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The Relation of Sleep Characteristics and Cognitive Impairment in Community-Dwelling Middle-Aged and Older Adults: Ardakan Cohort Study on Aging (ACSA)

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Keywords
Cognitive dysfunction · Geriatrics · Middle-aged · Sleep

Abstract

Introduction: The rise in the elderly population has brought attention to mild cognitive impairment (MCI). Sleep disorders also affect many older adults, indicating an important area of research for disturbed sleep and faster brain aging. This population-based study aimed to investigate the association of several sleep indicators with cognitive performance. ***Methods:*** This cross-sectional study focused on adults over 50 in the Ardakan Cohort Study on Aging (ACSA). MCI was evaluated using the Mini-Mental State Examination (MMSE) and the Abbreviated Mental Test score (AMTS) in literate and illiterate individuals. Sleep characteristics were collected using the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale, and Berlin questionnaire. The logistic regression models were used to analyze the data. ***Results:*** Overall, 3,380 literate and 1,558 illiterate individuals were included. In both groups, participants with MCI had a significantly higher PSQI global score ($p < 0.05$). Also, among the literate individuals, a significantly higher risk of having sleep-disordered breathing and poor sleep quality was observed in participants with MCI ($p < 0.05$). In illiterate individuals, higher sleep latency than 15 min increased odds of MCI ($p < 0.05$). However, after adjusting for all variables, only literate individuals with a sleep duration of more than 8 h had 66 percent increased odds of having MCI ($p = 0.033$). ***Conclusion:*** Sleep duration might be associated with cognitive function in the older Iranian population. Our findings underscore the importance of considering sleep patterns in relation to cognitive health.

Introduction

The world's population over 60 is predicted to double by 2050 [1]. Dementia and other kinds of cognitive impairment are expected to increase in the coming decades as the older population ages [2]. Mild

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cognitive impairment (MCI) is a condition characterized by cognitive deterioration that is more than predicted based on an individual's age and level of education but does not significantly interfere with daily living activities, as seen in Alzheimer's disease (AD) and other types of dementia [3]. There should be evidence, either by self-report or by an informant, of a change in cognitive abilities compared to the individual's previous level of functioning. According to a recent meta-analysis, approximately 15% of older adults are affected by MCI [4].

Identifying the factors behind MCI is crucial as it results in huge health and societal costs [5] and is considered a transitional phase between normal cognition and dementia, with a high incidence of progression to dementia [6, 7]. Various factors have been proposed to be associated with MCI. Demographic and social factors, including age progression [8], low educational attainment [9], and comorbidities such as diabetes mellitus [10], hypertension [11], depression, and anxiety [12], have been identified as risk factors for the development of MCI.

Associations have been observed between various parameters of disturbed sleep and faster cognitive decline [13, 14]. Sleep disorders affect a large proportion of older adults, ranging between 25 and 35% in population-based studies [15]. Along with several health problems related to disturbed sleep in the elderly, including cardiovascular diseases, several psychological and cognitive disorders are also proposed to be affected by sleep status [16]. Although aging is associated with several normative alterations that may be related to decreased cognitive functioning and altered sleep structure [17], as reported, alterations in both sleep and cognitive conditions can be out of the expected norms in a significant number of the elderly [17, 18], necessitating more exploration in relationships between sleep and cognition.

A meta-analysis has revealed several characteristics of sleep macrostructure, including sleep time, latency, and efficiency, which are altered in MCI patients [19]. In addition to general sleep quality, some other sleep conditions, such as sleep duration and daytime sleepiness, can affect cognitive status [20–22]; results regarding the link between cognitive function and sleep are not always consistent. Some prior cross-sectional and cohort studies [23, 24] have indicated lower sleep quality among subjects with MCI, while others could not find such an association [25–27]. Regarding the link between sleep-disordered breathing in some investigations, it may be considered a preventable risk factor for cognitive impairment [14, 26, 28]. However, it is important to note that in some of both cross-sectional and cohort studies, these results were not observed [25].

By 2050, nearly two-thirds of people with cognitive impairment are expected to reside in low- and middle-income countries [29]. Iran, classified as a rapidly aging low- and middle-income country, remains significantly understudied in terms of MCI. To the best of our knowledge, no study has investigated the relationship between various sleep indicators and cognitive performance in a population of illiterate older adults, a demographic common in developing countries [30]. Therefore, this population-based study aimed to evaluate the association of different sleep characteristics with the prevalence of MCI within a community comprising both literate and illiterate Iranian middle-aged and older adult individuals, using a large sample size.

