


Sleep Mediates the Relationship Between Depression and Cognitive Impairment in Older Men

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Abstract

Sleep and depression are strongly associated with cognitive impairment. The role of sleep disturbances in the adverse effect of depression on cognitive dysfunction in older adults remains unclear. This study explored the mediating effect of self-reported sleep disturbances on the relationship between depression and cognitive impairment in older adults according to sex differences. This study derived data from the 2009 Taiwan National Health Interview Survey and included 2,175 community-dwelling adults aged 65 years and older (men = 991; women = 1,184). Sleep disturbances were measured using self-reported survey questions. The Center for Epidemiological Studies Depression scale was used to assess depression. The Mini-Mental State Examination was used to evaluate cognitive impairment. A higher proportion of female older persons had cognitive impairment and depression than male older persons (cognition: 24.4% vs. 11.5%; depression: 17.0% vs. 10.8%). The mediating effect of sleep was detected in only men. Difficulty in initiating sleep was a complete mediator of the adverse effect of depression on cognitive impairment (Sobel test: $p = .03$). In summary, difficulty in initiating sleep may be a crucial, treatable mediator of the adverse effect of depression on cognitive impairment in older men.

Keywords

sleep, depression, cognitive impairment, older people

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With the average life expectancy in the developed world increasing, cognitive impairment has become a major public health problem among older adults, with its prevalence ranging from 11% to 20.8% (Jia et al., 2014; Mariani, Monastero, & Mecocci, 2007). Cognitive impairment has been connected with difficulties in performing daily activities, poor quality of life, increased risk of falling, and high mortality (Mariani et al., 2007; Muir, Gopaul, & Montero Odasso, 2012; Tilvis et al., 2004). To provide older adults with a healthy life and active aging, determining factors that can be controlled to prevent cognitive impairment and its related pathways is of clinical relevance.

Late-life depression has been shown to contribute to the development of subsequent cognitive decline (Dotson, Beydoun, & Zonderman, 2010; Gallagher, Kiss, Lanctot, & Herrmann, 2016). Neuroimaging studies have simultaneously determined progressive brain structural abnormalities in older adults with depressive symptoms caused

by pathogenetic mechanisms, including abnormal proinflammatory cytokine levels and hypercortisolemia (Moon et al., 2017; Morimoto & Alexopoulos, 2013; Sacuiu

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et al., 2016). Furthermore, depression has been recognized as a significant risk factor for sleep disturbances (Fok, Stewart, Besset, Ritchie, & Prince, 2010; Pedraza, Al Snih, Ottenbacher, Markides, & Raji, 2012), which are more likely to occur with increasing age in patients with depression (Stewart et al., 2006). Abnormal neurotransmitter levels (e.g., monoamine dysregulation) and an impaired hypothalamic–pituitary–adrenal axis may be responsible for this causal relationship (Murphy & Peterson, 2015). Accumulating evidence has indicated a strong connection between sleep disturbance and cognitive dysfunction in older adults (Chiu, Lai, Chen, & Tsai, 2016; Diem et al., 2016; Lo, Groeger, Cheng, Dijk, & Chee, 2016). Collectively, sleep disturbance may partially mediate the adverse effect of depression on cognitive dysfunction in older adults. The extent of the contribution of sleep disturbance to depression-related cognitive impairment remains unknown. If sleep disturbance is a considerable mediator of depression-related cognitive impairment in older adults, then sleep management might effectively attenuate this cognitive impairment.

Sex differences have been found to be associated with differences in depression, sleep disturbance, and cognitive impairment; women are more likely to experience more severe depressive symptoms, insomnia symptoms, and cognitive impairment than men (Chiu et al., 2016; Cole & Dendukuri, 2003; Jaussent et al., 2011; Rait et al., 2005). Sex differences should be considered when investigating the mediating effect of sleep disturbance on the relationship between depression and cognitive impairment in older adults.

