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Association between sleep quality and mild cognitive impairment in Chinese patients with type 2 diabetes mellitus: a cross-sectional study

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Abstract

Background Globally, the number of individuals with type 2 diabetes mellitus (T2DM) is increasing, and they are at a higher risk of developing mild cognitive impairment (MCI) than the general population. Sleep quality is thought to be a modifiable factor that may contribute to MCI, as previous studies have linked it to cognitive function in older adults. However, evidence concerning the association between sleep quality and MCI among patients with T2DM in China is limited. Therefore, this study aims to identify the association between sleep quality and MCI among patients with T2DM in China.

Methods This cross-sectional study was conducted among patients with T2DM who were referred to the Endocrinology Department of Xiangya Hospital, Central South University. Data regarding sociodemographic characteristics, lifestyle factors, T2DM-related information, and biochemical indicators were collected. Sleep quality and MCI were evaluated using the Pittsburgh Sleep Quality Index (PSQI) and the Mini-Mental State Examination (MMSE) scale, respectively. The association between sleep quality and MCI was analyzed using univariate and multivariate analyses.

Results This study included 1,001 patients with T2DM, with a mean age of 60.2 (standard deviation: 10.1) years. Pearson's correlation analysis showed that the total PSQI score was negatively associated with the MMSE score (r=-0.27, P<0.05). Multivariate analyses based on four models consistently showed that those with higher total PSQI score (aOR=1.09–1.11, P<0.05), as well as higher scores on the subjective sleep quality (aOR=1.32–1.46, P<0.05), sleep latency (aOR=1.25–1.32, P<0.05), sleep duration (aOR=1.30–1.32, P<0.05), sleep disturbance (aOR=1.66–1.86, P<0.05), and daily dysfunction (aOR=1.38–1.48, P<0.05) were associated with higher rates of MCI.

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Conclusions Among Chinese patients with T2DM, poor overall sleep quality, subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and daily dysfunction were associated with higher rates of MCI. Future studies are needed to examine whether sleep intervention could improve cognitive function in patients with T2DM. It is also suggested for clinicians working with T2DM patients to raise the awareness of cognitive impairment and sleep problems.

Keywords Type 2 diabetes mellitus, Sleep quality, Mild cognitive impairment, Chinese

Background

Diabetes mellitus is a common chronic disease, and its target organ injuries have distressing impacts on global public health and impose an enormous burden on the healthcare system [1-3]. The global prevalence of diabetes in adults was estimated to be 10.5% in 2021, rising to 12.2% by 2045 [2]; however, this rate had already reached 12.8% in mainland China in 2018 [4]. Additionally, diabetes-related medical costs reached at least USD 966 billion in 2021 globally, a 316% increase over the last 15 years [5]. Moreover, diabetes is a global killer and one of the top 10 causes of premature death, with disabilityadjusted life years from diabetes increasing by more than 80% between 2000 and 2019 [1, 3, 6]. Type 2 diabetes mellitus (T2DM) accounts for the majority of diabetes cases, and can cause long-term damage to the brain, neurons, and blood vessels and hence hasten brain aging and cognitive decline [7–9].

Mild cognitive impairment (MCI) is defined as an asymptomatic predementia stage on the cognitive decline continuum and characterized by objective cognitive impairment that is not severe enough to necessitate assistance with daily activities [10]. MCI is projected to occur at a rate of 41.0/1,000 person-years (PY), with patients converting to probable dementia at a high rate of 241.3/1,000 PY in the general population [11]. In addition, MCI is considered as a frequent complication of T2DM, with an estimated prevalence rate of 45.0% (95% confidence interval [CI]: 36.0–54.0%) worldwide [12, 13]. A recent national study reported that adults with T2DM had significantly poorer performance in delayed and total word recall than those with normoglycemia [14]. Another systematic review and meta-analysis involving 144 prospective studies reported that diabetes conferred a 1.25- to 1.91-fold excess risk for cognitive disorders (including cognitive impairment and dementia) [15]. T2DM patients with MCI were less likely to receive adequate diabetes care than those who have diabetes alone, which in turn affected their blood glucose, and made them vulnerable to hyper- and hypoglycemia [16]. Furthermore, patients with poorly controlled diabetes and MCI had 2.87 times (95% CI: 1.20-6.85) the risk of progressing to dementia [17]. Therefore, prevention of MCI in patients with T2DM is crucial.