Methods

Study Design and Participants

The present investigation is an observational cross-sectional study conducted on older adults who participated in the first wave of the Ardakan Cohort Study on Aging (ACSA) in 2020. The ACSA is a subset of the Persian cohort study named "IRanian Longitudinal Study on Aging (IRLSA)" [31]. ACSA participants were males and females over 50 who had resided in Ardakan city, located in the Province of Yazd, for at least 1 year. For eligible adults to participate in the study, informed consent, the ability to cooperation, and in-person attendance in the cohort implementation center were necessary. Thus, subjects with a severe or untreated mental or physical disability, blindness, and severe cognitive impairment that would prevent them from collaborating were excluded from the study. The study sample was identified using a stratified random sampling method based on the proportion of people aged 50 or more registered at each health center in the Ardakan urban area.

Data Collection and Variables

Data were collected on demographic factors such as age, gender, and educational levels (illiterate, elementary school, middle school, high school, and college) with a face-to-face interview by a general questioner. The categorization of the habitual smoking status was carried out utilizing the Glossary of the Center for Disease Control (CDC), which classifies a current smoker as an individual who has consumed a minimum of 100 cigarettes during their lifetime and continues to smoke regularly [32]. On the other hand, an ex-smoker is defined as an individual who has also smoked a minimum of 100 cigarettes in their lifetime but had quit smoking at the time of the interview [32]. The level of physical activity was assessed utilizing the Physical Activity Scale for the Elderly (PASE) [33]. This instrument has a scoring range from 0 to 400 points, with higher scores reflecting greater physical activity levels [33]. The Persian version of this tool has been previously evaluated and validated [34]. Body mass index was calculated based on each participant's weight and height and categorized into two groups: obese (>30) and nonobese (≤30).

Furthermore, depression was assessed as a potential confounding factor using the Persian version of the 10-item Center for Epidemiologic Studies Depression scale (CES-D-10) [35, 36]. A score of 10 or above on this scale was considered to be indicative of depression. The anxiety subscale in the Persian version of the Hospital Anxiety and Depression Scale (HADS) was used to evaluate anxiety level [37, 38]. According to this scale, a score of 7 or below was deemed negative, an 8–10 was deemed borderline, and an 11 or above was deemed positive. Furthermore, as the most prevalent underlying conditions, the presence of diabetes mellitus and hypertension were recorded according to the self-reports.

Cognitive Measurements

The study population was categorized into two groups based on their literacy status. The Mini-Mental State Examination (MMSE) was utilized to evaluate cognitive function in literate subjects. The MMSE is an 11-item exam that assesses cognitive performance in five areas: orientation, registration, attention and computation, recollection, and language [39]. Its scores range from 0 to 30, and subjects with scores 20–24 are categorized as MCI. The Persian version of MMSE has been previously found valid and reliable in the Iranian population [40].

The cognitive function of illiterate people was evaluated using the Abbreviated Mental Test score (AMTS). AMTS is a rapid tool proven valid and reliable among illiterate subjects and consists of ten questions on orientation, attention, and long and short-term memory. Its scores range between 0 and 10 [41]. The Persian version of AMTS has also been validated among the older Iranian population by Foroughan et al., and it has been suggested that a score of seven can be a reliable cutoff for MCI in the Iranian population [42]. Importantly, AMTS has been shown to have high similarity and concordance with MMSE scores, and it has been shown that there is a high correlation between having an AMTS score of less than seven and an MMSE score of less than 25 [41].

Since diagnosis of MCI cannot be made solely based on one screening test, such as the MMSE or AMTS, the results of the tests were confirmed by self-report or by an informant for participants with scores falling within the categories indicative of MCI, regarding a discernible change in their cognitive abilities compared to their previous level of functioning. Furthermore, it is important to note that all individuals identified with MCI did not show any impairments in performing their activities of daily living, including both basic activities and instrumental activities.