To fill the gap in the literature, the present study used data from a Taiwanese nationwide health survey and considered sex differences while investigating whether (self-reported) sleep disturbance mediates the relationship between depression and cognitive impairment in older adults. The current study hypothesized that the association between depressive symptoms and cognitive impairment in older adults is affected by sleep disturbances.

Methods

Data Source and Study Sample

This study examined representative data from the 2009 Taiwan National Health Interview Survey, which collected data of residents of Taiwan aged 12 years and older. A multistage stratified systematic sampling scheme was used. A total of 358 townships or districts of Taiwan were divided into 48 strata according to their geographical location and degree of urbanization. Townships or districts in each stratum were selected with a selection probability proportional to the size of the whole population so that the whole sample was nationally representative. Trained

interviewers conducted home interviews. A total of 3,294 people aged 65 years and older completed home interviews. The Mini-Mental State Examination (MMSE) and Center for Epidemiologic Studies Depression (CESD) scale scores were missing for 717 and 2 respondents, respectively. Data on the education level and insomnia subtype were unavailable for nine and one respondents, respectively, resulting in a final sample size of 2,175 for data analysis. This study was approved by the Research Ethics Review Committee of Far Eastern Memorial Hospital (protocol number: 106066-W), and the requirement of informed consent was waived because this study used retrospective secondary data.

Measures

Cognitive impairment. The MMSE is a 30-point cognitive test used to evaluate cognitive functioning, including retention, memory recall, attention, calculation, language, and visuospatial performance (Folstein, Folstein, & McHugh, 1975). The MMSE has been extensively used on older adults, with excellent test–retest reliability (Spearman's coefficient = .98, $p < .001$; Fountoulakis, Tsolaki, Chantzi, & Kazis, 2000). In this study, cognitive impairment was defined as an MMSE score of <24 or <20 for those with >8 or ≤ 8 years of education, respectively (Chiu et al., 2016; Ramos et al., 2013).

Self-reported sleep disturbances. Sleep disturbances, including short sleep duration, difficulty in breathing during sleep, difficulty in initiating sleep (DIS), difficulty in maintaining sleep (DMS), and early morning awakening (EMA), were measured using self-reported survey questions. For example, sleep duration was assessed using the question "How many hours do you usually sleep at night?" A self-reported sleep duration of ≤ 6.5 h was defined as a short sleep duration, with >6.5 h of sleep as the reference (Keage et al., 2012). Difficulty in breathing during sleep was evaluated using the question "Have you struggled to breathe or stopped breathing in your sleep?" (yes/no). DIS, DMS, and EMA were measured using three questions that prompted participants to recollect the occurrence of difficulty in falling asleep, difficulty in falling back asleep once awoken during the night, and difficulty in falling back asleep once awoken too early in the morning in the previous month. Responses to these questions were scored from 1 to 5, with 1 = *never*, 2 = *seldom (less than once per month)*, 3 = *sometimes (2–4 times per month)*, 4 = *usually (5–15 times per month)*, and 5 = *all the time (16–30 times per month)*. High internal consistency was found among our population, with Cronbach's α of .8. The occurrence of insomnia symptoms (DIS, DMS, and EMA) was defined as a score of 3–5 on any of the three questions.

Depressive symptoms. In this study, the 10-item CESD scale was used to measure depression; eight items measure depressive symptom frequency, and two items assess positive affect. A total score of 10 or more reflects clinically relevant symptoms of depression (Andresen, Malmgren, Carter, & Patrick, 1994; Chien & Cheng, 1985). Internal consistency with Cronbach's α and test-retest reliability of .86 and .49, respectively, were reported, and the sensitivity and specificity observed at a cutoff score of 5 were 82% and 70%, respectively, in the older population (Malakouti, Pachana, Naji, Kahani, & Saeedkhani, 2015).

