (1.197)	< .001
Spatial/executive ability	3.83 (1.175)	4.83 (0.453)	< .001
Naming	2.86 (0.355)	2.94 (0.236)	.243
Attention	5.86 (0.430)	5.97 (0.169)	.152
Language fluency	2.26 (0.561)	2.66 (0.482)	< .001
Abstract thinking	1.17 (0.514)	1.60 (0.497)	< .001
Memory	1.51 (0.818)	3.40 (0.881)	< .001
Orientation	6.00 (0.000)	5.97 (0.169)	.323
ISI items and score			
ISI score	10.32 (5.00)	11.50 (5.96)	.336
Item 1–Falling asleep	1.49 (0.87)	1.48 (1.06)	.953
Item 2–Staying asleep	1.54 (0.9)	1.78 (0.86)	.226
Item 3–Early awakenings	1.15 (0.94)	1.50 (0.93)	.093
Item 4–Satisfaction	1.83 (0.83)	1.90 (0.96)	.723
Item 5–Interference	1.49 (0.81)	1.65 (0.95)	.410
Item 6–Noticeable	1.37 (0.92)	1.55 (0.93)	.372
Item 7–Worry	1.46 (0.75)	1.63 (0.98)	.405

All test statistics are Student's *t* tests. Data are expressed as the mean (standard deviation). SD = standard deviation, MoCA = Montreal Cognitive Assessment Scale.

Multivariate analysis of the association between objective sleep characteristics and aMCI in patients with insomnia

After adjustment for age, sex, BMI, education, smoking, alcohol intake, depressive and anxiety symptoms (model 2), WASO, TST, SE%, N1%, and N3% were independently associated with aMCI in patients with insomnia disorder. Specifically, the increase per 1 hour of TST (adjusted odds ratio [aOR] = 0.56, 95% CI: 0.36–0.89), the increase of 10% in SE (aOR = 0.50, 95% CI: 0.32–0.77), and the increase of 10% in N3% (aOR = 0.02, 95% CI: 0.01–0.15) were associated with decreased odds of aMCI, while each increase of 15 minutes of WASO and each increase of 10% in N1% (aOR = 1.31, 95% CI: 1.11–1.55; aOR = 2.28, 95% CI: 1.36–3.82) increased the odds of aMCI 1.31-times and 2.28-times, respectively (**Figure S1** in the supplemental material). The results of multivariable logistic models (model 1: adjusted for age, sex, education, smoking, and alcohol intake; model 2: adjusted for model 1 + BMI, depressive symptoms, and anxiety symptoms) are shown in **Table 4**.

DISCUSSION

In this study, we examined the objective and self-reported sleep characteristics of insomnia disorder participants with aMCI and those with intact cognition. There were no significant differences in the self-reported sleep characteristics between the aMCI and control groups. The results of the objective sleep patterns from PSG showed that after adjusting for potential confounding factors, TST, SE, WASO, N1%, and N3% were independently associated with the presence of aMCI in the insomnia disorder population. Higher N1% and more time in WASO were the risk factors for aMCI, while increased TST, higher SE, and increased N3% were associated with decreased odds of aMCI. No significant difference in self-reported sleep was found between aMCI and IC group, but results from PSG did detect differences. The discrepant self-reported and PSG findings may have resulted from such possible reasons as sleep misperception in insomnia or cognitive deficits in aMCI, which also indicated that PSG monitoring may be sufficiently sensitive to reveal the characteristic sleep abnormality in patients with aMCI.

Most epidemiologic studies have not been specific to the insomnia population. However, consistent with our findings, previous studies have shown that MCI patients had less SWS[17,29,30], worse sleep continuity[16,17,29–31], and shorter sleep time[32] than participants with intact cognition in the general population. A large prospective study of sleep patterns measured by actigraphy reported that increased sleep fragmentation augmented the risk of AD and the rate of cognitive decline in older adults.[10] A recent meta-analysis of objective measures of sleep parameters in MCI patients showed that compared to healthy controls, those with MCI have pronounced changes in sleep architecture, with reduced TST, lower SE, longer sleep onset latency, longer REM latency, reduced REM, increased N1 sleep, and more severe hypoxemia.[32] Our findings indicate that the sleep architecture in the insomnia patient with aMCI is fundamentally consistent with that in MCI patients but with slight differences. In addition, some studies focused on insomnia did not use diagnostic criteria to assess insomnia disorder. Discrepant results across studies might have resulted partly from the heterogeneity in study methods and design, particularly for insomnia diagnosis.[33]