Sleep Characteristic Measurements

Pittsburgh Sleep Quality Index (PSQI) was utilized to assess total sleep quality. PSQI is a sleep quality measurement questionnaire that was first introduced by Buysse et al. [43] and consists of 19 questions that assess sleep characteristics in seven areas, including sleep quality, sleep latency, duration, efficiency, disturbance, use of medication, and daytime dysfunction. Each component can get 0 to 3 scores, with higher scores indicating more sleep problems. Thus, the total PSQI score ranges from 0 to 21, with higher scores indicating lower sleep quality and a total score of six or more categorized as poor sleep quality [43]. The validity and reliability of the Persian version of PSQI in the Iranian population have been previously confirmed [44].

The Epworth Sleepiness Scale (ESS), an instrument that assesses the frequency of daytime sleepiness in eight different daily situations and has scores ranging from 0 to 24, was utilized to evaluate daytime sleepiness [45], with a cutoff of ten used to identify patients suffering from daytime sleepiness based on higher ESS scores.

To assess the risk of sleep-disordered breathing, the Berlin questionnaire (BQ) was utilized, which is an instrument that evaluates three categories of risk factors for sleep apnea, and a score of two or more indicates the risk of having sleep-disordered breathing [46]. The Persian ESS and BQ versions were previously translated and validated for use in Iranian subjects [47, 48].

Statistical Analysis

Because different scaling systems were used to evaluate MCI in illiterate and literate subjects, the whole population was divided into two subgroups, and all analyses were conducted on each of these groups separately. Quantitative variables were expressed as mean, standard deviation (SD), and categorical variables were presented as frequency and percentage.

In the first step, the relationship between all factors introduced in Table 1 with the odds of having MCI was assessed through univariable logistic regression. Variables with $p < 0.2$ in the first step (univariable model) were entered into the final multivariable models 1 and 2.

Besides, in multivariable model 1, odds ratios (ORs) were calculated for sleep-related questionnaires, including the BQ, ESS, and PSQI. Considering that, in clinical practice, it is not always feasible for clinicians to inquire about all the items of the PSQI questionnaire, two questions of PSQI deemed more clinically significant, based on expert opinion, were utilized in model 2. The only difference between these two models lies in the fact that, in model 1, in addition to daytime sleepiness (from ESS questionnaire), and sleep-disordered breathing (from BQ questionnaire), the PSQI questionnaire, which contains all seven domains, was used. In contrast, in model 2, alongside daytime sleepiness (from ESS questionnaire), and sleep-disordered breathing (from BQ questionnaire), only the two clinically pertinent aspects of the PSQI – sleep latency and sleep duration – were included.

Statistical analyses were performed using STATA Statistical Software Version 15 (StataCorp. 2017). p values less than 0.05 were considered significant.

Results

Overall, 4,938 older adults were eligible to participate in the analysis. This population was composed of 3,380 literate and 1,558 illiterate individuals. Among the literate individuals, the mean age of participants with MCI and cognitively unimpaired individuals was 62.6 and 60.1, respectively. In the illiterate subjects, the mean age of participants with MCI and cognitively unimpaired individuals was 68.0 and 65.6, respectively. There were 1,466 (43.4%) and 1,102 (70.8%) females in the literate and illiterate groups, respectively. Regarding sleep quality, individuals with MCI showed higher PSQI scores and a lower prevalence of having good sleep quality. The characteristics in the literates' and illiterates' groups are shown in Table 1.