Possible confounders. Several confounders known to be associated with cognitive impairment were identified and divided into three categories: demographic characteristics (i.e., age, education level, marital status, and body mass index [BMI]), lifestyle factors (i.e., alcohol intake, exercise habits, tea intake, tobacco consumption, and coffee consumption), and comorbidities (i.e., history of hypertension, diabetes mellitus [DM], stroke, asthma, osteoporosis, presbyopia, body pain, and hypercholesterolemia; Chiu et al., 2016; Yen, Yang, Shih, & Lung, 2004). BMI was calculated as body weight in kilograms divided by height in meters squared. Exercise habits were evaluated using the survey question "Have you performed any exercise during the past 2 weeks?" (yes/no).

Statistical analysis. All statistical analyses were performed using SPSS, version 18.0 for Windows, and the significance level was set at $p < .05$. The results are presented as proportions for categorical variables and means and standard deviations for continuous variables. The distributions of demographic characteristics, lifestyle factors, comorbidities, CESD scores, and sleep parameters were analyzed using descriptive analyses and frequency distributions according to sex differences. Independent t test and chi-square test were used to examine disparities in demographic characteristics, lifestyle factors, comorbidities, CESD scores, and sleep parameters in respondents with and without cognitive impairment according to sex. Based on criteria proposed by Baron and Kenny (Baron & Kenny, 1986), the mediation effects of self-reported sleep disturbance on the association between depression and cognitive impairment in older men and women were examined. A series of multivariate linear regressions was used to test the associations between depression and cognitive impairment (a path), depression and self-reported sleep disturbance (b path), and self-reported sleep disturbance and cognitive impairment (c path) after controlling for confounders (i.e., age, educational level, marital status, BMI, alcohol intake, exercise habits, tea intake,

tobacco consumption, coffee consumption, hypertension, DM, stroke, asthma, osteoporosis, presbyopia, body pain, and hypercholesterolemia [Chiu et al., 2016; Yen et al., 2004]). After adjustment for self-reported sleep disturbance and confounders (a' path), the direct effect of depression on cognitive impairment was also analyzed. Complete mediation would be observed if the inclusion of self-reported sleep disturbance (mediator variable) reduced the observed association between depression (independent variable) and cognitive impairment (dependent variable) to zero. Partial mediation would occur if the observed relationship between depression (independent variable) and cognitive impairment (dependent variable) became weaker after the inclusion of self-reported sleep disturbance (mediator variable). The Sobel test (MacKinnon, Lockwood, Hoffman, West, & Sheets, 2002) was used to examine whether the indirect and direct effect of depressive symptoms (independent variable) on cognitive impairment (dependent variable) through self-reported sleep disturbance (mediator variable) was significant.

Results

Distributions of Demographic Characteristics, Lifestyle Factors, and Comorbidities in Elderly Adults With and Without Cognitive Impairment According to Sex Differences

Of 2,175 older adult respondents, 991 (45.6%) were men, and 1,184 (54.4%) were women, with average ages of 74.38 (± 6.56) and 73.43 (± 6.12) years, respectively. A total of 114 (12.0%) older men and 289 (24.4%) older women had cognitive impairment. A higher percentage of women ($n = 201$) had depression than men ($n = 107$; 17.0% vs. 10.8%). Women had more sleep complaints than men (Tables 1 and 2).

As presented in Table 1, significant differences were observed in age ($p < .001$), marital status ($p = .001$), BMI ($p = .04$), alcohol intake ($p < .001$), exercise habits ($p = .004$), coffee consumption ($p = .03$), stroke ($p = .03$), and presbyopia ($p = .002$) between older men with and without cognitive impairment. Furthermore, significant differences were observed in age ($p < .001$), educational level ($p < .001$), marital status ($p < .001$), exercise habits ($p = .001$), tea intake ($p = .02$), coffee consumption ($p < .001$), tobacco consumption ($p = .01$), DM ($p = .002$), hyperlipidemia ($p < .001$), stroke ($p = .002$), osteoporosis ($p = .001$), and presbyopia ($p < .001$) between older women with and without cognitive impairment. Variables that were different between the groups were entered into statistical models as confounders for further adjustment.