On the other hand, a few studies have focused on sleep structure in aMCI patients. A prior study revealed that a higher percentage of IC adults experience SWS compared to both AD and aMCI patients.[34] Compared to 18 IC adults, 10 aMCI patients were shown to have dramatically reduced SWS and borderline changes in REM, WASO, REM latency, and SE.[35] Contrary to our results, an analysis by actigraphy found that aMCI volunteers had less disturbed sleep (less movement in bed at night, less WASO, and fewer times up at night) than both non–amnesic MCIs and cognitively intact volunteers.[36] Other studies have focused on changes in the microstructure of sleep. Several studies that monitored with PSG have demonstrated less SWS accompanied by lower delta and theta power during sleep in aMCI patients.[34,35] AD patients had a decreased κ-complex density (one of the hallmarks of non–rapid eye movement sleep) compared to aMCI patients and IC participants, while no significant difference was observed between aMCI patients and IC participants[34]; these data indicate that sleep quality or quantity is dynamic and plays a role in AD progression, even though the changes in sleep parameters are not remarkable in the aMCI stage. In addition, several studies have demonstrated that memory consolidation has a relationship with SWS or slow-wave activities.[37,38]

Table 3—Sleep parameters in the IC group and aMCI group.

	Median (IQR)		*P*-Value
	aMCI (n = 45)	IC (n = 45)	
TIB, min	462.30 (439.60–497.65)	452.00 (419.00–483.50)	.341
TST, min	334.50 (275.75–378.80)	360.00 (316.50–422.00)	.049
SE, %	72.40 (58.75–81.45)	84.30 (72.05–90.00)	.002
WASO, min	102.00 (68.05–161.10)	56.00 (32.35–103.05)	.001
N1, % of TST	32.00 (20.00–45.30)	21.00 (17.00–30.30)	.002
N2, % of TST	49.00 (36.25–57.10)	52.00 (42.90–56.60)	.245
N3, % of TST	3.10 (1.00–7.00)	8.00 (4.15–11.35)	.001
REM, % of TST	15.00 (7.50–20.05)	17.50 (12.50–20.15)	.150
N1 latency, min	13.00 (7.05–35.55)	14.30 (6.10–23.30)	.521
N2 latency, min	30.20 (13.15–51.45)	21.30 (10.35–29.35)	.085
N3 latency, min	79.00 (39.85–145.25)	57.95 (35.70–108.08)	.316
REM sleep latency, min	116.00 (75.15–204.00)	111.30 (70.30–166.25)	.534
ArI	7.60 (5.15–10.55)	7.00 (4.00–10.00)	.480
LMI	2.00 (1.25–4.50)	2.00 (0.50–4.15)	.268
AHI, events/h	3.10 (1.90–4.40)	3.40 (2.20–4.30)	.467
SpO_2, %	96.00 (95.00–97.00)	96.00 (94.50–96.00)	.673
AHR, n/min	64.40 (58.75–72.05)	62.00 (58.35–68.00)	.252

Data are expressed as the median (interquartile range). All test statistics are Mann–Whitney *U* test. AHI = apnea-hypopnea index, AHR = average heart rate during sleep (n/min), ArI = arousal index, IQR, interquartile range, ISI = Insomnia Severity Index, LMI = leg movement index (n/h), N1 = stage 1 of non–rapid eye movement, N2 = stage 2 of non–rapid eye movement, N3 = stage 3 of non–rapid eye movement sleep, REM = rapid eye movement sleep, SE = sleep efficiency (%), SpO_2 (%) = average surplus pulse O_2 (%) in the TIB, TIB = time in bed (minutes), TST = total sleep time (minutes), WASO = waking time after sleep onset (min).

Table 4—Association of sleep indices with risk of aMCI in the patients with insomnia.