Sleep quality is a construct comprised of both one's subjective satisfaction with the sleep experience and quantitative components of sleep such as sleep duration, sleep onset latency, maintenance of sleep, and sleep efficiency [18]. Considerable evidence has suggested the benefits of good sleep quality on cognitive function [19, 20], and poor sleep quality can lead to cognitive decline, which may ultimately result in Alzheimer's disease (AD) by increasing β-amyloid burden [21]. A study conducted in the USA reported that sleep quality was related to both objective measures of sustained attention and self-awareness of memory decline in middle-aged and older adults [19]. Another study conducted in England showed that poor sleep quality was associated with deterioration in cognitive function [22]. However, studies of the association between sleep quality and MCI in Chinese patients with T2DM are limited. The only relevant study which was conducted in Shandong Province of China, evaluated sleep quality by asking participants "how well do you sleep and rest", and found a correlation between sleep quality and MCI [23]. However, no previous study has attempted to evaluate sleep quality using well-validated scales like the Pittsburgh Sleep Quality Index (PSQI) [24]. Therefore, this study aimed to identify the association between sleep quality and MCI in Chinese patients with T2DM by using the PSQI scale to comprehensively assess the role of overall sleep quality, subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, sleep medication, and daily dysfunction in the presence of MCI.

Methods

Study design and participants

This cross-sectional study was conducted at the Endocrinology Department of Xiangya Hospital, Central South University between March 2021 and December 2022. Those with T2DM diagnosed by specialized physicians, aged \geq 40 years, and voluntarily participating in this study with signed informed consent were included. Patients with dementia were excluded from the study. According to the sample size formula for categorical outcome (proportion) in cross-sectional studies (N = $Z^2p(1-p)/d^2$) [25], a sample size of 683 was obtained with Z = 1.96, p = 36.0%, d = 0.1p (p was the lower limit of the 95% CI of the pooled prevalence of MCI among patients with T2DM reported by a previous systematic review and meta-analysis) [13]. Finally, a minimum sample size of 910 was obtained with a response rate of 75%.

Data collection

Data regarding sociodemographic characteristics and lifestyle factors were collected through face-to-face interviews, and T2DM-related information and biochemical indicators were obtained by reviewing electronic medical records. Sociodemographic characteristics included age, sex, marital status, educational level, household income, and current work status; lifestyle factors included smoking and drinking status, and regular physical activity; T2DM-related factors included duration of diabetes, family history of diabetes, history of stroke, and diabetes-specific complications (including diabetic nephropathy, diabetic retinopathy, and diabetic foot); and laboratory indicators included fasting blood glucose (FBG), glycated hemoglobin A1c (HbA1c), total cholesterol (TC), triglycerides (TG), and uric acid (UA).

In reference to cigarette use and alcohol consumption, current smokers were defined as those who smoked at least one cigarette per day in the past month, and current drinkers were defined as those who drank at least one alcoholic beverage per day in the past month [26]. Regular physical activity was defined as performing at least one activity, such as walking or square dancing, for at least 30 min per day in the past month.

Measures

Cognitive function assessment

Cognitive function was evaluated using the Mini-Mental State Examination (MMSE) scale. The MMSE is a 30-point questionnaire widely used in clinical and research settings to measure cognitive impairment, including simple tasks related to five domains of cognitive function: orientation, registration, attention and calculation, recall, and language and praxis [27]. The total score ranges from 0 to 30, with higher scores indicating better cognitive function [28]. The cut-off values for MCI were \leq 19 points, \leq 22 points, and \leq 26 points for an educational level of illiterate, elementary school, and junior high school or above, respectively [29]. Specifically, those with a total score below and above the cut-off value were categorized into MCI and normal cognition (NC) groups, respectively.

