The Mediation Role of Sleep Quality in the Relationship Between Cognitive Decline and Depression

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Abstract

Objectives

Associations between cognitive decline and depression have been inconclusive. We examined 1) whether sleep quality mediates these relationships and 2) which factor of sleeping quality mediates these relationships.

Methods

This study utilized baseline data from the 2018 West China Health and Aging Trend study (WCHAT), a large cohort data-set that including participants aged over 50 years old. We defined depression using the 15-item Geriatric Depression Scale (GDS-15). Cognitive status was measured using the Short Portable Mental Status Questionnaire (SPMSQ) and sleeping quality was assessed using the Pittsburgh sleep quality index (PSQI). Direct relationships between cognitive decline, sleep quality and depression were assessed using multiple linear regression. Mediation models and structural equation model (SEM) pathway analysis were used to test the mediating role of specific aspects of sleep (e.g., quality, duration) in the relationship between cognitive decline and depression.

Results

Of 6828 participants aged 50 years old or older, the proportion of depression was 17.4%. Regression analysis indicated a direct association between cognitive scores (β= 0.251, 95% CI 0.211 to 0.29, $p < 0.001$) and depression status. After adjusted PSQI scores, the association between cognitive scores and depression status was still significant (β= 0.242, 95% CI 0.203 to 0.281, $p < 0.001$), indicating a partial mediation effect of sleeping quality. Mediation analysis verified sleep quality partially mediate the associations between cognitive decline and depression (indirect effect estimate = 0.0308, bootstrap 95% CI 0.0231 to 0.04; direct effect estimate = 0.3124, bootstrap 95% CI 0.2692 to 0.35). And daytime dysfunction had a highest mediation effect with a proportion of mediation up to 14.56%.

Conclusions

Sleep quality partially mediated the relationship between cognitive decline and depression. Daytime dysfunction had a highest mediation effect. Further research is necessary to examine the effects of sleep quality on the relationship of cognitive decline and depression.

Introduction

With an aging population, late-life depression has been a severe health problem in rural China which was a major cause of global disability and suicide, and associated with cardiovascular diseases and mortality[1]. Recent research reported the prevalence of depression was 15.5% in China in a large cross-sectional study which included 19,379 healthcare workers from 25 provinces[2]. However, in old people, the prevalence of depression was higher. It was found that 17.1% of males and 23.1% of females in 950

participants aged ≥ 60 years from 22 locations in China were identified as having depressive symptoms[3]. Many studies have identified that behavioral and psychosocial factors, such as alcohol abuse, smoking, sleep disturbance, physical inactivity, unhealthy eating habits, and stressful events, and sociodemographic factors, such as low income, unemployment, low education level, and low social support, are mostly related with an increased risk of depression[4,5].

Besides these risk factors, cognitive decline was found to be associated with depression in the recent years. It was found that cognitive impairment may be one of the more practically important aspects of depression[6]. And depression was also a risk factor for Alzheimer's disease[7]. Older adults who were diagnosed for the first time with depression after 65 years of age, showed a stronger association with cognitive impairment (OR = 6.65, 95% CI: 2.39; 10.9, $p < 0.01$)[8]. What's more, sleeping quality was both related with cognitive decline and depression[9]. Approximately half of older people report sleep disturbances, which are associated with various health conditions. Specifically, components of poorer sleep quality and greater sleep disturbance were related to worse sustained attention scores, while increased sleep latency and daytime sleepiness were associated with greater frequency and seriousness of forgetting[10]. Night sleep disturbances (OR = 1.95, 95% CI: 1.17–3.25) and daytime sleepiness (OR = 1.93, 95% CI: 1.16–3.20) were also associated with depression[11]. Particularly, a study found that daytime sleepiness and poor efficiency were significantly associated with loss of interest; and poor satisfaction, daytime sleepiness, mid-sleep time, and efficiency were significantly associated with having at least one depressive symptom[12].

Both the quality of sleep and cognitive decline impact depression while they influence each other. However, the underlying mechanisms are not yet clear. In our study, we we hypothesized that participants with depression would have poorer scores on cognitive tests and that this association would be mediated by sleep quality. This leads us to explore the mediating effect of sleeping quality between cognitive decline and depression in older adults and further test the components of sleeping quality in this relationship.

Method

Study design and sample population

Our study was a cross-sectional analysis obtaining baseline data of the west China health and aging trend (WCHAT) study which was conducted from 2018 to 2020[13]. The research was approved by the Ethical Review Committee of West China Hospital with the committee's reference number 2017(445) and the registration number is ChiCTR 1800018895. In our study, participants aged 50 years old or older were enrolled. Participants were recruited by the local government and asked verbally by the researchers about their willingness to take part in the study. Before investigation, informed consent was signed and obtained by each participant. Initially, 7536 participants were enrolled. Then we excluded subjects who were under 50 years old and 97 participants were excluded. Then we kept on excluding 545 subjects

without doing sleeping quality assessment. Besides, 59 participants were excluded without doing depression assessment. After that, 7 subjects were excluded without life style data. Therefore, 6828 participants were analyzed in our study (Fig. 1).

