

# Sleep quality of spousal caregivers is associated with neuropsychiatric symptoms and living ability of patients with Alzheimer disease

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*To the Editor:* Alzheimer disease (AD) is the most common neurodegenerative disorder, accounting for the majority of cases of dementia. The global prevalence of AD is rising, representing an increasing challenge for older individuals and their families.<sup>[1]</sup> Seven out of every ten patients with AD receive informal care at home, relying on co-resident family members, especially spouses.<sup>[2]</sup> However, cultural differences exist in the effects of the disorder. For example, Chinese caregivers of patients with dementia had higher scores on measures of depression and caregiver burden compared with caregivers of patients with dementia in Western societies.<sup>[3]</sup> It is important to consider that AD not only affects the patient but also their caregivers, particularly spousal caregivers who spend more than half their time with the patient.<sup>[4]</sup> As AD progresses, patients become increasingly dependent on caregivers. Meanwhile, there is an increasingly heavy caregiver burden, characterized as the physical, psychological, or emotional, social, and financial problems experienced by family members who care for impaired older adults.<sup>[5]</sup> Additionally, it is frequently reported that sleep disturbance symptoms are associated with health consequences among AD caregivers.<sup>[6]</sup>

It is reported that approximately a third of patients with AD complain of sleep problems, while approximately two-thirds of AD caregivers have trouble sleeping.<sup>[7]</sup> However, little is known about the features of sleep disorder in AD spousal caregivers, as well as the relationship between neuropsychiatric problems of patients with AD and sleep quality of their spousal caregivers. Given the patterns of the main sleep disturbances experienced by patients with AD, we examined features of sleep disturbance in AD caregivers. We also aimed to further explore whether functional abilities and psychiatric symptoms of patients with AD were significantly linked to caregivers' sleep quality.

We recruited 98 patients clinically diagnosed with probable AD, and their spousal caregivers. We also

recruited 75 age-, sex-, and education-matched cognitively healthy non-caregiving controls. The study was conducted at the Memory Clinic of the Neurology Unit, First Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China. Trained neurologist and neuropsychological evaluators conducted the diagnosis. All participants had to complete all neuropsychological questionnaires and scales with two blinded evaluators. The inclusion criteria for patients with AD were: (1) Diagnostic and Statistical Manual of Mental Disorders—Fourth Edition (DSM-IV) diagnosis of probable AD conforming to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria<sup>[8]</sup>; (2) a decline in cognitive and physical function for more than 2 years, and need for a caregiver for over 6 months; (3) completion of all clinical assessments, including the Mini-Mental State Examination (MMSE),<sup>[9]</sup> Clinical Dementia Rating ( $\geq 1$ ), activities of daily living (ADL) assessment ( $\geq 25$ ); and (4) exclusion of vascular dementia or other types of dementia caused by systemic diseases with neuroimaging. Exclusion criteria included: (1) severe malnourishment, infection, indwelling catheter, constipation, or pain; (2) presence of alcohol or drug abuse, or other diseases potentially related to sleep disturbance; and (3) a diagnosis of schizophrenia, schizoaffective disorder, or primary affective disorder, and severe primary diseases of the heart, brain, liver, kidney, and hematopoietic system.

Spousal caregivers that were willing to take part in the study were included where they: (1) were the main caregivers of the patient with AD; (2) had taken care of the patient with AD for at least 6 months at home; and (3) were informal or professional caregivers. We excluded caregivers if they had: (1) a history of primary sleep disturbance or sleep problems before caregiving; (2) diagnosis of a mental disorder or primary affective disorder before caregiving; (3) alcohol dependence or a history of drug

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**Table 1: Demographics and neuropsychiatric tests in patients with AD, spousal caregivers, and controls.**