Sleep quality

The PSQI was used to assess sleep quality [30]. It is a self-report questionnaire with 19 items and seven sleep indices, namely subjective sleep quality (including very good, good, poor, and very poor), sleep latency, which is a composite index including two questions "how long it takes from bedtime to sleep (including ≤ 15 min, 16-30 min, 31-60 min, and ≥ 60 min) and "how often it is hard to fall asleep (including not at all, < 1 time/week, 1-2 times/week, and ≥ 3 times/week)", sleep duration (including ≥ 7 h, 6-7 h, 5-6 h, and < 5 h), sleep efficiency

(including 85%, 75–84%, 65–74%, and <65%), sleep disturbance (including not at all, <1 time/week, 1–2 times/week, and ≥ 3 times/week), sleep medication (including not at all, <1 time/week, 1–2 times/week, and ≥ 3 times/week), and daily dysfunction, which is a composite index including two questions "do you often feel sleepy" (including not at all, <1 times/week, 1–2 times/week, and ≥ 3 times/week) and "have you had less energy to do things" (including not at all, occasionally, sometimes, and often)". Each index has a score ranging from 0 to 3, making up the total PSQI score ranging from 0 to 21, with a higher total PSQI score indicating poorer overall sleep quality [31]. This scale has been widely used in the Chinese populations with a Cronbach's α coefficient of 0.842 and good construct validity [31].

Statistical analyses

Missing data were complemented using multiple interpolation. Continuous variables distributed normally or non-normally were described as mean (standard deviation [SD]) or median (interquartile range), respectively. Categorical variables were described as frequency (n) and proportion (%). The differences in PSQI scores between the MCI and NC groups were compared using the Student's t-test. Pearson's correlation was used to identify the linear relationship between PSQI and MMSE scores. Chi-square goodness-of-fit and trend chi-square tests were used to identify the associations between sleep quality indices and MCI. Multivariate logistic regression analyses were used to determine the association between sleep quality and MCI, and four models were developed for multivariate analyses to identify the robustness of the contribution of sleep quality to MCI. A two-tailed P value of <0.05 was considered statistically significant. Data were analyzed using IBM SPSS software (version 26.0) and R software (version 4.2.1) [32].

Results

Characteristics of study participants

A total of 1,001 patients with T2DM aged 40–96 years were included in this study, with the majority (61.2%) being male. The mean age and duration of diabetes were 60.2 (SD: 10.1) and 11.4 (SD: 7.6) years, respectively. The sociodemographic characteristics and lifestyle factors of the study population are summarized in Table 1; T2DM-related characteristics and biochemical indicators are shown in Tables 2 and 3, respectively.

Correlation matrix of PSQI and MMSE

The correlation matrix of the PSQI and MMSE scores is shown in Table 4. The total PSQI score (r=-0.27, P<0.05), subjective sleep quality (r=-0.23, P<0.05), sleep latency (r=-0.20, P<0.05), sleep duration (r=-0.16, P<0.05), sleep efficiency (r=-0.26, P<0.05), sleep disturbance (r=-0.24,

Table 1 Sociodemographic characteristics and lifestyle factors of participants (n = 1,001)

Variables	Description	N (%)		
Age (year)	40–59	520 (51.9)		
	≥60	481 (48.1)		
Sex	Male	613 (61.2)		
	Female	388 (38.8)		
Marital status	Married	924 (92.3)		
	Single	77 (7.7)		
Educational level	Middle school or below	542 (54.1)		
	High school or above	459 (45.9)		
Household income (RMB)	≤ 5,000	638 (63.7)		
	> 5,000	363 (36.3)		
Current work status	Employed	326 (32.6)		
	Unemployed	675 (67.4)		
Current smoker	No	800 (79.9)		
	Yes	201 (20.1)		
Current drinker	No	874 (87.3)		
	Yes	127 (12.7)		
Regular physical activity	No	393 (39.3)		
	Yes	608 (60.7)		