Data collection

We used electronic questionnaire and instruments to collect the required data. All interviewers were medical students who were trained on collecting questionnaire data through face to face, one-on-one personal interviews. Other anthropometric and bioimpedance measurements were collected by trained technicians[13]. Depression was assessed using the 15-item Geriatric Depression Scale (GDS-15). The scale, which contains 15 items that require only a yes/no answer, is the most widely used scale for the detection of depression and scores ≥ 5 indicate depression[14]. Sleeping quality was assessed using the Pittsburgh sleep quality index (PSQI). The questionnaire included 7 components and component scores range from 0 to 3 and a global score ranging from 0 to 21, with higher scores indicating worse sleep quality. Mostly, scores > 5 are considered as poor self-reported sleep quality[15]. Cognitive status was measured using a 10-item Short Portable Mental Status Questionnaire (SPMSQ). For SPMSQ scoring, 0 ~ 2 indicated complete cognitive function, 3 ~ 4 indicated mild cognitive functional impairment, 5 ~ 7 indicated moderate cognitive function impairment, and 8 ~ 10 indicated severe cognitive function impairment and this assessment should be based on the education level[16]. Other baseline demographic information included age, gender, occupation, educational level, ethnic groups background. A medical history of chronic disease was self-reported. These disease conditions included hypertension, diabetes, osteoarthrosis, coronary heart disease, tumor, deafness and having two or more disease was considered as comorbidity.

Statistical analysis

Information was processed and analyzed using R version 4.0.2. Characteristics of baseline data were presented with mean values, standard deviation (SD), and frequencies. Differences between the categories of depression and the variables studied were analyzed through analysis of variance (ANOVA) in the continuous variables and the chi squared test on categorical variables[17]. Direct effects of cognitive decline (operationalized by SPMSQ scores) and poor sleep quality (operationalized by PSQI scores) on depression were assessed using three multi-variable regression models that included relevant variables from previous covariate analyses. 95% confidence intervals were generated for all regression coefficients. Mediation hypotheses of 7 components of PSQI questionnaire and PSQI total score on the relationship between cognitive decline and depression were done using the bias-corrected bootstrap method with 6828 samples to calculate confidence intervals (95%). The results were statistically significant with $p < 0.05$. An indirect effect was considered significant when the confidence interval did not include zero. Besides, path analysis of 7 components of PSQI questionnaire was shown in the SEM framework which was done using a SEM package in R version 4.0.2[18].

Results

Overall, we enrolled 6828 participants (2562 men and 4266 women) aged 50 years old or older in the study. The mean age of the group was 62.43 ± 8.28 years. Table 1 shows descriptive characteristics of the participants according to depression assessment. The prevalence of depression according to the GDS-15 was 17.4%, with a higher prevalence of depression in women than in men and a lower prevalence in Han compared to other ethnic groups. Subjects with depression tended to be farmers and has a lower educational level ($P < 0.001$). It was observed that individuals in the depression group presented higher scores in subjective sleep quality, sleep latency, habitual sleep efficiency, sleep disturbance, used sleep medication, daytime dysfunction and PSQI total scores ($P < 0.001$). Subjects who enjoy dancing, drinking tea and smoking has a lower prevalence of depression ($P < 0.001$). And subjects with anxiety or cognitive decline has a higher prevalence of depression ($P < 0.001$). Besides, subjects with coronary heart disease (CHD), osteoarthrosis, deafness has a higher prevalence of depression ($P < 0.05$).

Table 1
Sample characteristics stratified by depressed status (N = 6828).

Characters	Total n = 6828	Depressed n = 1185(17.4)	Non-depressed n = 5643(82.6)	P value
Ethnic group, n(%)				< 0.001
Han	2472(36.2)	338(28.52)	2134(37.82)	
Others	4356(63.8)	847(71.48)	3509(62.18)	
Gender, n(%)				< 0.001
Male, n(%)	2562(37.52)	367(30.97)	2195(38.9)	
Female, n(%)	4266(62.48)	818(69.03)	3448(61.1)	
Age, mean ± SD	62.43 ± 8.28	62.78 ± 8.50	62.36 ± 8.23	0.1245
Age group, n(%)				0.2967
50–59	2697(39.5)	454(38.31)	2243(39.75)	
60–69	2723(39.88)	463(39.07)	2260(40.05)	
70–79	184(2.69)	33(2.78)	151(2.68)	
80 +	1224(17.93)	235(19.83)	989(17.53)	
Occupation				< 0.001
Farmers	4456(65.26)	910(76.79)	3546(62.84)	
Others	2372(34.74)	275(23.21)	2097(37.16)	
Educational level, n(%)				< 0.001
No formal education	1897(27.78)	434(36.62)	1463(25.93)	
Elementary school	2318(33.95)	425(35.86)	1893(33.55)	
Middle school	1468(21.5)	200(16.88)	1268(22.47)	
High school and above	1145(16.75)	126(10.63)	1019(18.04)	
Dwelling status, n(%)				0.006
Solitude	339(4.96)	78(6.58)	261(4.63)	
Non-solitude	6489(95.04)	1107(93.42)	5382(95.37)	

Note. Means ± standard deviation was shown. Others = other nationalities including Zhuang, Manchu, Hui, Mongolia, Tujia nationalities. Data are shown using % or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.* These variables are presented as median (interquartile range).