Variables	Model 1		Model 2	
	OR (95% CI)	*P*-Value	OR (95% CI)	*P*-Value
TST (increase per 1 h)	0.63 (0.42, 0.93)	.021	0.56 (0.36, 0.89)	.014
SE% (increase per 10%)	0.53 (0.36, 0.79)	.002	0.50 (0.32, 0.77)	.002
N1, % of TST (increase per 10%)	2.19 (1.37, 3.50)	< .001	2.28 (1.36, 3.82)	.002
N2, % of TST (increase per 10%)	0.77 (0.52, 1.14)	.196	0.80 (0.53, 1.22)	.308
N3, % of TST (increase per 10%)	0.03 (0.01, 0.16)	< .001	0.02 (0.01, 0.15)	< .001
REM, % of TST (increase per 10%)	0.51 (0.24, 1.04)	.066	0.52 (0.25, 1.10)	.086
Latency (increase per 15 min)	1.05 (0.95, 1.15)	.297	1.08 (0.97, 1.20)	.181
WASO (increase per 15 min)	1.27 (1.09, 1.47)	.002	1.31 (1.11, 1.55)	.001
AHI	0.97 (0.89, 1.07)	.667	0.96 (0.87, 1.07)	.457
ArI	1.04 (0.94, 1.16)	.380	1.04 (0.93, 1.15)	.497

Model 1: adjusted for age, sex, education, smoking, and alcohol intake. Model 2: model 1 adjusted for body mass index, depressive symptoms, and anxiety symptoms. AHI = apnea-hypopnea index, ArI = arousal index, CI = confidence interval, OR = odds ratio, REM = rapid eye movement sleep, TST = total sleep time (minutes), WASO = waking time after sleep onset (min).

There are several possible explanations for the relationship between physiological sleep and cognitive decline observed in our study. Previous studies have identified that sleep, especially slow rhythms in neural activity, is interlinked with cerebrospinal fluid waves and enhances the removal of potentially neurotoxic waste products that accumulate in the awake central nervous system.[39,40] In addition, sleep loss may negatively impact cognitive performance by promoting inflammation. Sleep deprivation or sleep restriction can activate the systemic inflammatory response and increase proinflammatory cytokines.[41,42] This leads to reductions in amyloid β clearance caused by dysfunctional microglia, neuronal injury, and local inflammation of the central nervous system, all of which are pathological manifestations of AD.[43]

The main strengths of this study are: First, all of the patients with insomnia disorder were diagnosed by physicians strictly in accordance with clinical standards, based not only on insomnia complaints but also the effects on cognitive function of such other factors as hypoxia, which cannot be ruled out. Second, PSG monitoring was conducted to provide a detailed record of sleep parameters. However, some limitations should be considered: First, this study was not prospective, so we cannot conclude whether sleep disturbances preceded or followed the development of aMCI. Second, although we adjusted for many potential confounders, we could not completely rule out the possibility of residual confounding by unmeasured factors (eg, ApoE genotype, physical activity).

In conclusion, sleep fragmentation, longer light sleep, lower sleep efficiency, short sleep duration, and SWS may be related to cognitive impairment in patients with insomnia disorder. Although the findings may not be exclusive to insomnia patients with aMCI, they still propose to clinical physicians the important goal of paying more attention to the cognitive status of patients with insomnia. In view of effective targeted treatments for improving sleep disturbances, such as cognitive behavioral therapy for insomnia and medication,[18] if the association between sleep features and aMCI in patients with insomnia disorder is clarified definitively, prospects are promising for reducing the risk of cognitive decline from sleep abnormalities as early as possible in patients with insomnia disorder.

ABBREVIATIONS

AD, Alzheimer disease
aMCI, amnesic mild cognitive impairment
aOR, adjusted odds ratio
CI, confidence interval
IC, intact cognition
MCI, mild cognitive impairment
MoCA, Montreal Cognitive Assessment scale
N1%, percentage of stage 1 of non-rapid eye movement sleep in TST
N3%, percentage of stage 3 of non-rapid eye movement sleep in TST
PSG, polysomnography
REM, rapid eye movement sleep
SDS, self-rating depression scale
SE, sleep efficiency
SWS, slow-wave sleep
TST, total sleep time
WASO, wake time after sleep onset

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