N, Frequency; %, Percentage of N; RMB, renminbi

Table 2 T2DM-related factors of participants (n = 1,001)

Variables	Description	N (%)
Duration of diabetes (year)	< 10	462 (46.2)
	≥10	539 (53.8)
Family history of diabetes	No	563 (56.2)
	Yes	438 (43.8)
Stroke	No	876 (87.5)
	Yes	125 (12.5)
Diabetic nephropathy	No	493 (49.3)
	Yes	508 (50.7)
Diabetic retinopathy	No	613 (61.2)
	Yes	388 (38.8)
Diabetic foot	No	922 (92.1)
	Yes	79 (7.9)

N, frequency; %, percentage of N; T2DM, type 2 diabetes mellitus

Table 3 Laboratory indicators of participants (n = 1,001)

Laboratory infareators of participants (if 1,001)				
Variables	M (P ₂₅ , P ₇₅)			
FBG (mmol/l)	7.10 (5.89, 8.97)			
HbA1c (%)	8.10 (6.70, 9.70)			
TC (mmol/l)	4.60 (3.73, 5.52)			
TG (mmol/l)	1.62 (1.10, 2.34)			
UA (mmol/l)	358.00 (288.00, 434.00)			

M, median; FBG, fasting blood glucose; HbA1c, glycated hemoglobin A1c; TC, total cholesterol; TG, triglycerides; UA, uric acid

P<0.05), and daily dysfunction (r=-0.25, P<0.05) were significantly correlated with the total MMSE score. In addition, the total PSQI score and its seven sleep indices were correlated with most of the five MMSE dimensions. The strongest correlation was found between daily dysfunction and language and praxis (r=-0.28, P<0.05),

while the weakest correlation was found between sleep efficiency and registration (r=-0.07, P<0.05).

Univariate association between sleep quality and MCI

The univariate analyses of sleep quality and MCI are shown in Table 5. According to the MMSE screening criteria, 274 and 727 individuals were classified into the MCI and NC groups, respectively. The rate of MCI was higher among those with poor sleep quality compared to those with good sleep quality (Fig. 1). In addition, higher total PSQI scores, as well as higher scores on subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and daily dysfunction were associated with higher rates of MCI. Table 6 shows the dose-response association between the seven sleep quality indices and MCI.

Multivariate association between sleep quality and MCI

The multivariate analyses of sleep quality and MCI are shown in Table 7. The four models consistently showed that patients with higher total PSQI scores (aOR = 1.09– 1.11, P<0.05), as well as higher scores on the subjective sleep quality (aOR = 1.32–1.46, P<0.05), sleep latency (aOR = 1.25–1.32, P<0.05), sleep duration (aOR = 1.30– 1.32, P<0.05), sleep efficiency (aOR = 1.36–1.41, P<0.05), sleep disturbance (aOR = 1.66–1.86, P<0.05), and daily dysfunction (aOR = 1.38–1.48, P<0.05) were associated with higher rates of MCI.

Discussion

This study explored the association between sleep quality and MCI among Chinese patients with T2DM using a large sample size of 1,001. Four models based on multivariate analyses consistently showed that poorer overall sleep quality (higher total PSQI score), as well as worse subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and daily dysfunction were associated with higher rates of MCI. To the best of our knowledge, this is the first study to identify the association between sleep quality and MCI among patients with T2DM in China using the PSQI to comprehensively assess sleep quality.