Table 1. Characteristics of study participants

Variables	Literate individuals		Illiterate individuals	
	MCI (*N*: 214)	CU (*N*: 3,166)	MCI (*N*: 567)	CU (*N*: 991)
Age, years	62.6±7.9	60.1±6.6	68.0±7.8	65.6±7.8
Male sex	117 (54.7)	1,796 (56.7)	61 (10.8)	394 (39.8)
Body mass index				
Obese (>30)	86 (40.2)	1,210 (38.2)	305 (53.8)	470 (47.4)
Nonobese (≤30)	128 (59.8)	1,956 (61.8)	262 (46.2)	521 (52.6)
Educational status				
Elementary school	156 (72.9)	1,343 (42.5)	N/A	N/A
Middle school	38 (17.8)	680 (21.5)		
High school	13 (6.1)	581 (18.3)		
College	7 (3.2)	562 (17.7)		
Smoking				
Never smoked	147 (69.3)	2,267 (71.8)	538 (95.1)	771 (78.1)
Ex-smoker	30 (14.2)	366 (11.6)	16 (2.8)	118 (11.9)
Current smoker	35 (16.5)	523 (16.6)	12 (2.1)	99 (10.0)
Physical activity	133.64±91.2	149.37±86.7	99.5±63.5	117.53±78.2
PSQI global score	8.41±4.5	7.32±4.1	9.57±4.3	8.71±4.2
Sleep quality				
Good (PSQI ≤5)	46 (21.5)	917 (29.0)	82 (14.5)	178 (18.0)
Poor (PSQI >5)	168 (78.5)	2,249 (71.0)	485 (85.5)	813 (82.0)
Sleep duration				
<6 h	118 (55.2)	1,748 (55.4)	374 (66.4)	647 (65.5)
6 ≤ to <8 h	66 (30.8)	1,123 (35.6)	140 (24.9)	262 (26.5)
≥8 h	30 (14.0)	286 (9.0)	49 (8.7)	78 (8.0)
Sleep latency				
≤15 min	84 (39.2)	1,466 (46.4)	133 (23.5)	309 (31.2)
15 < to ≤60 min	110 (51.4)	1,488 (47.0)	327 (57.6)	554 (56.0)
>60 min	20 (9.4)	210 (6.6)	107 (18.9)	127 (12.8)
Epworth Sleepiness Scale global score	4.45±3.3	4.88±3.07	3.90±3.0	4.11±2.7
Daytime sleepiness				
Yes (ESS >10)	17 (7.9)	270 (8.5)	35 (6.2)	46 (4.6)
No (ESS ≤10)	197 (92.1)	2,896 (91.5)	532 (93.8)	945 (95.4)
Sleep disordered breathing				
Yes (Berlin questionnaire score ≥2)	187 (87.4)	2,541 (80.3)	505 (89.1)	858 (86.6)
No (Berlin questionnaire score <2)	27 (12.6)	625 (19.7)	62 (10.9)	133 (13.4)
Depressive symptom (CES-D 10)				
Yes (≥10)	52 (24.4)	423 (13.4)	177 (31.4)	197 (20.0)
No (<10)	161 (75.6)	2,725 (86.6)	386 (68.6)	789 (80.0)
Anxiety (HADS-A)				
Abnormal	32 (14.9)	311 (9.8)	706 (71.2)	106 (18.7)
Mild to borderline	31 (14.6)	401 (12.7)	150 (15.2)	109 (19.2)
Normal	151 (70.5)	2,454 (77.5)	135 (13.6)	352 (62.1)
Hypertension	117 (55.2)	1,345 (43.2)	368 (66.4)	601 (61.4)
Diabetes	71 (33.6)	889 (28.8)	244 (44.4)	362 (37.3)

Quantitative values are presented as mean ± standard deviation. Qualitative values are presented as *n* (%). MCI, minimal cognitive impairment; CU, cognitively unimpaired; N/A, not applicable; PSQI, Pittsburgh Sleep Quality Index; CES-D 10, Center for Epidemiologic Studies Short Depression Scale; HADS-A, The Hospital Anxiety and Depression Scale (anxiety subscale).

Table 2. OR of sleep characteristics associated with MCI in literate individuals (MMSE <25)

