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Featured Article

Sleep duration, cognitive decline, and dementia risk in older women

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Abstract

Introduction: Consistent evidence linking habitual sleep duration with risks of mild cognitive impairment (MCI) and dementia is lacking.

Methods: We conducted a prospective study on 7444 community-dwelling women (aged 65–80 y) with self-reported sleep duration, within the Women's Health Initiative Memory Study in 1995–2008. Incident MCI/dementia cases were ascertained by validated protocols. Cox models were used to adjust for multiple sociodemographic and lifestyle factors, depression, cardiovascular disease (CVD), and other clinical characteristics.

Results: We found a statistically significant ($P = .03$) V-shaped association with a higher MCI/dementia risk in women with either short (≤6 hours/night) or long (≥8 hours/night) sleep duration (vs. 7 hours/night). The multicovariate-adjusted hazard for MCI/dementia was increased by 36% in short sleepers irrespective of CVD, and by 35% in long sleepers without CVD. A similar V-shaped association was found with cognitive decline.

Discussion: In older women, habitual sleep duration predicts the future risk for cognitive impairments including dementia, independent of vascular risk factors.

Keywords: Sleep duration; Elderly; Cognition; Cognitive decline; Mild cognitive impairment; Dementia; Longitudinal analysis; Cohort studies

1. Introduction

Since the first experimental sleep deprivation study on humans reported in 1896 [1], considerable evidence has shown that sleep loss impairs cognitive performance [2]. However, the focus of previous clinical studies has been on "short-term" sleep deprivation. As insufficient sleep was increasingly recognized as an important public health

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problem (e.g., 32% reporting ≤6 hours of sleep on weekdays among people aged >60 years in a US national survey [3]), a growing attention has been directed to studying the "long-term" neurocognitive effects of sleep deprivation. Cross-sectional analyses of population studies on older people worldwide (e.g., in the United States [4], United Kingdom [5], Finland [6], France [7], and China [8]) have revealed an inverse U-shaped or V-shaped association between cognitive function and self-reported sleep duration. Only a small number of longitudinal studies have begun to examine whether habitual short or long sleep duration increases the risk for cognitive declines [9–12] or dementia [13–15] in the elderly, but the results were mixed. Interpretation of previous findings was uncertain due to short follow-up time or lack of rigorous control of potential confounders. To examine associations of cognitive decline and mild cognitive impairment (MCI)/dementia with habitual sleep duration, we conducted a longitudinal analysis based in the Women's Health Initiative Memory Study (WHIMS), 1995–2008.

2. Methods

2.1. Study population

The WHIMS [16] was an ancillary study to the Women's Health Initiative trials of hormone therapy (WHI-HT), two large, randomized, double-blind, placebo-controlled, clinical trials of conjugated equine estrogen treatment alone (E-alone) for women with prior hysterectomy or in combination with medroxyprogesterone acetate (E + P) for women without prior hysterectomy [17]. The WHIMS was designed to test the hypothesis that HT reduces the incidence of all-cause dementia in women aged ≥65 years. Community-dwelling women were recruited during 1995–1998 from WHI-HT participants who were aged 65–80 years at enrollment, free of dementia defined by WHIMS protocols. After discovering an unfavorable risk-to-benefit ratio of its noncognitive end points, the E + P trial was discontinued in July, 2002. The E-alone trial also ended earlier than planned in February, 2004 because of a greater risk of stroke and a lack of benefit for coronary heart disease. These decisions also ended the WHIMS trial, but annual follow-up was continued for cognitive assessment. The WHIMS study design, eligibility criteria, and recruitment procedures have been described elsewhere [16]. The current analyses are based on 7444 participants who had complete data on sleep duration at WHIMS baseline.

2.2. Study variable

The measures of sleep disturbance in the WHI cohort were developed by sleep research consultants to the WHI Behavioral Advisory Committee [18]. As part of the baseline examination, each WHI participant was asked to report "hours of sleep on a typical night during the past 4 weeks" (≤5, 6, 7, 8, 9, and ≥10). Levine et al. [19] assessed the psychometric properties of these sleep measures and showed that self-reported sleep duration did not cluster with other subconstructs of sleep disturbance, such as insomnia and sleepiness. Very good test-retest reliability was found for self-reported sleep duration (Spearman $R = 0.97$ for same-day administration and 0.89 for 8–14 days).

2.3. Neurocognitive outcome variables

Our analyses included two end points: defined significant decline in global cognitive function, as assessed by the modified mini-mental state (3MS) examination [20], and the incidence of MCI or probable dementia, as determined by the validated 4-phase WHIMS protocols [16,21]. In phase 1, trained, masked, and certified technicians administered the 3MS test at baseline and annually. Women who screened positively for cognitive impairment, according to education-adjusted 3MS cut points, proceeded to more extensive neuropsychological testing (phase 2), including a modified Consortium to Establish a Registry for Alzheimer's Disease (CERAD) battery [22]. Participants subsequently received a detailed clinical neurologic and neuropsychiatric evaluation by physicians (i.e., neurologists, geriatricians, or geriatric psychiatrists) with experience in diagnosing dementia (phase 3). Each suspected case of dementia then underwent cranial computerized axial tomography (CAT) scan and a series of laboratory tests to rule out possible reversible causes of cognitive decline and dementia (phase 4). Cognitive decline during the follow-up, regardless of subsequent clinical classification, was defined as loss of 3MS score by eight units (∼two standard errors) from baseline, corresponding to a clinically significant decline [15,23]. Following the accepted criteria [24] at WHIMS baseline, MCI was defined as poor performance (≤10th percentile in CERAD norms) on at least one CERAD test, evidence of functional impairment (but not severe enough to interfere with activities of daily living), and absence of psychiatric or other medical disorders (including probable dementia) that could explain the cognitive impairment. All clinical/testing data were then transmitted to the central adjudication committee for final confirmation of dementia, based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [25].

2.4. Measurement of covariates

Participants completed structured questionnaires to provide baseline information on demographics (age and race-ethnicity), socioeconomic status (SES, including education in years, family income, and employment status), lifestyle factors (smoking, alcohol consumption, and physical activity), and relevant clinical characteristics (use of menopausal HT, prior depression, cardiovascular disease [CVD], and related risk factors). Women were grouped according to body mass index (BMI, in kg/m^2) categories (<25.0 vs. 25.0–29.9 vs. ≥30.0). Hypertension was defined as antihypertensive medication or elevated blood pressure (systolic