A positive association between overall sleep quality and cognitive function has been reported in elderly individuals [33, 34]. For example, a study conducted in Egypt found that poor sleep quality was related to cognitive impairment among elderly people [35], and a population-based study reported that poor sleep quality, rather than sleep-disordered breathing, was associated with MCI in the general population [36]. However, evidence concerning the relationship between overall sleep quality and MCI in patients with T2DM was limited and inconclusive. Specifically, Gupta et al. [37] found that sleep quality was not independently associated with cognitive decline

Table 4 Correlation matrix of PSQI and MMSE (n = 1,001)

	Orientation	Registration	Attention and Calculation	Recall	Language and Praxis	MMSE score
Total PSQI score	-0.17**	-0.06	-0.22**	-0.16**	-0.25**	-0.27**
Subjective sleep quality	-0.19**	-0.08*	-0.18**	-0.16**	-0.17**	-0.23**
Sleep latency	-0.12**	-0.05	-0.17**	-0.08**	-0.20**	-0.20**
Sleep duration	-0.09**	-0.00	-0.13**	-0.08**	-0.18**	-0.16**
Sleep efficiency	-0.14**	-0.07*	-0.20**	-0.18**	-0.24**	-0.26**
Sleep disturbance	-0.18*	-0.05	-0.20**	-0.12**	-0.22**	-0.24**
Sleep medication	-0.02	-0.00	-0.05	-0.09**	-0.01	-0.05
Daily dysfunction	-0.19**	-0.01	-0.17**	-0.12**	-0.28**	-0.25**

MMSE, Mini-Mental State Examination; PSQI, Pittsburgh Sleep Quality Index; * P < 0.05; ** P < 0.01

Table 5 Univariate analyses between sleep quality and MCI (n = 1,001)

Variables	Total population	MCI group	NC group	t	P value	Crude OR
	(M [SD])	(n=274, M [SD])	(n=727, M [SD])			(95% CI)
Total PSQI score	6.2 (4.1)	7.8 (4.4)	5.6 (3.8)	-7.22	< 0.001	1.14 (1.10–1.18)
Subjective sleep quality	1.4 (0.9)	1.7 (1.0)	1.3 (0.9)	-6.00	< 0.001	1.64 (1.40-1.92)
Sleep latency	1.4 (1.2)	1.7 (1.2)	1.3 (1.1)	-5.39	< 0.001	1.40 (1.24–1.57)
Sleep duration	0.8 (1.1)	1.1 (1.2)	0.7 (1.0)	-4.63	< 0.001	1.38 (1.21–1.57)
Sleep efficiency	1.1 (1.2)	1.5 (1.3)	0.9 (1.1)	-6.85	< 0.001	1.50 (1.34–1.68)
Sleep disturbance	1.4 (0.6)	1.7 (0.7)	1.4 (0.6)	-6.70	< 0.001	2.22 (1.76-2.80)
Sleep medication	0.1 (0.5)	0.1 (0.5)	0.1 (0.5)	-1.35	0.178	1.22 (0.93-1.60)
Daily dysfunction	1.2 (1.2)	1.7 (1.3)	1.0 (1.2)	-7.77	< 0.001	1.57 (1.40-1.76)

M, mean; SD, standard deviation; OR, odds ratio; CI, confidence interval; MCI, mild cognitive impairment; NC, normal cognition; PSQI, Pittsburgh Sleep Quality Index

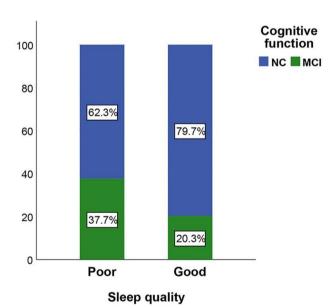


Fig. 1 Rate of MCI among patients with poor and good sleep quality. MCI, mild cognitive impairment; NC, normal cognition

with a limited sample size of 250, whereas the only relevant study among Chinese population found that sleep quality was associated with MCI by using the question "how well do you sleep and rest" [23].