Table 1. Distribution of Demographic Characteristics, Lifestyle Factors, and Comorbidities in Respondents With and Without Cognitive Impairment According to Sex.

Characteristic	Male (n = 991)						Female (n = 1,184)						
	Total		Cognitive impairment (n = 114)		No cognitive impairment (n = 877)		Total		Cognitive impairment (n = 289)		No cognitive impairment (n = 895)		
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	p
<i>Demographic characteristics</i>													
Age, mean (SD)	74.38	(6.56)	77.94	(7.13)	73.67	(6.21)	73.43	(6.12)	75.94	(6.78)	72.26	(5.41)	<.001
Education levels >8 years	345	(34.8)	34	(29.8)	311	(35.5)	169	(14.3)	11	(3.8)	158	(17.7)	<.001
Married	790	(78.3)	78	(68.4)	712	(81.2)	638	(53.9)	130	(45.0)	508	(56.8)	.001
Body mass index, mean (SD)	23.71	(3.08)	23.71	(3.07)	23.87	(3.13)	24.43	(3.54)	24.45	(3.47)	24.43	(3.55)	.98
<i>Lifestyle factors</i>													
Alcohol intake	603	(60.8)	47	(41.2)	556	(63.4)	226	(19.1)	46	(15.9)	180	(20.1)	.12
Exercise habits	550	(55.5)	49	(43.0)	501	(57.1)	603	(50.9)	102	(35.3)	501	(56.0)	.001
Tea	487	(49.1)	47	(41.2)	440	(50.2)	350	(29.6)	69	(23.9)	281	(31.4)	.02
Coffee	102	(10.3)	5	(4.4)	97	(11.1)	106	(9.0)	10	(3.5)	96	(10.7)	<.001
Tobacco consumption	261	(26.3)	76	(66.7)	550	(62.7)	54	(4.6)	21	(7.3)	33	(3.7)	.01
<i>Comorbidities</i>													
Hypertension	458	(46.2)	47	(41.2)	411	(46.9)	624	(5.41)	160	(55.4)	464	(51.8)	.30
Diabetes mellitus	165	(16.6)	20	(17.5)	145	(16.5)	244	(20.6)	78	(27.0)	166	(18.5)	.002
Hyperlipidemia	205	(36.3)	16	(14.0)	189	(21.6)	360	(30.4)	63	(21.8)	297	(33.2)	<.001
Stroke	59	(51.8)	12	(10.5)	47	(5.4)	55	(4.6)	23	(8.0)	32	(3.6)	.002
Asthma	59	(6.0)	7	(6.1)	52	(5.9)	49	(4.1)	11	(3.8)	38	(4.2)	.74
Osteoporosis	150	(15.1)	18	(15.8)	132	(15.1)	423	(35.7)	79	(27.3)	344	(38.4)	.001
Presbyopia	695	(70.1)	66	(57.9)	629	(71.7)	803	(67.8)	168	(58.1)	635	(70.9)	<.001
Body pain	260	(26.2)	33	(28.9)	227	(25.9)	530	(44.8)	150	(51.9)	380	(42.5)	.005

Note. Chi-square test for categorical data to test the disparities between older adults with and without cognitive impairment.

Table 2. Distribution of Depressive Symptom and Self-Reported Sleep Disturbances in Respondents With and Without Cognitive Impairment According to Sex.