Characteristics	AD patients (n = 98)	Spousal caregivers (n = 98)	Non-caregiving controls (n = 75)	P value
Age (years)	75.0 ± 5.1	74.7 ± 4.9	76.1 ± 4.1	0.143
Sex ratio (male/female)	57/41	41/57	36/39	0.379
Education level (years)	7.5 ± 2.6	7.7 ± 2.4	8.0 ± 2.7	0.454
Hypertension	51/98 (52.0)	47/98 (48.0)	36/75 (48.0)	0.813
Diabetes	22/98 (22.4)	18/98 (18.4)	17/75 (22.7)	0.720
Hyperlipidemia	49/98 (50.0)	46/98 (46.9)	39/75 (52.0)	0.797
Smoking	27/98 (27.6)	31/98 (31.6)	21/75 (28.0)	0.794
Drinking (>100 mL/day)	11/78 (19.4)	15/98 (15.3)	20/75 (26.7)	0.082
Symptomatic treatment	95/98 (96.9)	NA	NA	/
PSQI score	15.0 ± 4.1	11.0 ± 2.1	7.1 ± 2.7	<0.010
MMSE score	10.6 ± 2.7	25.5 ± 3.0	25.9 ± 2.1	<0.010
NPI score	16.4 ± 4.2	ND	ND	/
BADL score	11.6 ± 2.4	ND	ND	/
IADL score	21.3 ± 3.3	ND	ND	/
HAMA score	17.8 ± 4.6	18.9 ± 3.2	8.5 ± 3.9	<0.010
HAMD score	23.1 ± 5.7	16.1 ± 3.9	6.5 ± 4.3	<0.010

The data are shown as mean ± standard deviation, n/N (%), or n. AD: Alzheimer disease; BADL: Basic activities of daily living; HAMA: Hamilton anxiety scale; HAMD: Hamilton depression scale; IADL: Instrumental activities of daily living; MMSE: Mini-Mental State Examination; NA: Not available; ND: Not detect; NPI: Neuropsychiatric inventory; PSQI: Pittsburgh sleep quality index.

abuse that may impact sleep quality; (4) chronic active diseases of the heart, brain, liver, kidney, and hematopoietic system. Healthy controls that were willing to take part in the study were not taking care of patients with dementia. Moreover, all subjects enrolled have a family income of at least RMB 5000 yuan monthly to maintain a normal livelihood.

All participants were required to undergo a detailed clinical history interview and neurological examination. Participants were screened with neuropsychological scales including the MMSE, Hamilton Depression Scale (HAMD), Hamilton Anxiety Scale (HAMA), Neuropsychiatric Inventory (NPI), ADL assessment and Pittsburgh Sleep Quality Index (PSQI). The study was approved by the Ethics Committee of First Affiliated Hospital of Zhejiang University on Human Clinical Research.

We express values as mean ± standard deviation (SD) for quantitative data. One-way analysis of variance (ANOVA) and Tukey test or Games-Howell test were used for pairwise comparison. Quantitative data were assessed with Pearson Chi-Squared test and the Bonferroni method. Correlation among ADL, NPI scores, and PSQI scores was tested using Spearman correlation analysis. All data were analyzed using SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA). A *P* value <0.05 was seen as significant.

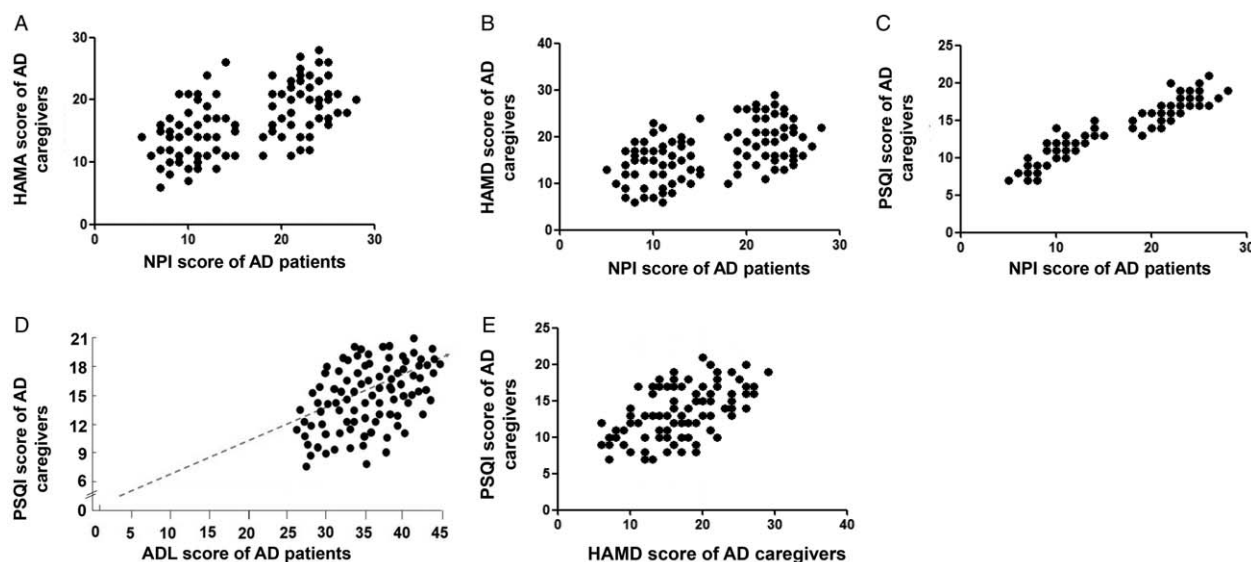
Table 1 presents demographic characteristics and the prevalence of risk factors (hypertension, diabetes, hyperlipidemia, smoking, and drinking) in 98 patients, 98 spousal caregivers, and 75 healthy non-caregiving controls. We did not observe any statistically significant differences between the three groups in age, sex ratio, education levels, and vascular risk factors proportion. However, compared with non-caregiving controls, caregivers had a significantly increased severity of sleep disturbance (PSQI: 11.0 ± 2.1 *vs.* 7.1 ± 2.7, *P* < 0.010), and increased severity of anxiety (HAMA: 18.9 ± 3.2 *vs.* 8.5 ± 3.9, *P* < 0.010) and depression (HAMD: 16.1