The current study assessed overall sleep quality by the PSQI with a large sample size. It was found that poorer overall sleep quality was associated with higher rates of MCI among T2DM patients, and this association was

consistent across the four models in multivariate analyses. Therefore, this study provides new insights into the association between sleep quality and MCI among Chinese patients with T2DM, and it underscores the importance of raising the awareness of cognitive impairment and sleep problems for clinicians working with T2DM patients. Future clinical trials are still needed to ascertain whether sleep intervention can protect T2DM patients from cognitive impairment.

In addition, this study found that poor subjective sleep quality was associated with higher rates of MCI, which is consistent with several population-based studies [38, 39]. It may be explained by the fact that poor subjective sleep quality can contribute to increased amyloid deposition, which is an important biomarker of MCI [40]. Sleep efficiency was also found to be associated with MCI in this study. Saetung al. [41] found that decreased sleep efficiency was independently associated with poorer cognitive function among patients with impaired glucose tolerance, and that a 10% change in sleep efficiency was equivalent to an effect of eight years of age on cognitive function scores. The underlying mechanism may be that worse sleep efficiency, as measured by actigraphy, increases cerebrospinal fluid amyloid-ß plaque 42 (Aß42) levels, which is a key molecule involved in AD pathogenesis [42]. Therefore, special attention should be paid to the subjective sleep quality and sleep efficiency for the management of cognitive function in patients with T2DM.

Table 6 Distribution of sleep quality indices between MCI and NC groups (n = 1,001)

Sleep quality indices	Scores of sleep indices	MCI group (<i>n</i> = 274, %)	NC group (<i>n</i> = 727, %)	Chi-square goodness- of-fit test		Trend chi- square test	
				χ^2	P value	χ^2	P value
Subjective sleep quality	0	36 (20.2)	142 (79.8)	180.00	< 0.001	38.42	< 0.001
	1	81 (20.8)	308 (79.2)				
	2	95 (30.4)	218 (69.6)				
	3	62 (51.2)	59 (48.8)				
Sleep latency	0	65 (22.2)	228 (77.8)	70.50	< 0.001	30.14	< 0.001
	1	55 (18.6)	241 (81.4)				
	2	44 (32.4)	92 (67.6)				
	3	110 (39.9)	166 (60.1)				
Sleep duration	0	123 (22.9)	415 (77.1)	461.00	< 0.001	24.50	< 0.001
	1	52 (25.5)	152 (74.5)				
	2	50 (32.5)	104 (67.5)				
	3	49 (46.7)	56 (53.3)				
Sleep efficiency	0	96 (19.6)	394 (80.4)	322.00	< 0.001	50.56	< 0.001
	1	45 (25.4)	132 (74.6)				
	2	34 (27.6)	89 (72.4)				
	3	99 (46.9)	112 (53.1)				
Sleep disturbance	0	5 (20.8)	19 (79.2)	819.00	< 0.001	47.99	< 0.001
	1	107 (19.2)	450 (80.8)				
	2	139 (36.8)	239 (63.2)				
	3	23 (54.8)	19 (45.2)				
Sleep medication	0	254 (26.7)	699 (73.3)	11.44	< 0.01	2.02	0.155
	1	8 (47.1)	9 (52.9)				
	2	8 (61.5)	5 (38.5)				
	3	4 (22.2)	14 (77.8)				
Daily dysfunction	0	74 (17.3)	353 (82.7)	182.00	< 0.001	60.38	< 0.001
	1	43 (25.0)	129 (75.0)				
	2	46 (28.7)	114 (71.3)				
	3	111 (45.9)	131 (54.1)				

 $MCI, mild\ cognitive\ impairment;\ NC,\ normal\ cognition$

Table 7 Multivariate analyses between sleep quality and MCI among patients with T2DM