Characteristic	Male (n = 991)						Female (n = 1,184)							
	Total		Cognitive impairment (n = 114)		No cognitive impairment (n = 877)		Total		Cognitive impairment (n = 289)		No cognitive impairment (n = 895)			
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	p	
Depression (CES-D \geq 10)	107	(10.8)	24	(21.1)	83	(9.5)	<.001	201	(17.0)	72	(24.9)	129	(14.4)	<.001
Difficulty initiate sleep	290	(29.3)	44	(38.6)	246	(28.1)	.02	593	(50.1)	159	(51.6)	444	(49.6)	.57
Difficulty maintain sleep	303	(30.6)	40	(35.1)	263	(30.0)	.23	596	(50.3)	172	(59.5)	424	(47.4)	<.001
Early-morning awake	304	(30.7)	43	(37.7)	261	(29.8)	.08	570	(48.1)	159	(55.0)	411	(45.9)	.007
Sleep duration \leq 6.5	542	(54.7)	54	(47.4)	488	(55.6)	.10	711	(60.1)	154	(53.3)	557	(62.2)	.007
Difficulty breathing during sleep	89	(9.0)	20	(17.5)	69	(7.9)	.001	127	(10.7)	34	(11.8)	93	(10.4)	.51

Note. Chi-square test for categorical data to test the disparities between older adults with and without cognitive impairment. CES-D = Center for Epidemiologic Studies Depression Scale.

Association of Depression With Self-Reported Sleep Disturbance and Cognitive Impairment in Older Adults According to Sex Differences

A considerably higher percentage of older men with depression had cognitive impairment (22.4% [$n = 22$] vs. 10.2% [$n = 90$]), DIS (65.4% [$n = 70$] vs. 24.9% [$n = 220$]), DMS (64.5% [$n = 69$] vs. 26.5% [$n = 234$]), EMA (60.7% [$n = 65$] vs. 27.0% [$n = 239$]), and difficulty breathing during sleep (15.0% [$n = 16$] vs. 8.3% [$n = 73$]) than did those without depression (all $p < .05$, Table 3). A considerably higher percentage of older women with depression had cognitive impairment (35.8% [$n = 72$] vs. 22.1% [$n = 217$]), DIS (79.1% [$n = 159$] vs. 44.2% [$n = 434$]), DMS (82.6% [$n = 166$] vs. 43.7% [$n = 430$]), EMA (82.1% [$n = 165$] vs. 41.2% [$n = 405$]), and difficulty breathing during sleep (15.9% [$n = 32$] vs. 9.7% [$n = 95$]) than did those without depression (all $p < .05$, Table 3).

Mediating Effects of Self-Reported Sleep Disturbance on the Relationship Between Depression and Cognitive Impairment in Older Adults According to Sex Differences

Because depression was not significantly associated with cognitive impairment in the whole sample or older women (the first step, a path), the mediating effect of self-reported sleep disturbance on the association between depression and cognitive impairment in older adults was evaluated in only men. Only DIS was found to fit in the mediation model after adjustment for confounders (Figure 1). In step 1, depression was associated with a higher risk of cognitive impairment (adjusted odds ratio [aOR] = 1.98, 95% CI [1.14, 3.45]). In step 2, depressive symptoms was correlated with DIS (aOR = 5.82, 95% CI [3.72, 9.11]). In step 3, DIS was associated with a higher risk of cognitive impairment (aOR = 1.62, 95% CI [1.05, 2.50]). The relationship between depressive symptoms and cognitive impairment was completely mediated by DIS (aOR = 2.11, 95% CI [1.01, 4.39]) when the adverse effect of depression on cognitive impairment decreased to zero (aOR = 0.09, 95% CI [0.91, 3.02]). The Sobel test revealed that the model adequately fit the data and that DIS was a significant complete mediator of the association of depressive symptoms with cognitive impairment ($p = .03$).

Discussion

In this population-based cross-sectional study, older women had an approximately two-fold prevalence of cognitive impairment and depression than did men (cognition: 24.4% vs. 11.5% and depression: 17.0% vs. 10.8%).

These findings are consistent with those for Western and Asian populations (Jia et al., 2014; Mariani et al., 2007; Yen et al., 2004). The respondents' socioeconomic status (i.e., educational level) might explain this relationship because only 3.8% of women with cognitive impairment had more than 8 years of education; this proportion was much lower than the proportion of men with this education level (29.8%). Because this study did not determine the mechanism underlying the relationship between sex differences and cognitive impairment, future research is required to explore this issue.