Characters	Total n = 6828	Depressed n = 1185(17.4)	Non-depressed n = 5643(82.6)	P value
Subjective Sleep Quality, n(%)				< 0.001
0 score	1243(18.2)	163(13.76)	1080(19.14)	
1 score	3597(52.68)	584(49.28)	3013(53.39)	
2 score	1688(24.72)	351(29.62)	1337(23.69)	
3 score	300(4.39)	87(7.34)	213(3.77)	
Sleep Latency, n(%)				< 0.001
0 score	1451(21.25)	172(14.51)	1279(22.67)	
1 score	2654(38.87)	425(35.86)	2229(39.5)	
2 score	1940(28.41)	431(36.37)	1509(26.74)	
3 score	783(11.47)	157(13.25)	626(11.09)	
Sleep Duration, n(%)				0.0563
0 score	3336(48.86)	550(46.41)	2786(49.37)	
1 score	1546(22.64)	263(22.19)	1283(22.74)	
2 score	1228(17.98)	225(18.99)	1003(17.77)	
3 score	718(10.52)	147(12.41)	571(10.12)	
Habitual Sleep Efficiency, n(%)				< 0.001
0 score	4800(70.3)	763(64.39)	4037(71.54)	
1 score	1041(15.25)	214(18.06)	827(14.66)	
2 score	425(6.22)	81(6.84)	344(6.1)	
3 score	562(8.23)	127(10.72)	435(7.71)	
Sleep Disturbance, n(%)				< 0.001
0 score	258(3.78)	25(2.11)	233(4.13)	
1 score	4422(64.76)	676(57.05)	3746(66.38)	
2 score	2053(30.07)	446(37.64)	1607(28.48)	

Note. Means ± standard deviation was shown. Others = other nationalities including Zhuang, Manchu, Hui, Mongolia, Tujia nationalities. Data are shown using % or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.* These variables are presented as median (interquartile range).

Characters	Total n = 6828	Depressed n = 1185(17.4)	Non-depressed n = 5643(82.6)	P value
3 score	95(1.39)	38(3.21)	57(1.01)	
Used Sleep Medication, n(%)				< 0.001
0 score	6630(97.1)	1131(95.44)	5499(97.45)	
1 score	80(1.17)	14(1.18)	66(1.17)	
2 score	50(0.73)	15(1.27)	35(0.62)	
3 score	68(1)	25(2.11)	43(0.76)	
Daytime Dysfunction, n(%)				< 0.001
0 score	2815(41.23)	307(25.91)	2508(44.44)	
1 score	2125(31.12)	424(35.78)	1701(30.14)	
2 score	1392(20.39)	298(25.15)	1094(19.39)	
3 score	496(7.26)	156(13.16)	340(6.03)	
PSQI, mean ± SD	6.16 ± 3.29	7.18 ± 3.52	5.95 ± 3.20	< 0.001
Dancing status, n(%)				0.0295
Yes	1346(19.71)	206(17.38)	1140(20.2)	
No	5482(80.29)	979(82.62)	4503(79.8)	
Smoking status, n(%)				< 0.001
Yes	1315(19.26)	179(15.11)	1136(20.13)	
No	5513(80.74)	1006(84.89)	4507(79.87)	
Drinking alcohol status, n(%)				0.2663
Yes	1315(19.26)	214(18.06)	1101(19.51)	
No	5513(80.74)	971(81.94)	4542(80.49)	
Drinking tea status, n(%)				< 0.001
Yes	3042(44.55)	471(39.75)	2571(45.56)	
No	3786(55.45)	714(60.25)	3072(54.44)	

Note. Means ± standard deviation was shown. Others = other nationalities including Zhuang, Manchu, Hui, Mongolia, Tujia nationalities. Data are shown using % or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.* These variables are presented as median (interquartile range).

Characters	Total n = 6828	Depressed n = 1185(17.4)	Non-depressed n = 5643(82.6)	P value
Anxiety status, n(%)				< 0.001
Yes	1490(21.82)	530(44.73)	960(17.01)	
No	5338(78.18)	655(55.27)	4683(82.99)	
Cognitive score	1.13 ± 1.50	1.64 ± 1.85	1.03 ± 1.39	< 0.001
Cognitive status, n(%)				< 0.001
No cognitive decline	5776(84.59)	871(73.5)	4905(86.92)	
Mild cognitive decline	755(11.06)	207(17.47)	548(9.71)	
Moderate to severe cognitive decline	297(4.35)	107(9.03)	190(3.37)	
Hypertension, n(%)				0.757
Yes	1736(25.42)	306(25.82)	1430(25.34)	
No	5092(74.58)	879(74.18)	4213(74.66)	
Diabetes, n(%)				0.8324
Yes	500(7.32)	89(7.51)	411(7.28)	
No	6328(92.68)	1096(92.49)	5232(92.72)	
Coronary heart disease (CHD), n(%)				0.0114
Yes	276(4.04)	64(5.4)	212(3.76)	
No	6552(95.96)	1121(94.6)	5431(96.24)	
Osteoarthrosis, n(%)				0.0387
Yes	756(11.07)	152(12.83)	604(10.7)	
No	6072(88.93)	1033(87.17)	5039(89.3)	
Tumour, n(%)				0.4499
Yes	49(0.72)	11(0.93)	38(0.67)	
No	6779(99.28)	1174(99.07)	5605(99.33)	
Deafness, n(%)				0.0081

Note. Means ± standard deviation was shown. Others = other nationalities including Zhuang, Manchu, Hui, Mongolia, Tujia nationalities. Data are shown using % or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.* These variables are presented as median (interquartile range).

Characters	Total n = 6828	Depressed n = 1185(17.4)	Non-depressed n = 5643(82.6)	P value
Yes	49(0.72)	16(1.35)	33(0.58)	
No	6779(99.28)	1169(98.65)	5610(99.42)	
Disease comorbidity, n(%)				0.5049
Yes	1560(22.85)	280(23.63)	1280(22.68)	
No	5268(77.15)	905(76.37)	4363(77.32)	

Note. Means ± standard deviation was shown. Others = other nationalities including Zhuang, Manchu, Hui, Mongolia, Tujia nationalities. Data are shown using % or mean (standard deviation). P values were calculated with chi-squared tests and Student's t tests for categorical and continuous variables, respectively.* These variables are presented as median (interquartile range).