Sleep quality	Model 1 ^a	odel 1 ^a		Model 2 ^b		Model 3 ^c		Model 4 ^d	
	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	aOR (95% CI)	P value	
Total PSQI score	1.11 (1.07–1.15)	< 0.001	1.11 (1.06–1.45)	< 0.001	1.10 (1.05-1.14)	< 0.001	1.09 (1.05-1.14)	< 0.001	
Subjective sleep quality	1.46 (1.24-1.73)	< 0.001	1.39 (1.17–1.65)	< 0.001	1.33 (1.11–1.58)	0.001	1.32 (1.11–1.57)	0.002	
Sleep latency	1.32 (1.16–1.51)	< 0.001	1.29 (1.13–1.47)	< 0.001	1.25 (110-1.43)	0.001	1.25 (1.09–1.43)	0.001	
Sleep duration	1.32 (1.45-1.51)	< 0.001	1.32 (1.14–1.52)	< 0.001	1.30 (1.13-1.50)	< 0.001	1.30 (1.12-1.50)	< 0.001	
Sleep efficiency	1.41 (1.25-1.59)	< 0.001	1.39 (1.23–1.58)	< 0.001	1.36 (1.20-1.54)	< 0.001	1.37 (1.20–1.55)	< 0.001	
Sleep disturbance	1.86 (1.45-2.38)	< 0.001	1.77 (1.38–2.27)	< 0.001	1.66 (1.28–2.15)	< 0.001	1.66 (1.28–2.15)	< 0.001	
Sleep medication	1.07 (0.80-1.44)	0.631	1.05 (0.78-1.41)	0.748	1.02 (0.75-1.38)	0.907	0.99 (0.73-1.35)	0.960	
Daily dysfunction	1.48 (1.31–1.67)	< 0.001	1.44 (1.27–1.63)	< 0.001	1.38 (1.21–1.57)	< 0.001	1.38 (1.21–1.57)	< 0.001	

 $a OR, adjusted\ odds\ ratio; CI, confidence\ interval; MCI, mild\ cognitive\ impairment; PSQI, Pittsburgh\ Sleep\ Quality\ Index$

The association between sleep duration and MCI found in this study is consistent with several large population-based studies [38, 43, 44]. For example, a study using data drawn from the 2011, 2013, and 2015 waves of the China

Health and Retirement Longitudinal Study reported that short and long sleep durations were associated with consistently lower cognition scores with increasing age [38], and a pooled cohort study found an inverted U-shaped

^a Model 1 was adjusted for sociodemographic characteristics

 $^{^{\}rm b}$ Model 2 was adjusted for sociodemographic characteristics and lifestyle factors

 $[^]c\, Model\, 3\, was\, adjusted\, for\, socio demographic\, characteristics, lifestyle\, factors, and\, T2DM-related\, factors$

 $^{^{}d}\,\text{Model}\,4\,\text{was}\,\text{adjusted}\,\text{for}\,\text{sociodemographic}\,\text{characteristics},\,\text{lifestyle}\,\text{factors},\,\text{T2DM-related}\,\text{factors},\,\text{and}\,\text{laboratory}\,\text{indicators}$

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association between sleep duration and global cognitive decline [43, 44]. Additionally, Li et al. [44] found that long sleep duration was associated with lower mental status scores (β =-0.43, P=0.001) and lower memory scores (β = -0.26, P = 0.006) than normal sleep duration [44]. To our knowledge, this is the first study to explore the relationship between sleep duration and cognitive function in patients with T2DM. This study found that insufficient sleep duration is associated with higher rates of MCI. The mechanism underlying this association may be that both T2DM and sleep deprivation increase hippocampal synaptic plasticity and deposition of Aß, which may lead to impaired cognitive function [45-49]. Therefore, for patients with T2DM who are sleep deprived, appropriate prolonged sleep duration may be an effective measure to maintain cognitive function.