± 3.9 *vs.* 6.5 ± 4.3, *P* < 0.010), but similar cognitive levels (MMSE: 25.5 ± 3.0 *vs.* 25.9 ± 2.1, *P* > 0.050). As for the sleep quality in patients with AD and their spousal caregivers, there was a significant difference of PSQI score between two groups (15.0 ± 4.1 *vs.* 11.0 ± 2.1, *P* < 0.010).

The caregivers and non-caregiving controls had significantly different scores for the seven items of the PSQI, including sleep quality, time to fall asleep, sleep duration, sleep efficiency, sleep interruption, sleep drugs, and daytime sleep. Caregivers had higher scores on these items than did controls, indicating that caregivers are more troubled by sleep problems than non-caregiving controls.

There was a statistically positive correlation between the HAMA score (*r* = 0.54, *P* < 0.010), HAMD score (*r* = 0.47, *P* < 0.010), PSQI score of spousal caregivers and NPI scores of patients with AD (*r* = 0.95, *P* < 0.010), indicating higher NPI scores in patients with AD were accompanied by higher PSQI and HAMA, HAMD scores in their caregivers [Figure 1A–1C]. We also observed a positive correlation between PSQI scores of AD caregivers and ADL scores of patients (*r* = 0.61, *P* < 0.010) [Figure 1D]. This suggests that sleep quality scores of caregivers increase as the ADL scores of patients increased. There was also a positive correlation between caregivers' HAMD and PSQI scores (*r* = 0.52, *P* < 0.010) [Figure 1E], indicating that caregivers' PSQI scores increase as HAMD scores increase.

In this study, we demonstrate the caregivers' sleep problems were more severe than that of non-caregiving controls. More severe psychiatric symptoms in patients with AD were associated with a worse degree of depression and anxiety in their caregivers. Consistently, higher ADL scores in patients were associated with higher PSQI scores in caregivers. Moreover, the severity of psychiatric symptoms in patients with AD was positively correlated with sleep quality of caregivers.



**Figure 1:** The correlation of neuropsychological assessment scores between spousal caregivers and patients with AD. (A) The HAMA score of spousal caregivers is positively correlated with NPI score of patients with AD. (B) The HAMD score of spousal caregivers is positively correlated with NPI score of patients with AD. (C) The PSQI score of spousal caregivers is positively correlated with NPI score of patients with AD. (D) The PSQI score of spousal caregivers is positively correlated with ADL score of patients with AD. (E) The HAMD score is positively correlated with PSQI score in spousal caregivers. Using the Spearman correlation test with the significant difference of  $P < 0.05$ . AD: Alzheimer disease; ADL: Activities of daily living; HAMA: Hamilton anxiety scale; HAMD: Hamilton depression scale; NPI: Neuropsychiatric inventory; PSQI: Pittsburgh sleep quality index.