Table 2 showed the results of three multiple linear regression analysis in three models. Model 1 was multiple linear regression analysis between depression status and cognitive score. Model 2 was multiple linear regression analysis between depression status and cognitive scores adjusted by PSQI scores. Model 3 was multiple linear regression analysis between PSQI scores and cognitive scores. All the three models adjusted related covariates including gender, age, and ethnic group, life styles (dancing, smoking and drinking tea), chronic diseases (deafness, CHD and osteoarthrosis) and anxiety. In model 1, the results from regression analysis indicated a significant association between cognitive scores ($\beta = 0.251$, 95% CI 0.211 to 0.29, $p < 0.001$) and depression status. Model 2 showed that after adjusted PSQI scores, the association between cognitive scores and depression status was still significant ($\beta = 0.242$, 95% CI 0.203 to 0.281, $p < 0.001$), indicating a partial mediation effect of sleeping quality. While model 3 showed a significant association between cognitive scores ($\beta = 0.101$, 95% CI 0.047 to 0.154, $p < 0.001$) and PSQI scores.

Table 2
Associations between cognitive status and sarcopenia in older adults.

Outcome variable	Model 1: Depressed			Model 2: Depressed			Model 3: PSQI		
	β	P vaule	95% CI	β	P vaule	95% CI	β	P vaule	95% CI
PSQI	–	–	–	0.088	< 0.001	0.071 to 0.106	–	–	–
Cognitive score	0.251	< 0.001	0.211 to 0.29	0.242	< 0.001	0.203 to 0.281	0.101	< 0.001	0.047 to 0.154
Ethnic group: Han	-0.236	< 0.001	-0.353 to -0.119	-0.281	< 0.001	-0.398 to -0.165	0.509	< 0.001	0.349 to 0.669
Gender: Female	-0.094	0.207	-0.241 to 0.052	-0.191	0.011	-0.338 to -0.044	1.094	< 0.001	0.893 to 1.295
Age	-0.002	0.568	-0.009 to 0.005	-0.005	0.195	-0.012 to 0.002	0.029	< 0.001	0.019 to 0.038
Educational: Elementary school	-0.066	0.369	-0.211 to 0.078	-0.066	0.367	-0.21 to 0.078	-0.003	0.975	-0.201 to 0.195
Educational: Middle school	-0.21	0.016	-0.381 to -0.039	-0.193	0.026	-0.363 to -0.023	-0.19	0.111	-0.424 to 0.044
Educational: High school and above	-0.563	< 0.001	-0.761 to -0.364	-0.522	< 0.001	-0.719 to -0.324	-0.463	0.001	-0.735 to -0.19
Occupation: Farmers	0.447	< 0.001	0.312 to 0.581	0.433	< 0.001	0.3 to 0.567	0.152	0.106	-0.032 to 0.336

Note.

Model 1: multiple linear regression analysis between depressed and cognitive score;

Model 2: multiple linear regression analysis between depressed and cognitive score adjusted by PSQI;

Model 3: multiple linear regression analysis between PSQI and cognitive score;

Adjusted by gender, age, and ethnic group, life styles (dancing, smoking and drinking tea), chronic diseases (deafness, CHD, osteoarthrosis) and anxiety.

Outcome variable	Model 1: Depressed			Model 2: Depressed			Model 3: PSQI		
Dancing, Yes	-0.207	0.004	-0.348 to -0.066	-0.182	0.011	-0.322 to -0.042	-0.289	0.003	-0.482 to -0.096
Smoking: Yes	-0.177	0.035	-0.342 to -0.013	-0.203	0.015	-0.367 to -0.04	0.292	0.011	0.067 to 0.518
Drinking tea: Yes	-0.096	0.095	-0.208 to 0.017	-0.101	0.077	-0.213 to 0.011	0.059	0.456	-0.096 to 0.213
Anxiety: Yes	1.828	< 0.001	1.695 to 1.962	1.689	< 0.001	1.554 to 1.824	1.574	< 0.001	1.392 to 1.757
Deafness: Yes	0.561	0.084	-0.076 to 1.197	0.425	0.188	-0.208 to 1.057	1.535	0.001	0.664 to 2.406
CHD: Yes	0.09	0.526	-0.187 to 0.367	-0.043	0.762	-0.319 to 0.234	1.498	< 0.001	1.119 to 1.877
Osteoarthrosis, Yes	-0.074	0.405	-0.249 to 0.101	-0.177	0.047	-0.352 to -0.003	1.167	< 0.001	0.928 to 1.406
Constant	2.309	< 0.001	1.802 to 2.817	2.06	< 0.001	1.554 to 2.566	2.826	< 0.001	2.132 to 3.519
Observations	6828			6828			6828		
R^2	0.1675			0.1796			0.1271		
Adjusted R^2	0.1656			0.1777			0.1251		
Residual standard error	2.249 (df = 6812)			2.233 (df = 6811)			3.077 (df = 6812)		
F Statistic (df; P value)	91.36 (df = (15, 6812);P value < 0.001)			93.22 (df = (16,6811);P value < 0.001)			66.1 (df = (15,6812); P value < 0.001)		
Note.									
Model 1: multiple linear regression analysis between depressed and cognitive score;									
Model 2: multiple linear regression analysis between depressed and cognitive score adjusted by PSQI;									
Model 3: multiple linear regression analysis between PSQI and cognitive score;									
Adjusted by gender, age, and ethnic group, life styles (dancing, smoking and drinking tea), chronic diseases (deafness, CHD, osteoarthrosis) and anxiety.									