This study also found that sleep latency, sleep disturbance, and daily dysfunction were associated with MCI, which is consistent with previous studies among the elderly [50, 51]. Specifically, a systematic review involving 71 studies reported that sleep alterations, including sleep efficiency and sleep latency, can generate or accelerate cognitive decline, even in the absence of overt pathology [50], and another study conducted in older adults without dementia found that sleep disturbance was significantly correlated with memory recall and processing speed, and this relationship could be mediated by depression [51]. However, this is the first study to identify an association between MCI and sleep latency, sleep disturbance, and daily dysfunction in patients with T2DM. The proposed link between the above sleep quality indices and MCI among patients with T2DM is that both diabetes and sleep quality problems influence the glymphatic system, which is the key system for clearing toxic compounds from the brain, and accumulation of toxic substances in the brain leads to cognitive impairment [52–55]. Moreover, because the glymphatic system requires physiological sleep to function properly, sleep quality problems can stimulate the development of Aß in the brain and lead to AD [56]. Therefore, when attempting to identify potentially modifiable factors that could cause MCI in patients with T2DM, it is important to consider the role of sleep quality indices.

This study has several limitations. First, given that this was a cross-sectional study, the relationship between sleep quality and MCI may be bidirectional, and future longitudinal studies including baseline information on sleep disorders are still needed to ascertain the causal link between sleep quality and cognitive function. Second, some factors, including shift work, napping, and depressive symptoms, which may be associated with poor sleep quality in a bidirectional manner [57, 58], were not considered in this study. Third, since PSQI was a subjective measurement of sleep quality, the use

of other measurements like polysomnography, which is the gold standard for sleep assessment, is highly recommended to diagnose sleep problems for future research. Additionally, this study assessed sleep quality at a single timepoint. Future studies are also suggested to use actigraphy to measure sleep quality as it is able to objectively measure sleep across a longer period of time in the home environment.

Conclusions

Poor overall sleep quality, subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, and daily dysfunction were associated with higher rates of MCI in Chinese patients with T2DM. Future studies are still needed to ascertain whether sleep intervention could improve cognitive function in patients with T2DM. It is also recommended for clinicians working with patients with T2DM to raise the awareness of cognitive impairment and sleep problems.

Abbreviations

aOR Adjusted odds ratio
AD Alzheimer's disease
BMI Body mass index
CI Confidence Interval
FBG Fasting blood glucose
HbA1c Hemoglobin A1c

MMSE Mini Mental State Examination
MCI Mild cognitive impairment
NC Normal cognition

OR Odds ratio PY Person-years

PSQI Pittsburgh Sleep Quality Index

RMB Renminbi
SD Standard deviation
T2DM Type 2 diabetes mellitus
TC Total cholesterol
TG Triglycerides
UA Uric acid

Acknowledgements

The authors are grateful to all the participants and staff of the Xiangya Hospital of Central South University who participated in or assisted with the study. An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR. The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

Author contributions

W.D. contributed to the concept and design of this study, project administration, resources, conceptualization, funding acquisition. R.M., W.C., J.X., R.X., XY.W., L.C., J.Y. and A.L. contributed to the methodology, investigation, data curation, supervision. R.M. and H.W. contributed to the methodology, software, formal analysis, visualization and validation. R.M. drafted the main manuscript text. S.D. contributed to the supervision and validation. R.M., H.W., S.D. and W.D. critically revised the manuscript for important intellectual content. All authors approved the final version of publication.

Funding

This study was supported by the National Natural Science Foundation of China (grant number, 82103939), National Natural Science Foundation of Hunan Province (grant number, 2021JJ40805), Start-up Research Fund of Central South University (grant number, 202044003), National Key R&D Program of China (grant number, 2020YFC2008600).

Data availability

The datasets generated and/or analyzed during the present study are not publicly available but are available from the corresponding author Wenjie Dai (Email: m18673965791@163.com) on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Xiangya School of Public Health, Central South University (No. XYGW-2019-47). All participants voluntarily participated in the study and provided written informed consent.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 27 August 2023 / Accepted: 14 March 2025 Published online: 22 March 2025

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