Variables (reference level)			Adjusted models			
	Univariable		model 1**		model 2***	
	OR (95% CI)	*p* value	OR* (95% CI)	*p* value	OR* (95% CI)	*p* value
Age	1.05 (1.03–1.07)	<0.001	1.05 (1.03–1.07)	<**0.001**	1.05 (1.03–1.07)	<**0.001**
Male (female)	0.91 (0.69–1.21)	0.554				
BMI (nonobese ≤30)						
Obese (>30)	1.08 (0.81–1.44)	0.567				
Educational status (elementary)						
Middle school	0.48 (0.33–0.69)	<0.001	0.45 (0.31–0.66)	<**0.001**	0.44 (0.30–0.65)	<**0.001**
High school	0.19 (0.10–0.34)	<0.001	0.18 (0.10–0.33)	<**0.001**	0.18 (0.09–0.32)	<**0.001**
College	0.10 (0.04–0.23)	<0.001	0.11 (0.05–0.24)	<**0.001**	0.11 (0.05–0.24)	<**0.001**
Smoking (never smoked)						
Ex-smoker	1.26 (0.84–1.90)	0.260				
Current smoker	1.03 (0.70–1.51)	0.871				
Physical activity	0.99 (0.99–0.99)	0.011	0.99 (0.99–1.00)	0.435	0.99 (0.99–1.00)	0.532
Depressive symptom (no <10)						
Yes (≥10)	2.08 (1.49–2.89)	<0.001	1.81 (1.17–2.80)	**0.007**	1.81 (1.17–2.80)	**0.008**
Anxiety (HADS-A) (normal)						
Mild to borderline	1.25 (0.84–1.87)	0.264	1.02 (0.64–1.60)	0.924	1.05 (0.67–1.66)	0.805
Abnormal	1.67 (1.12–2.49)	0.012	1.03 (0.61–1.73)	0.902	1.07 (0.63–1.80)	0.794
Hypertension (no)	1.61 (1.22–2.14)	0.001	1.22 (0.89–1.66)	0.201	1.22 (0.90–1.67)	0.191
Diabetes (no)	1.25 (0.93–1.68)	0.132	1.04 (0.75–1.44)	0.784	1.05 (0.76–1.45)	0.725
PSQI global score	1.06 (1.02–1.09)	<0.001				
Epworth Sleepiness Scale global score	0.95 (0.90–0.99)	0.047				
Sleep quality (good PSQI ≤5)						
Poor (PSQI >5)	1.48 (1.06–2.08)	0.020	1.04 (0.72–1.50)	0.808		
Daytime sleepiness (no, ESS ≤10)						
Yes (ESS >10)	0.92 (0.55–1.54)	0.767	0.99 (0.58–1.69)	0.994	1.01 (0.59–1.74)	0.951
Sleep-disordered breathing (no, Berlin questionnaire score <2)						
Yes (Berlin questionnaire score ≥2)	1.70 (1.12–2.57)	0.011	1.28 (0.82–2.00)	0.272	1.31 (0.83–2.08)	0.233
Sleep duration (6 ≤ to <8)						
<6	1.14 (0.84–1.56)	0.382			0.90 (0.64–1.26)	0.567
≥8	1.78 (1.13–2.80)	0.012			1.66 (1.04–2.66)	**0.033**
Sleep latency, min (≤15)						
15 < to ≤60	1.29 (0.96–1.72)	0.088			1.06 (0.77–1.47)	0.691
>60	1.66 (0.99–2.76)	0.050			1.17 (0.66–2.06)	0.581

Bold numbers indicate statistical significance ($p < 0.05$) in multivariable-adjusted models. CI, confidence interval; OR, odds ratio. *OR adjusted for sleep-related variables in the model and variables with $p < 0.2$ in the univariable model including age, educational status, physical activity, depression, anxiety, hypertension, and diabetes mellitus. **In model 1: as sleep-related variables, daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and all seven domains of the PSQI were entered. ***In model 2: As sleep-related variables, daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and only the two clinically pertinent aspects of the PSQI – sleep latency and sleep duration – were included.

Table 2 demonstrates the logistic regression results of factors associated with MCI in the literate individuals. A higher PSQI global score was associated with higher odds of MCI (OR: 1.06, 95% CI: 1.02–1.09). Those with poor sleep quality (PSQI >5) had 1.48 times higher odds of having MCI compared to those with good sleep quality. Moreover, sleep-disordered breathing was also associated with higher odds of having MCI. In the univariable analysis, baseline characteristics factors including age, educational level, physical activity,

hypertension, diabetes, depression, and anxiety had $p < 0.2$ with the odds of having MCI and therefore entered into multivariable models 1 and 2.

In the first multivariable model, in addition to the above factors, for sleep-related variables, the following were entered: daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and sleep quality (from all seven domains of the PSQI). No significant association was observed between sleep quality, daytime sleepiness, and sleep-disordered breathing with the odds of MCI. In the second multivariable model, in addition to the mentioned factors (baseline characteristics' factors with $p < 0.2$ in the univariable analysis), for sleep-related variables, the following were entered: daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and sleep latency and sleep duration (as two more clinically relevant domains of the PSQI). Results showed that a sleep duration of more than 8 h had a 66 percent increased odds of having MCI in literate individuals.

Table 3 demonstrates the logistic regression results of factors associated with MCI in the illiterate individuals. A higher PSQI global score was associated with higher odds of MCI (OR: 1.04, 95% CI: 1.02–1.07). Those with sleep latency of 15 < to ≤60 and >60 had 1.37 and 1.95 times higher odds of having MCI compared to those with sleep latency of ≤15 min.