Table 3 showed the relative total, direct and indirect effects for the mediating role of sleeping quality on the relationship between cognitive decline and depression in mediation models. Our mediation hypothesis was confirmed because bootstrapping revealed significant relative indirect effects for depression (ACME = 0.0308, 95% CI 0.0231 to 0.04), indicating that sleeping quality mediated the association between cognitive decline and depression. And most of sleeping components also has mediation effect like subjective sleep quality (ACME = 0.0145, 95% CI 0.0092 to 0.02), sleep latency (ACME = 0.0103, 95% CI 0.0061 to 0.02), sleep duration (ACME = 0.0026, 95% CI 0.005 to 0.01), sleep disturbance (ACME = 0.018, 95% CI 0.0123 to 0.02) and daytime dysfunction (ACME = 0.0503, 95% CI 0.0403 to 0.06). Among these components, daytime dysfunction had a highest mediation effect with a proportion of mediation up to 14.56%. And these mediation effects were also shown in Fig. 2.

Table 3
Mediation models: relative total, direct and indirect effects for the mediating role of sleeping quality on the relationship between cognitive decline and depression.

Mediator Variable		β	P-value	95% CI
PSQI	ACME	0.0308	< 0.001	0.0231 to 0.04
	ADE	0.3124	< 0.001	0.2692 to 0.35
	Total Effect	0.3432	< 0.001	0.2976 to 0.39
	Prop. Mediated	0.0885	< 0.001	0.0686 to 0.12
Subjective Sleep Quality	ACME	0.0145	< 0.001	0.0092 to 0.02
	ADE	0.3281	< 0.001	0.2873 to 0.37
	Total Effect	0.3426	< 0.001	0.3025 to 0.39
	Prop. Mediated	0.0419	< 0.001	0.0274 to 0.06
Sleep Latency	ACME	0.0103	< 0.001	0.0061 to 0.02
	ADE	0.3331	< 0.001	0.2913 to 0.37
	Total Effect	0.3435	< 0.001	0.3028 to 0.38
	Prop. Mediated	0.0296	< 0.001	0.0173 to 0.05
Sleep Duration	ACME	0.0026	0.008	0.0005 to 0.01
	ADE	0.3408	< 0.001	0.2964 to 0.38
	Total Effect	0.3433	< 0.001	0.3016 to 0.39
	Prop. Mediated	0.0071	0.008	0.0015 to 0.02
Habitual Sleep Efficiency	ACME	-0.0007	0.68	-0.0039 to 0
	ADE	0.3443	< 0.001	0.2985 to 0.39
	Total Effect	0.3436	< 0.001	0.2974 to 0.39
	Prop. Mediated	-0.0024	0.68	-0.0117 to 0.01
Sleep Disturbance	ACME	0.018	< 0.001	0.0123 to 0.02
	ADE	0.325	< 0.001	0.2803 to 0.37
	Total Effect	0.343	< 0.001	0.297 to 0.39
	Prop. Mediated	0.0518	< 0.001	0.0357 to 0.07

Note. ACME, average causal mediation effects (indirect effect); ADE, average direct effects; Prop. Mediated, the mediator variable explains the percentage of the association between cognitive and depressed.

Mediator Variable		β	P-value	95% CI
Used Sleep Medication	ACME	0.0002	0.91	-0.0033 to 0
	ADE	0.3445	< 0.001	0.3006 to 0.38
	Total Effect	0.3446	< 0.001	0.3015 to 0.38
	Prop. Mediated	0.0006	0.91	-0.0101 to 0.01
Daytime Dysfunction	ACME	0.0503	< 0.001	0.0403 to 0.06
	ADE	0.2924	< 0.001	0.2519 to 0.34
	Total Effect	0.3428	< 0.001	0.3035 to 0.39
	Prop. Mediated	0.1456	< 0.001	0.1162 to 0.18

Note. ACME, average causal mediation effects (indirect effect); ADE, average direct effects; Prop. Mediated, the mediator variable explains the percentage of the association between cognitive and depressed.

We then performed path analysis using the structural equation model (SEM) framework. As shown in Fig. 3, SEM pathway analysis showed that the correlation between cognitive decline and depression was positive (SEM co-efficient: 0.18). 7 components of PSQI assessment were also shown different correlation between cognitive decline and depression. Most correlation was positive, while only the correlation between sleep duration and depression was negative (SEM co-efficient: -0.01) and the correlation between cognitive decline and habitual sleep efficiency was negative (SEM co-efficient: -0.01). These results further confirmed the association between cognitive decline, sleeping quality and depression.

Discussion

The current study evaluated the mediating role of sleeping quality in the relationship between cognitive decline and depression. Several mechanisms have been proposed to explain how sleep quality impacts both cognition and depression. 60 to 70% of people with cognitive impairment or dementia have sleep disturbances. Research has shown that poor sleep quality as measured by the PSQI is associated with multiple markers of metabolic dysfunction, including insulin resistance which is related with bad performance on executive function tasks among older adults[19,20]. Furthermore, several mouse models have demonstrated strong relationships between diet induced insulin resistance and memory dysfunction[21,22]. Besides, good sleep plays a protective role in human emotional homeostasis and regulation[23]. And in depressed individuals, dysregulated sleep was often-reported[24]. As many as 90% of patients with depression will have sleep quality complaints[25]. It was reported that as many as 24–58% of individuals with sleep disordered breathing (eg, obstructive sleep apnea) meet the criteria for depression[26]. And it was found that all the symptoms of depression, sleep problems were the most, prevalent, (13.6%), and those with sleep problems had the highest, relative odds (7.6 times) of developing

a new-onset major depressive episode during the next year compared with those without sleep problems. Thus, sleep disturbance was associated with having more depressive symptoms[27]. Another mechanism through which poor sleep could affect both cognitive function and depression is through oxidative stress. Higher levels of oxidative stress biomarkers were found in patients with bad sleeping quality[28]. In addition, sleep deprivation is related with an increased rate of oxidative pentose phosphate pathway activity[29]. High levels of oxidative stress has also been implicated in depression among older adults[30] as well as those with cognitive decline[31]. Our study demonstrates that bad sleeping quality partially mediates the effects of cognitive decline on depression in older adults. Our results thus contribute to the current knowledge by providing evidence that improving sleeping quality may ameliorate the negative impact of cognitive decline on depression.