In this study, older adults with depressive symptoms had more complaints of cognitive impairment than did those without depressive symptoms. One possible mechanism is that depression may be a psychological response to decreased self-awareness, interfere with daily functioning, and result in an inability to expend greater effort on tasks; thus, this poor performance may be perceived as cognitive impairment (Austin, Mitchell, & Goodwin, 2001). Regarding the physiological mechanism, hippocampal volume has been linked to verbal and spatial memory function. Depression might dysregulate the hypothalamic–pituitary–adrenal axis and thus cause prolonged hypercortisolemia, resulting in hippocampal atrophy and impairment in verbal and spatial memory functions (Butters et al., 2008; Saito et al., 2016).

The findings of the current study revealed that self-reported sleep disturbance was correlated to cognitive impairment in both male and female older adults. The peptide β -amyloid has been associated with neurodegenerative diseases, causing learning and memory impairment (Xie et al., 2013). An *in vivo* mouse study discovered that β -amyloid clearance occurred through the lymphatic system of the brain. That study further revealed that the interstitial space increased during sleep, resulted in a striking increase in the convective exchange of cerebrospinal fluid with interstitial fluid, and eventually elevated the rate of β -amyloid clearance during sleep (Mander et al., 2015). Collectively, sleep deprivation reduces the convective exchange of cerebrospinal fluid with interstitial fluid and reduces the rate of β -amyloid clearance, which is correlated with cognitive impairment.

DIS was found to be a complete mediator of the relationship between depressive symptoms and cognitive impairment in men. Testosterone plays a critical role in mediating the relationship between sleep and cognitive impairment. Testosterone increases nerve growth factor levels in the hippocampus, which is known to maintain forebrain neurons and regulate neurobehavioral functions, including memory and learning functions (Tirassa et al., 1997). Testosterone can reduce the secretion of β -amyloid peptides from primary cerebrocortical neurons, as reported in an animal study (Gouras et al., 2000). Sleep deprivation may lead to reductions in the circulating

Table 3. Distribution of Self-Reported Sleep Disturbances in Respondents With and Without Depressive Symptom According to Sex.

Characteristic	Male (n = 991)				Female (n = 1,184)						
	CES-D ≥ 10 (n = 107)		CES-D < 10 (n = 884)		Total		CES-D ≥ 10 (n = 201)		CES-D < 10 (n = 983)		
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
Cognitive impairment	114	(11.5)	24	(2.4)	90	(10.2)	289	(24.4)	217	(22.1)	<.001
Difficulty initiate sleep	290	(29.3)	70	(6.4)	220	(24.9)	593	(50.1)	434	(44.2)	<.001
Difficulty maintain sleep	303	(30.6)	69	(6.5)	234	(26.5)	596	(50.3)	430	(43.7)	<.001
Early-morning awake	304	(30.7)	65	(6.0)	239	(27.0)	570	(48.1)	405	(41.2)	<.001
Sleep duration ≤ 6.5	542	(54.7)	61	(5.7)	481	(54.4)	711	(60.1)	579	(58.9)	.074
Difficulty breathing during sleep	89	(9.0)	16	(1.5)	73	(8.3)	127	(10.7)	95	(9.7)	.009

Note. Chi-square test for categorical data to test the disparities between older adults with and without cognitive impairment.
CES-D = Center for Epidemiologic Studies Depression Scale.