It has been reported that spousal caregivers are at particularly high risk of sleep disturbances, which are associated with adverse health consequences.<sup>[10]</sup> Our results suggest that caregivers have significantly higher sleep quality scores than non-caregiving controls. Clearly, nighttime wakening in patients with AD will precipitately impact on a caregiver's sleep.<sup>[11]</sup> Among patients with dementia, studies have suggested that severe cognitive impairment, poorer physical function, sleep disturbance symptoms, and higher NPI psychosis are associated with sleeping difficulties in caregivers.<sup>[5,12]</sup> In the early study that using Chinese population, the authors found that the poorer physical condition, lower life satisfaction, and a higher degree of depression and anxiety were associated with a higher caregiver burden.<sup>[3]</sup> However, we enrolled only the spousal caregivers and we paid more attention on the factors in patients with AD that may influence the sleep quality of their caregivers. We also analyzed the characteristic of sleep disorder in spousal caregivers. Our findings support the existence of a positive correlation between physical function of patients and sleep quality of spousal caregivers, which indicate that poorer physical function of patients is related with sleep problems. For caregivers, higher NPI and distress scores of patients are suggested to be linked to more frequent sleep disturbances among spousal caregivers in our study and caregivers in others.<sup>[10,13,14]</sup> Notably, depression in caregivers is a subjective risk factor for sleep problems, and AD caregivers vary in the degree of sleep disturbance they experience, which besides the above-mentioned factors.

Furthermore, we observed a direct correlation between neuropsychiatric symptoms of patients with AD and spousal caregiver anxiety/depression. Both depression and anxiety in caregivers are reported to precipitate caregiver sleep disturbances, even when patient factors were reduced

or eliminated.<sup>[15]</sup> This is consistent with our results showing that caregiver depression was associated with caregiver sleep quality, and that higher PSQI scores are associated with higher HAMD scores. And as suggested, the model proposed by Moore *et al*,<sup>[6]</sup> could be used to identifying the sleep quality of AD caregivers.

In fact, the burden of long-term care has been implicated as a vital mediator for caregiver sleep problems, and depression and anxiety are strongly related to caregiver burden. Moreover, there is a well-established relationship between depression and insomnia. Though similar relationship was also found in another study,<sup>[16]</sup> the authors did not observe the sleep quality of patients with AD as well as whether neuropsychiatric symptoms in the patients was an influencing factor of sleep disorder in their caregivers.

Actually, the problems incorporate multiple aspects of caregiver life, including health concerns and various underlying impairments, and they indicate that attention and intervention are necessary for AD caregivers as well as patients with AD. Within informal caregiving situations, seeking professional support should be a key part of care.<sup>[3]</sup> Behavioral interventions targeting on leisure time may benefit for improving sleep outcomes and depressive symptoms.<sup>[6]</sup> In line with this, the authors applied a longitudinal design and found that elevated levels of positive affect are positively associated with better subjective sleep in AD caregivers.<sup>[17]</sup> Therefore, spousal caregivers may hire in-home care, and take care of their own health issues and stay emotionally healthy. Only with a good health including mental health and good sleep, spousal caregivers could give much more help on patients with AD to slow down the progress of disease.

This study is subject to some limitations. First, the sample comprises heterosexual spousal caregivers, which limits the generalizability of our results. Second, the small sample size may have led to different results to previous studies. Third, the dynamic data of sleep quality and neuropsychiatric scale assessments are lacking. Therefore, these factors and their relationships should be investigated in larger samples with a longitudinal observation are necessary in the future study.

In summary, sleep disturbance is common among informal spousal caregivers and is associated with patients' mental and physical function, as well as caregiver anxiety and depression. Given the increasing numbers of people with AD both in mainland China and worldwide, it is crucial to prevent and provide effective interventions for sleep problems, depression, and anxiety in caregivers. Therefore, the interventions and preventative measures to improve mental and physical function in patients will also benefit vulnerable caregivers for their sleep quality.

### Declaration of patient consent

The authors certify that they have obtained informed consent from all participants or their assigned surrogate decision makers. In the form the subjects have given their consent for their images and other clinical information to be reported in the journal. They understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

None.

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