Among the 7 components of sleeping assessment, we found that daytime dysfunction had a highest mediation effect with a proportion of mediation up to 14.56%, the following was sleep disturbance which had a mediation effect of 5.18% and subjective sleep quality which had a mediation effect of 4.19%. This was consistent with previous studies. A recent research found that the effects of sleep disturbance, subjective sleep quality and daytime dysfunction scores were most obvious on anxiety in the elderly aged 60 years and older in China, and the ORs (95%CI) were 4.63 (3.55–6.04), 2.75 (2.33–3.23) and 2.50 (2.19–2.86), respectively[32]. An earlier study also found that symptoms of short sleep duration, daytime sleepiness and sleep disturbances are independently related to anxiety while the use of sleep medication is independently associated to depression in a random sample of 2393 individuals aged 65 years or older[33]. Another longitudinal study found that short sleep duration, especially on weekdays, was significantly associated with subsequent depressive (OR = 0.86, 95%CI: 0.80–0.92)[34]. Besides, shorter sleep duration has been found to be associated with a greater rate of ventricular enlargement, which similarly reflects loss of brain volume[35]. And sleep disturbances were studied to be linked to cortical thinning, a marker of cortical atrophy found in many dementia subtypes[36,37]. As we discussed before, numerous studies provide findings indicating the remarkable relationship between sleep alterations and depression. Our study found the most three relevant components (eg. daytime dysfunction, sleep disturbance, subjective sleep quality) mediated the relationship between cognitive decline and depression, which might be the target to focus on improving sleeping quality.

According to the World Health Organization, depression is the leading cause of disability, affecting over 300 million people. Depression is also the commonest mental disorder in older adults worldwide, affecting 7% of the world's older population and accounting for 5.7% of years lived with disability among adults aged over 60 years[38]. For many individuals with depression, the major impairment they experience is cognitive decline[39]. Our study found a high prevalence of depression that was 17.4% and after adjusting numerous confounders, the association between cognitive decline and depression was still significant. This is most likely regulated by several mechanisms. Firstly, depression's duration has a significant impact on left hippocampal volume, indicating that the time since first depressive episode plays an important role in hippocampal degeneration which leading to cognitive decline[40]. And lower

hippocampal volumes are associated with a poorer clinical outcome and more depressive episodes[41]. Secondly, accumulated evidence highlighting the major role of systemic inflammation, which were existed both in cognitive decline and depression[42]. Thirdly, as we discussed before, oxidative stress was a common mechanism in cognitive decline and depression[30,31]. Thus, the relationship between cognitive decline and depression is complex and bidirectional. The ultimate goal of treatment in depression is full functional recovery, and assessing patients for cognitive impairment and selecting treatments that address cognitive dysfunction.

There are several limitations in this study. Firstly, our sampling did not cover all the cities in west China. Secondly, our study design was a cross-sectional study. Thirdly, we conducted a centralized investigation and not a household survey. Furthermore, most of the participants who came to the site of investigation on their own were relatively healthy. This might existed some bias in the analysis. So a critical next step would be to replicate this study with longitudinal data to establish the relationship. In addition, it would be crucial to examine if clinically established sleep interventions are able to prevent or reverse depression in cognitive decline adults.

Conclusions

In conclusion, our study demonstrated that the relationship between cognitive decline and depression was partially mediated by sleeping quality. Therefore, our study suggests that improving sleeping quality in older adults with cognitive decline might counteract the progression of depression.

Abbreviations

WCHAT
West China Health and Aging Trend study; GDS-15:15-item Geriatric Depression Scale; SPMSQ:Short Portable Mental Status Questionnaire; PSQI:Pittsburgh sleep quality index; SEM:structural equation model; SD:standard deviation; ACME:average causal mediation effects (indirect effect); ADE:average direct effects.

Declarations

Availability of Data and Materials

The data-set generated and analyzed during the current study will be available two years later and is also available now from the corresponding author on a reasonable request.

Acknowledgement

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Statement of Ethics

Subjects (or their guardians) have given their written informed consent. The current research was approved by the Ethical Review Committee of West China Hospital with the committee's reference number 2017(445) and the registration number is ChiCTR 1800018895.

Competing Interest

None.

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Authors Contributions

Xiaolei Liu and Xin Xia contributed to conceptualization, data collection, data curation, formal analysis, writing the original draft, and review and editing of the paper. Fengjuan Hu contributed to data collection, data curation, and review and editing of the paper. Qiukui Hao contributed to data collection, data curation. Lisha Hou contributed to data collection, data curation. Xuelian Sun contributed to data collection, data curation. Gongchang Zhang contributed to data collection, data curation. Jirong Yue and Birong Dong contributed to study conceptualization, funding acquisition, investigation, methodology, project administration, supervision, and review and editing of the paper.

Consent for publication

Not Applicable.

