ONLINE SUPPLEMENT

DECREASED SLOW WAVE SLEEP INCREASES RISK OF DEVELOPING HYPERTENSION IN ELDERLY MEN

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Online supplemental methods.

Study participants.

2,860 participants from the original cohort did not participate in the sleep study as they were unwilling (1997), not screened because recruitment goals were met (332), death before the sleep study visit (334), ineligible due to exclusion criteria such as use of mechanical devices during sleep, including positive airway pressure devices, oral appliances for snoring or sleep apnea, or oxygen therapy (150), and quitting the MrOS study before the sleep study was offered (37). Among the 49 men who reported use of one of the sleep devices, 17 men were able to forego use of their sleep devices during the night of the in-home PSG study and had sleep studies performed. Of the 3,135 enrolled participants, 2,911 had valid PSG data. Of these, sleep staging could not be performed on 39 studies (due to poor EEG quality), and in 132 records there was difficulty differentiating stage 2 and SWS due to artifact; 5 people fell into both categories.

Other measures. Self-administered questionnaires were used at the time of the sleep study to ascertain participant demographic and lifestyle information and their personal and family medical history, including self-reported HTN, diabetes, and cardiovascular disease (which included history of myocardial infarction, angina, congestive heart failure, coronary bypass surgery, transient ischemic attack, stroke, or rheumatic heart disease). Race/ethnicity was self-reported using a questionnaire with a choice of 5 categories (Caucasian/White, African American/Black, Asian, Hispanic, and Other). Due to the small percentiles of non-Caucasian participants (<10% total) and no difference by SWS or incident hypertension, they were then simplified to Caucasian and Non-Caucasian. Interviews and examinations by trained study staff members included measures of functional status and anthropometric data. Physical activity was assessed by using the physical activity scale for the elderly (PASE)[1]. Depressed mood was assessed using the Geriatric Depression Scale (GDS), a 15 point scale of yes or no questions, and a standard cut point of >6 was used to define depressed mood[2]. Participants also reported tobacco use (current, past, or never) and alcohol use (drinks per week). Alcohol use was assessed by <1 or >1 drink per week and also by 0, <1, 1-2, 3-5, 6-13, or 14+ drinks per week). Participants were asked to bring in all current medications used within the preceding 30 days. All prescription and nonprescription medications were entered into an electronic database and each medication was matched to its ingredient(s) based on the Iowa Drug Information Service (IDIS) Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA)[3]. They were also asked whether each medication was used for sleep, and if so, the subject was considered to have "Use of Sleep Medication." Zolpidem, diphenhidramine, acetaminophen, trazadone, and melatonin were the most common medications reported for this purpose.

Sleep studies.

The recording montage consisted of C_3/A_2 and C_4/A_1 electroencephalograms, bilateral electroculograms, electrocardiogram, a bipolar submental electromyogram, thoracic and abdominal respiratory inductance plethysmography, airflow (using nasal-oral thermocouple and nasal pressure cannula), finger pulse oximetry, electrocardiogram, body position (mercury switch sensor), and bilateral leg movements (piezoelectric sensors). Trained certified staff members performed home visits for setup of the sleep study units. After sensors were placed and calibrated, signal quality and impedance were checked, and sensors were repositioned as needed to improve signal quality, replacing electrodes if impedances were > 5000 ohms, using approaches similar to those in the Sleep Health Heart Study[4]. After studies were downloaded, they were transferred to the Case Western Reserve University Reading Center (Cleveland, OH) for centralized scoring by a trained technician using standard criteria[5, 6]. PSG data quality was excellent, with > 70% of studies graded as being of excellent or outstanding quality and a failure rate < 4%. Quality codes for signals and studies were graded using previously described approaches, including coding of the duration of artifact-free data per channel and overall study quality (reflecting the combination of grades for each channel)[4].

The inter-scorer reliability of percent time in SWS was high (intraclass correlation coefficient [ICC] = 0.958, 95% CI = 0.921-0.982). The intra-scorer reliability was also high, with the ICC ranging from 0.964-0.998.

Pre-hypertension subgroup analysis. In a subgroup analysis, determined whether the association between SWS and incident HTN persisted after excluding men who were pre-hypertensive at baseline. The normotensive participants were further divided into normotensive, pre-hypertensive or hypertensive groups at follow-up. ANOVA, Kruskal-Wallis and chi square tests were analyzed for significant differences in SWS and the other sleep stages in this subset.

Results.

Subgroup analysis of sleep architecture in normotensive subjects.