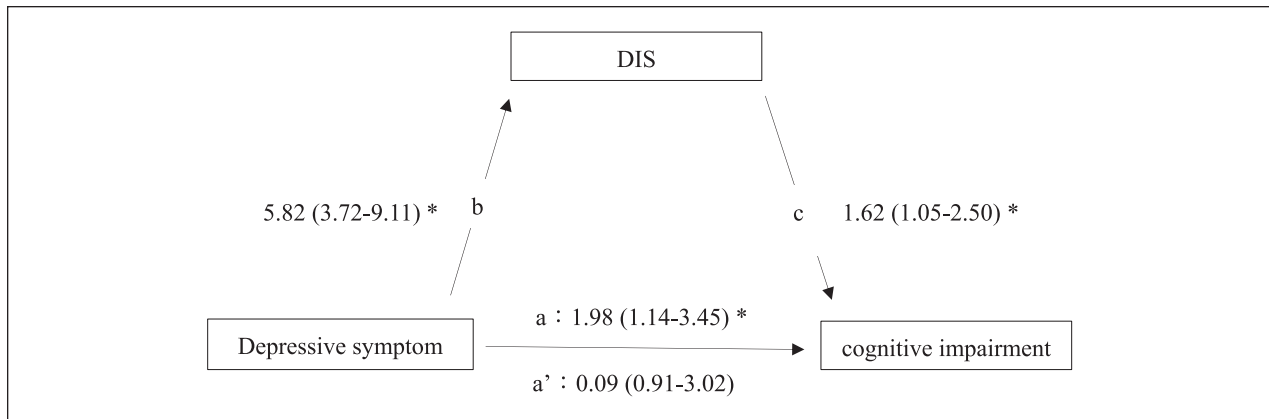


Figure 1. Mediating effect of difficulty in initiating sleep on relationship between depressive symptom and cognitive impairment in elderly men ($n = 991$).

Note. Models for mediation effect were adjusted for DIS, DMS, EMA, DIB during sleep, age, marital status, body mass index, alcohol intake, exercise habit, coffee, stroke, and presbyopia. DIS = difficulty in initiating sleep. DMS = difficulty in maintaining sleep. EMA = early morning awaking. DIB = difficulty in breathing. Data were presented by odds ratio with 95% confidence interval.

levels of testosterone (Wu et al., 2011). The current study did not find particular evidence to explain why DIS could completely mediate the relationship between depressive symptoms and cognitive impairment. Further investigation is warranted.

In this study, no significant correlation was observed between depression and cognitive impairment in older women when a potential confounder, tobacco consumption, was entered into the analyzed model. Coincidentally, previous studies have suggested that tobacco consumption plays a crucial role in the development of cognitive impairment in older adults (Chen et al., 2013; Ferri et al., 2011). Furthermore, the current study reported that older women with cognitive impairment consumed more tobacco than did those without cognitive impairment (7.3% [$n = 21$] vs. 3.7% [$n = 33$], $p = .01$). Future research is required to explore this topic according to sex differences.

The present study has several limitations. First, because this was a cross-sectional study, the causal relationships between insomnia symptoms, depressive symptoms, and cognitive functional status could not be determined. Second, the use of self-reported sleep disturbance might contribute to record bias. The study finding should therefore be interpreted with caution.

In conclusion, the current study suggests that DIS is a complete mediator of the association of late-life depression with cognitive impairment in men aged 65 years and older. Therefore, sleep disturbance likely plays a critical role in the adverse effect of depression on the development of cognitive impairment in older men. The findings of the current study suggest that when targeting depressive symptoms to alleviate cognitive impairment, interventions should focus on managing sleep disturbances in the older population, particularly in men.

Author Contributions

Study concept and design: Dr. HYC, Miss CRW, and Dr. PYC. Acquisition of patients and data: Dr. PYC. Analysis and interpretation of data: Miss CRW, Dr. HYC, Dr. PYC, Dr. HCH, and Dr. YTC. Preparation of manuscript: Miss CRW, Dr. HYC, Mrs. SHH, and Miss TJC.

Impact Statement

We certify that this work is novel. This study suggests that difficulty in initiating sleep is a treatable mediator of the adverse effect of depression on cognitive impairment in male older adults.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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