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Figures

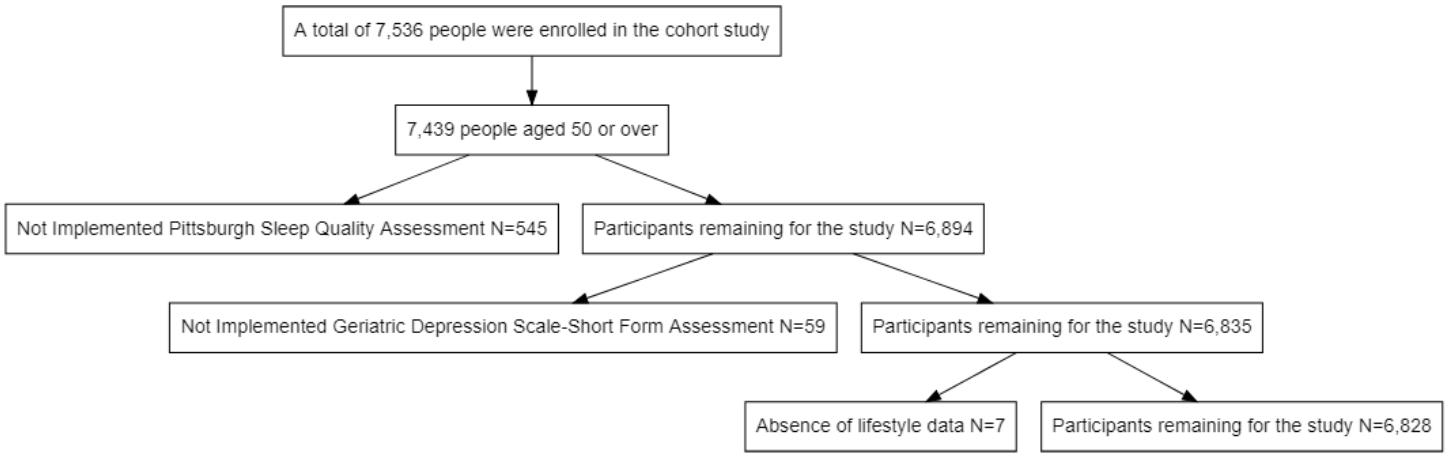

Figure 1

Initially, 7536 participants were enrolled. Then we excluded subjects who were under 50 years old and 97 participants were excluded. Then we kept on excluding 545 subjects without doing sleeping quality assessment. Besides, 59 participants were excluded without doing depression assessment. After that, 7 subjects were excluded without life style data. Therefore, 6828 participants were analyzed in our study (figure 1).