In the univariable analysis, age, sex, body mass index, smoking history, physical activity, hypertension, diabetes, depression, and anxiety had $p < 0.2$ with the odds of having MCI and therefore entered into multivariable models 1 and 2.

In the first multivariable model, in addition to the above baseline characteristics' factors, for sleep-related variables, the following were entered: daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and sleep quality (from all seven domains of the PSQI). No significant association was observed between sleep-related variables and MCI. In the second multivariable model, in addition to the mentioned factors (baseline characteristics' factors with $p < 0.2$ in the univariable analysis), for sleep-related variables, the following were entered: daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and sleep latency and sleep duration (as two more clinically relevant domains of the PSQI). Results showed no significant association between sleep-related variables and MCI.

Discussion

This study examined the association of several sleep indicators with cognitive performance in literate and illiterate over 50-year-old Iranian participants. We, in our previous study [49], showed that age, educational level, history of depression, and sex are the factors that might be associated with the cognitive function in Iranian middle-aged and older adults. In the current study, after adjusting for associated factors, among all the sleep indicators, only sleep duration remained associated with cognition. Besides, this result has been observed solely in literate individuals and we did not find such an association in illiterate individuals.

Our findings, consistent with most prior cross-sectional and cohort studies [23, 24, 50], indicated lower sleep quality, defined by higher PSQI scores, among subjects with MCI in both groups. Nevertheless, in our cross-sectional study, lower sleep quality was not associated with higher odds of MCI after controlling for other related factors, including comorbidities and demographic characteristics. This could be due to the fact that cognitive decline is time-bound and often occurs during follow-up periods, while our study only involved a cross-sectional analysis of baseline characteristics. For example, in a 5-year population-based cohort study of the German elderly, PSQI remained an independent predictor of MCI even after adjustments [51], while in a cross-sectional analysis of the same group, PSQI scores did not remain significant after adjustment, and sleep-disordered breathing was only significantly correlated with MCI [26]. However, there are also cohort studies in which PSQI scores were not significant [27, 52]. It is noteworthy that a discrepancy frequently exists between PSQI reports and polysomnography results due to the subjective nature of PSQI [53–55], and the fact that many of the subjects in the studies mentioned above are elderly individuals with cognitive impairments who may struggle with recalling their sleep patterns [50]. Additionally, our study observed a high relationship between conditions such as depressive symptoms, anxiety, educational level, comorbidities, and the presence of MCI [49] which means that the association between MCI and sleep status could be influenced by many comorbid conditions [56].

The relationship between sleep quality and cognitive status has been widely studied, with various explanations suggesting a bidirectional association between sleep characteristics and cognitive impairment. For example, MCI an early symptom of AD, and β-amyloid accumulation in animal studies, has been associated with sleep issues [57]. Conversely, declining sleep quality has been associated with an increase in β-amyloid deposits [58, 59].

Table 3. OR of sleep characteristics associated with MCI in illiterate individuals (AMTS <7)