In evaluating only normotensive subjects at the start of the study (without blood pressure medication or other evidence of pre-hypertension), there was an association with decreased percent time in SWS (P=0.004) and percent increased time in stage 2 (N2; P=0.042) sleep as subjects either stayed normotensive, or progressed to pre-hypertension or HTN, shown in Online Supplemental Figure S1. There was no difference in percent time in REM sleep or stage 1 (N1) sleep and HTN progression. These results were unchanged after adjustment for age and covariates.

References:

1. Washburn RA, Ficker JL. Physical Activity Scale for the Elderly (PASE): the relationship with activity measured by a portable accelerometer. *J Sports Med Phys Fitness.* 1999;39:336-340.
2. Almeida OP, Almeida SA. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. *Int J Geriatr Psychiatry.* 1999;14:858-865.
3. Pahor M, Chrischilles EA, Guralnik JM, Brown SL, Wallace RB, Carbonin P. Drug data coding and analysis in epidemiologic studies. *Eur J Epidemiol.* 1994;10:405-411.
4. Redline S, Sanders MH, Lind BK, Quan SF, Iber C, Gottlieb DJ, Bonekat WH, Rapoport DM, Smith PL, Kiley JP. Methods for obtaining and analyzing unattended polysomnography data for a multicenter study. Sleep Heart Health Research Group. *Sleep.* 1998;21:759-767.
5. Rechtschaffen A and Kales A. A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects. Los Angeles: Brain Information Service, Brain Research Institute, UCLA; 1973.
6. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep.* 1992;15:173-184.

Table S1. Adjusted odds ratios of incident hypertension (HTN) in the lowest quartile compared to the highest quartile in sleep characteristics.

Variable	Odds ratio of lowest quartile to highest quartile	95% CI	P value for trend
Sleep disordered breathing			
Respiratory disturbance index (RDI)	0.89	0.56, 1.42	0.82
Hypoxemia (% sleep time Pao2 <80%)	0.62*	0.31, 1.24	0.18
Central apnea index	1.00*	0.73,1.38	0.98
Sleep duration			
Total sleep duration (minutes)	0.68	0.44, 1.06	0.088
Sleep architecture			
Overall arousal index	1.26	0.82, 1.94	0.26
Sleep efficiency	0.93	0.59, 1.47	0.81
Wake after sleep onset (minutes)	0.89	0.56, 1.40	0.57
% time in stage 1 (N1) sleep	0.69	0.44, 1.08	0.075
% time in stage 2 (N2) sleep	0.77	0.50, 1.19	0.068
% time in slow wave (N3) sleep	1.83	1.18, 2.85	**0.012**
% time in REM	0.97	0.62, 1.52	0.93

*Denotes variables dichotomized as zero or greater than zero rather than quartiles due to distributions not suitable for quartiles. Models are adjusted for age, non-white race, study site, and body mass index. (Models are not significantly changed when additionally adjusting for alcohol use or smoking).

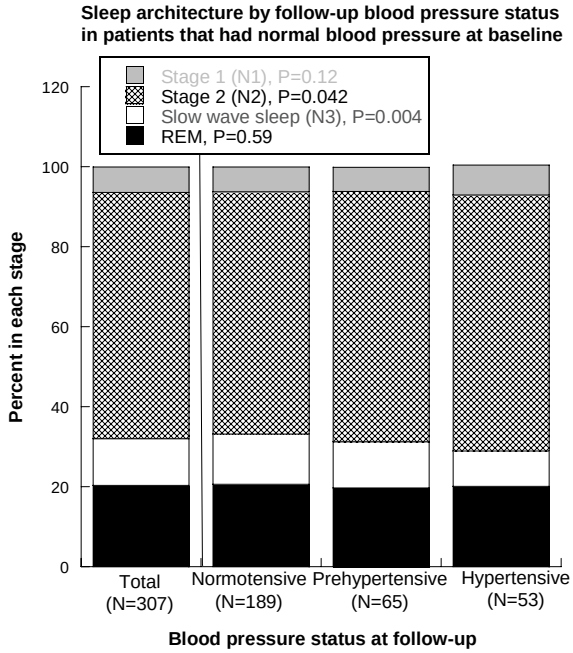

Figure S1

Online Supplemental Figure S1 Legend

Sleep architecture of normotensive subjects at baseline based on hypertension progression ~3.4 years later. In subset analysis of participants who were normotensive at baseline (not pre-hypertensive but with SBP<120 mmHg and DBP <80 mmHg; N=307), we found an association with percent time in slow wave sleep (SWS; P=0.004) and stage 2 sleep (P=0.042) as subjects progressed to pre-hypertension or hypertension. There was no difference in percent time in REM sleep or stage 1 sleep.