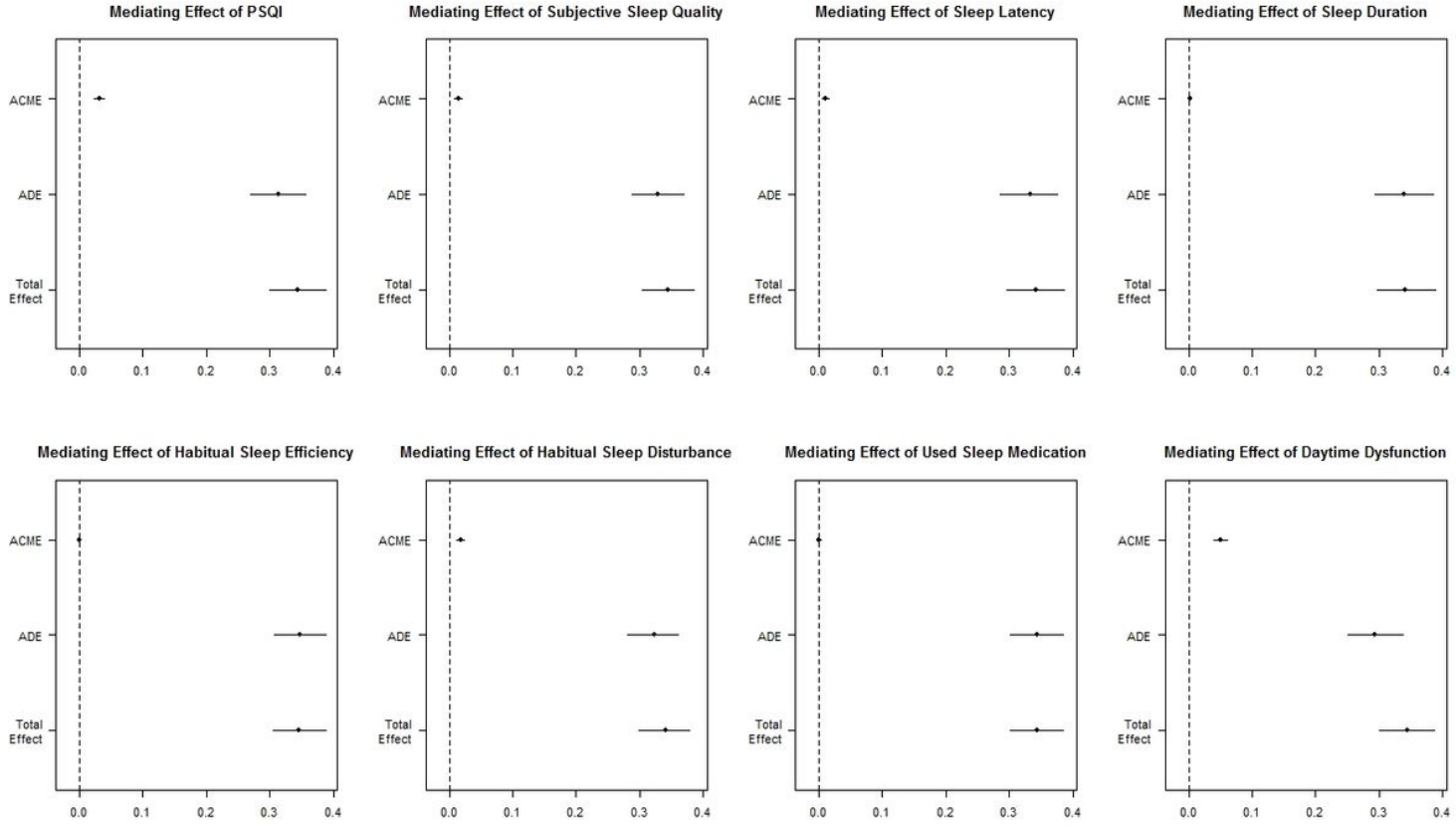

Figure 2

Our mediation hypothesis was confirmed because bootstrapping revealed significant relative indirect effects for depression (ACME = 0.0308, 95% CI 0.0231 to 0.04), indicating that sleeping quality mediated the association between cognitive decline and depression. And most of sleeping components also has mediation effect like subjective sleep quality (ACME = 0.0145, 95% CI 0.0092 to 0.02), sleep latency (ACME = 0.0103, 95% CI 0.0061 to 0.02), sleep duration (ACME = 0.0026, 95% CI 0.005 to 0.01), sleep disturbance (ACME = 0.018, 95% CI 0.0123 to 0.02) and daytime dysfunction (ACME = 0.0503, 95% CI 0.0403 to 0.06). Among these components, daytime dysfunction had a highest mediation effect with a proportion of mediation up to 14.56%. And these mediation effects were also shown in figure 2.

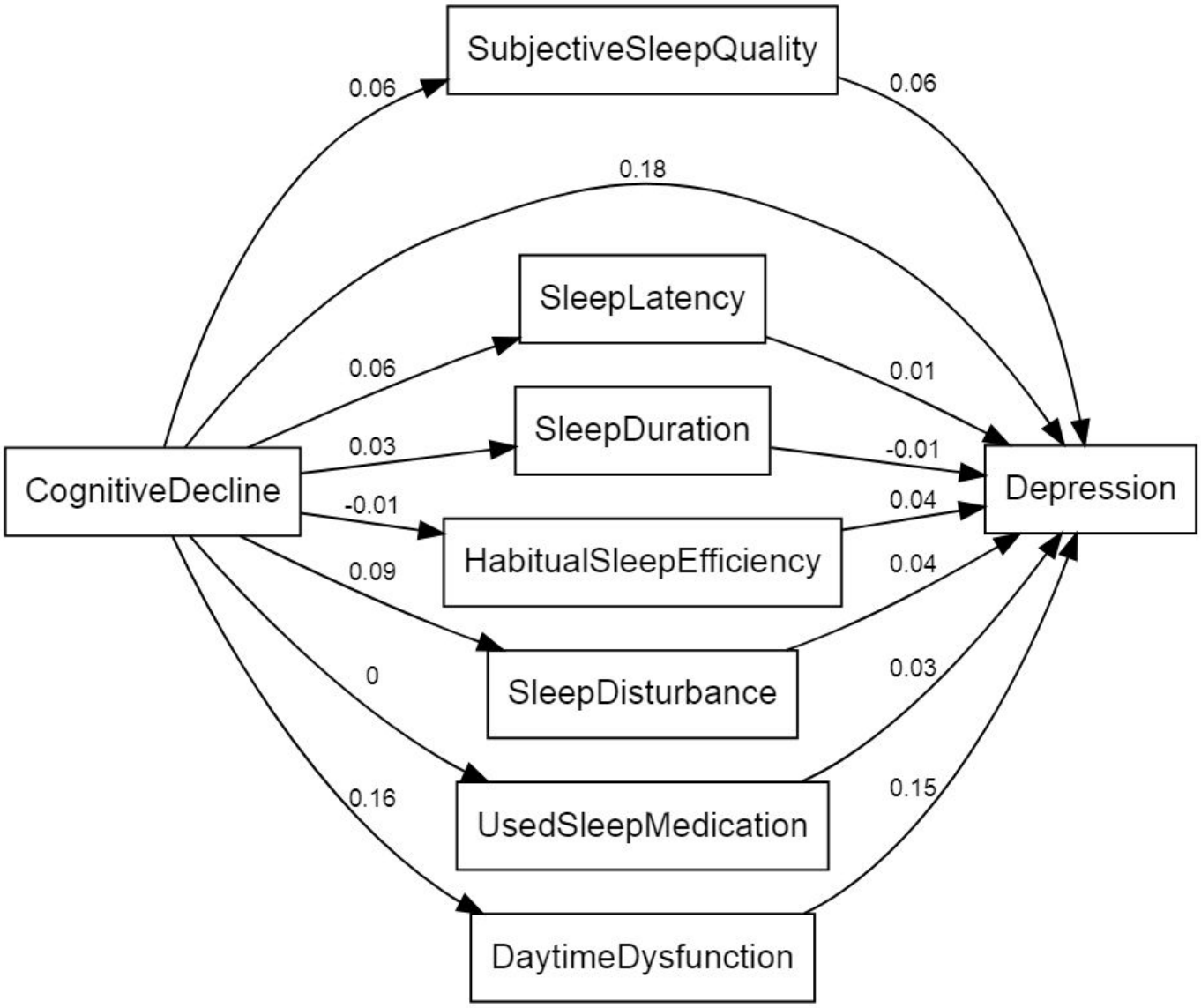

Figure 3

We then performed path analysis using the structural equation model (SEM) framework. As shown in Figure 3, SEM pathway analysis showed that the correlation between cognitive decline and depression was positive (SEM co-efficient: 0.18). 7 components of PSQI assessment were also shown different correlation between cognitive decline and depression.