Variables (reference level)	Univariable		Adjusted models			
			model 1**		model 2***	
	OR (95% CI)	*p* value	OR* (95% CI)	*p* value	OR (95% CI)	*p* value
Age	1.03 (1.02–1.05)	<0.001	1.06 (1.04–1.08)	<**0.001**	1.06 (1.04–1.08)	<**0.001**
Male (female)	0.18 (0.13–0.24)	<0.001	0.15 (0.09–0.23)	<**0.001**	0.15 (0.10–0.24)	<**0.001**
BMI (nonobese, ≤30)						
Obese (>30)	1.29 (1.04–1.58)	0.016	0.98 (0.77–1.24)	0.904	0.97 (0.77–1.24)	0.864
Smoking (never smoked)						
Ex-smoker	0.19 (0.11–0.33)	<0.001	0.62 (0.32–1.20)	0.158	0.63 (0.32–1.22)	0.171
Current smoker	0.17 (0.09–0.31)	<0.001	0.94 (0.45–1.95)	0.885	0.94 (0.45–1.94)	0.869
Physical activity	0.99 (0.99–0.99)	<0.001	0.99 (0.99–1.00)	0.154	0.99 (0.99–1.00)	0.160
Depressive symptom (no, <10)						
Yes (≥10)	1.83 (1.44–2.32)	<0.001	1.57 (1.13–2.19)	**0.006**	1.46 (1.04–2.03)	**0.025**
Anxiety (HADS-A) (normal)						
Mild to borderline	1.45 (1.10–1.92)	0.008	0.94 (0.67–1.30)	0.713	0.91 (0.65–1.26)	0.585
Abnormal	1.57 (1.18–2.09)	0.002	0.79 (0.53–1.16)	0.240	0.78 (0.53–1.16)	0.224
Hypertension (no)	1.24 (0.99–1.54)	0.053	0.82 (0.63–1.06)	0.142	0.82 (0.63–1.06)	0.154
Diabetes (no)	1.34 (1.08–1.66)	0.006	0.96 (0.75–1.22)	0.768	0.97 (0.76–1.24)	0.849
PSQI global score	1.04 (1.02–1.07)	<0.001				
Epworth Sleepiness Scale global score	0.97 (0.93–1.00)	0.150				
Sleep quality (good PSQI ≤5)						
Poor (PSQI >5)	1.29 (0.97–1.72)	0.075	0.84 (0.60–1.17)	0.313		
Daytime sleepiness (no, ESS ≤10)						
Yes (ESS >10)	1.35 (0.85–2.12)	0.192	1.18 (0.71–1.97)	0.514	1.22 (0.73–2.05)	0.435
Sleep-disordered breathing (no, Berlin questionnaire score <2)						
Yes (Berlin questionnaire score ≥2)	1.26 (0.91–1.74)	0.154	0.93 (0.65–1.35)	0.738	0.94 (0.65–1.35)	0.744
Sleep duration (6 ≤ to <8)						
<6	1.08 (0.84–1.37)	0.523			0.96 (0.72–1.26)	0.779
≥8	1.17 (0.77–1.77)	0.441			1.20 (0.76–1.91)	0.418
Sleep latency, min (≤15)						
15 < to ≤60	1.37 (1.07–1.75)	0.012			1.10 (0.82–1.46)	0.499
>60	1.95 (1.41–2.71)	<0.001			1.30 (0.88–1.93)	0.179

Bold numbers indicate statistical significance ($p < 0.05$) in multivariable-adjusted models. CI, confidence interval; OR, odds ratio. *OR adjusted for sleep-related variables in the model and variables with $p < 0.2$ in the univariable model including age, sex, obesity, smoking, physical activity, depression, anxiety, hypertension, and diabetes mellitus. **In model 1: as sleep-related variables, daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and all seven domains of the PSQI were entered. *** In model 2: as sleep-related variables, daytime sleepiness (from ESS questionnaire), sleep-disordered breathing (from BQ questionnaire), and only the two clinically pertinent aspects of the PSQI – sleep latency and sleep duration – were included.

The glymphatic system, which is responsible for the clearance of neurotoxic substances such as β-amyloid, is most active during sleep, and sleep deprivation results in reduced clearance of these substances [24, 60], thereby affecting cognition. Additionally, it has been demonstrated that sleep deprivation decreases cognitive reserve and the efficacy of brain networks [61]. Another theory is that sleep deprivation induces inflammatory responses, which can negatively impact cognitive function [62].

In our study, the sleep-disordered breathing was associated with elevated odds of MCI in the literate subgroup but not in the illiterate subgroup. However, this

result was no longer significant after controlling for other variables. This is in contrast to the results from a previous population-based cross-sectional study, in which sleep-disordered breathing was the only variable that significantly affected the odds of MCI after adjusting for demographic factors [26]. A prior meta-analysis by Leng et al. observed that sleep-disordered breathing increased the risk of developing cognitive impairment in prospective cohort studies but not cross-sectional studies [25]. Another meta-analysis, which evaluated the impact of various sleep characteristics on the risk of AD or MCI, revealed that sleep-disordered breathing was associated with the highest increase in risk among the analyzed variables [14]. The study also indicated that more extended follow-up periods were generally associated with an increased risk ratio [14]. In a separate meta-analysis, which only included cohort studies, sleep-disordered breathing increased the risk of cognitive decline in female subjects but not male subjects [28]. According to the authors, sleep-disordered breathing may be a preventable risk factor for cognitive impairment, and measures such as continuous positive airway pressure therapy may be beneficial to delay the deterioration [28, 63].

