A Change in Sleep Pattern May Predict Alzheimer Disease

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Objective: *Sleep problems may adversely affect neuronal health. We examined a subjective report of change (reduced duration and/or depth) in sleep pattern in relation to subsequent risk of incident all-cause dementia and Alzheimer disease (AD) over 9 years.* **Methods:** *This longitudinal study used data from a population-based sample of 214 Swedish adults aged 75 and over who were dementia-free both at baseline and at first follow-up (3 years later). The sample was 80% female and, on average, 83.4 years of age at baseline. All participants underwent a thorough clinical examination to ascertain all-cause dementia and AD.* **Results:** *Forty percent of participants reported a change in sleep duration at baseline. Between the 6th and 9th year after baseline, 28.5% were diagnosed with all-cause dementia, 22.0% of whom had AD. Reduced sleep was associated with a 75% increased all-cause dementia risk (hazard ratio: 1.75; 95% confidence interval: 1.04−2.93; Wald = 4.55, df = 1, p = 0.035) and double the risk of AD (hazard ratio: 2.01; 95% confidence interval: 1.12−3.61; Wald = 5.47, df = 1, p = 0.019) after adjusting for age, gender, and education. The results remained after adjusting for lifestyle and vascular factors but not after adjusting for depressive symptoms. No evidence supported a moderating effect of the use of sleeping pills, and the sleep−dementia relationship remained after controlling for the presence of the apolipoprotein E ε4 allele.* **Conclusion:** *Self-reported sleep problems may increase the risk for dementia, and depressive symptoms may explain this relationship. Future research should determine whether treatment, in particular, behavioral or nonpharmacologic treatment, may represent one avenue toward reduction of dementia risk in late life.* (Am J Geriatr Psychiatry 2013; ■:■−■)

Key Words: Sleep disturbances, dementia, older adults, longitudinal

INTRODUCTION

Approximately 50% of older adults report problems regarding their sleep,[1] and sleep problems may be particularly common in a variety of clinical health settings older adults may be more likely to encounter, including hospice[2] and assisted living facilities.[3] Sleep problems are likely to increase with age[4−6]

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and may adversely affect overall well-being.[7] Two separate cross-sectional studies found that self-reported sleep quality was associated with poorer cognitive performance[8] and that reporting reduction in sleep duration may be associated with poorer global cognitive status.[9] A change in sleep pattern (shorter or greater sleep duration) was also associated with worse memory[10] and greater cognitive decline.[11] Finally, insomnia accelerated cognitive decline over 3 years of follow-up, although only in men and not in women.[12]

Sleep disturbances were also identified as a potentially important area in research on risk factors for dementia.[13] This was partially based on evidence that more sleep disruptions (e.g., insomnia, restless legs) were associated with increased risk of vascular dementia after 10 years.[14] However, the contribution of sleep problems to the risk of dementia is still poorly understood.

There is also evidence that reduced duration and/or quality of sleep may adversely affect brain health specifically, likely via weakened neuronal structures, increased risk of cell death, and via cardiovascular pathways. Middle-aged adults who average 5 hours of sleep per night are more likely to have hypertension than those averaging 7 hours.[15] Also, having poor sleep quality may increase the risk of stroke and raise blood pressure.[16,17] Together, these findings may point to a potential cardiovascular pathway toward poor brain health.[18,19]

Sleep may also be associated with increased dementia risk because of its interplay with psychological stress. Insomnia is one of the diagnostic criteria for Major Depressive Episode and Major Depressive Disorder,[20] and sleep problems have been identified as a possible risk factor for subsequent depression.[21,22] Depressive symptoms may therefore be an important variable in any association between sleep problems and dementia.

We examined whether a subjective report of change (reduced duration and/or depth) in sleep pattern was associated with an increased risk of incident all-cause dementia and Alzheimer disease (AD). In addition, we tested whether an association between change in sleep pattern and dementia may be explained by vascular health and/or depressive symptoms. We also considered the influence of demographic factors, lifestyle factors, apolipoprotein E epsilon 4 allele (apoE ε4), and the potential modification effect of sleeping pills. Finally, we examined change in sleep pattern categorized in three groups and introduced into the model as a continuous variable to test for a potential dose−response association.

METHODS

Sample

We used data from the population-based Kungsholmen Project, a longitudinal study of aging and dementia among adults aged 75 years and older residing in Kungsholmen district, Stockholm, Sweden. Data collection included a baseline and four follow-up examinations.[23,24] Individuals living in Kungsholmen born before 1913 were invited to participate in the initial measurement, which took place from 1987 to 1989. Follow-up data collections occurred approximately every 3 years until 2000 for a total of up to five measurement occasions per person and up to 9 years of follow-up.

Of the initial sample of 1,810 participants (Phase I), the current study includes only participants from the pool of 668 individuals who underwent clinical examination (phase II) that included assessment of different psychiatric symptoms and sleep problems (Fig. 1). Of these 668 individuals, 225 were diagnosed with dementia, resulting in a dementia-free cohort of 443 people. Then, to decrease the likelihood of reverse causation in the main analyses, we excluded from this cohort (1) 98 persons with scores of 23 or lower on the Mini-Mental State Exam (MMSE)[25] at baseline and (2) 43 persons diagnosed with dementia at first follow-up. As shown in Figure 1, we also did not include 24 participants who refused study participation after baseline testing and 62 participants who died between baseline and first follow-up.

The Kungsholmen project was approved by the ethics committee at the Karolinska Institute, and written informed consent was obtained from either a participant or proxy (close relative). Refusal to participate was respected at any time throughout the project.

Diagnosis of All-Cause Dementia and AD

All-cause dementia cases included all new (incident) dementia patients identified between the