The role of sleep-disordered breathing on cognitive function is a matter of debate. It has been proposed that the sleep-disordered breathing-related intermittent hypoxia may contribute to the hippocampus's irreversible damage and apoptosis [64], or serve as an accelerating factor of AD through increased β-amyloid plaque formation, as seen in animal models [65]. Additionally, sleep-disordered breathing can decrease sleep efficiency, resulting in an increased time spent in bed, which is a risk factor for MCI when exceeding 8–9 h [66, 67]. However, a meta-review of studies on sleep-disordered breathing, chronic obstructive pulmonary disease, and insomnia suggested that the effect of sleep-disordered breathing is multidimensional, encompassing factors other than sleep disturbance seen in insomnia and hypoxia/hypercapnia seen in chronic obstructive pulmonary disease [68]. This might be partially explained by the genetic evidence linking sleep-disordered breathing and cognitive impairments, such as the high incidence of the ApoE 4 allele [28, 69], which may result in a more pronounced effect of sleep-disordered breathing on cognitive function in individuals with these alleles [25, 70, 71]. Moreover, sleep-disordered breathing correlates with a higher prevalence of cardiovascular risk factors, which are independent cognitive impairment risk factors [72].

In our analysis of the association between sleep duration and the prevalence of MCI, we observed a significant relationship between sleep duration of more than 8 h and the chance of having MCI in the literate individuals, which is consistent with the results of some other studies [23, 66, 73]. A cross-sectional study of a large Korean elderly population group found that a sleep duration of more than 9 h increases the odds of MCI the most [23]. Additionally, a dose-response meta-analysis found that a sleep duration of approximately 7 h was associated with the minimum risk of MCI in older adults [74]. Another meta-analysis showed that sleep duration exceeding 8.5–9 h was associated with an increased risk of MCI [66]. It is crucial to emphasize that neither excessive nor insufficient sleep is recommended for cognitive health.

In our study, the relationship between prolonged sleep latency and MCI did not remain significant after adjusting for other related variables. A prior cohort study on sleep characteristics found that sleep latency can predict the incidence of MCI during follow-up [75]. This study suggested that prolonged sleep latency is not a risk factor but an early indicator of neurodegeneration [75]. This is in line with a meta-analysis by Bubu et al. [14], which demonstrated that increased sleep latency increases the risk of cognitive impairment. Furthermore, a previous neuroimaging study showed a correlation between increased sleep latency and higher deposition of β-amyloids in the prefrontal cortex, a brain region showing β-amyloid deposition at the early stages of AD development [76]. Sleep latency can also be measured using objective polysomnography-based methods, and a meta-analysis of objective studies showed that increased objective sleep latency is also associated with cognitive impairment [19].

Limitations and Strengths

Our study's limitations should be considered when interpreting the results. First, this study is cross-sectional, and the impact of certain sleep characteristics on cognitive impairment may only be evident after a prolonged follow-up period. Second, all sleep parameters included in the study were based on self-reports by the subjects, and considering that these subjects are elderly, which may decrease the accuracy of the detailed data taken of them as they may have difficulty remembering. Additionally, in the ACSA study, any form of a cognitive or physical disability that prevented the subjects from attending the cohort study center was considered exclusion criteria, which could exclude those with worse conditions that may be more vulnerable to both studied conditions.

However, our study also has several methodological strengths. First, it is a large, population-based study that has included thousands of elderly subjects and encompasses data from various subjective sleep characteristics,

and employs a multiple regression model adjusted for various domains to minimize confounding effects. Second, to our knowledge, this is the first study that categorized the study population into illiterate and literate subjects and used the AMTS scoring system to evaluate MCI in illiterate subjects with improved reliability.

Conclusion

The present study provides evidence of a relationship between sleep patterns and MCI. The results suggest the importance of considering the potential link between sleep and cognitive function.

Statement of Ethics

In accordance with the principles of the Declaration of Helsinki, this research was carried out and authorized by the Research Ethics Committee of the University of Social Welfare and Rehabilitation Sciences (record number IR.USWR.REC.1394.490). All of the participants provided written informed consent in the assessment and collection of data.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization: A.D. and F.S.T. Data collection: A.D., E.H. and M.S. Formal analysis: M.S. and M.B. Methodology: P.J., A.A., and F.T. Visualization: M.F., F.T., and A.A. Writing – original draft: F.S.T., P.J., and A.A. Writing – review and editing: F.S.T., M.F., and M.B.

Data Availability Statement

The data cannot be made open individually by the authors because they contain information that could compromise the privacy of research participants. Data are available to all investigators for scientific objectives upon request on the ACSA website.

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