Decrease in Daytime Sleeping Is Associated with Improvement in Cognition After Hospital Discharge in Older Adults

Joseph M. Dzierzewski, PhD,*† Constance H. Fung, MD, MSHS,*† Stella Jouldjian, MSW, MPH,* Cathy A. Alessi, MD,*† Michael R. Irwin, MD,‡ and Jennifer L. Martin, PhD*†

OBJECTIVES: To examine the relationship between changes in objectively assessed sleep and global cognitive functioning from inpatient postacute rehabilitation to 6-month follow-up.

DESIGN: Secondary analysis of two prospective, longitudinal studies.

SETTING: Inpatient rehabilitation units at a Veterans Affairs Medical Center.

PARTICIPANTS: Older adults (mean age 73.8 ± 9.4) undergoing inpatient rehabilitation (n = 192).

MEASUREMENTS: All participants completed 7 nights and days of ambulatory sleep monitoring using wrist actigraphy (yielding an estimate of nighttime wakefulness and daytime sleep) and the Mini-Mental State Examination (MMSE) during a postacute inpatient rehabilitation stay and 6 months after discharge. The 5-item Geriatric Depression Scale, Geriatric Pain Measure, and Cumulative Illness Rating Scale for Geriatrics were completed during inpatient rehabilitation.

RESULTS: Growth curve modeling (controlling for baseline age, education, sex, body mass index, depression, pain, and comorbidity burden) revealed that individuals whose amount of daytime sleep decreased from inpatient postacute rehabilitation to 6-month follow-up also experienced improvements in MMSE score (β = -0.01, t(80 = -3.22, P = .002)). Change in nighttime wakefulness was not a significant predictor of change in MMSE score.

CONCLUSION: Older adults whose daytime sleeping decreased after hospital discharge also experienced improvements in cognitive functioning at 6 month follow-up. As such, daytime sleep may represent a promising candidate for targeted interventions aimed at promoting

From the *Geriatric Research, Education and Clinical Center, Veterans Affairs Greater Los Angeles Healthcare, †David Geffen School of Medicine, University of California Los Angeles, and ‡Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience and Human Behavior, University of California Los Angeles, Los Angeles, California.

Address for correspondence to Jennifer L. Martin, VA Greater Los Angeles Healthcare System, 16111 Plummer Street (11E), North Hills, CA 91343. E-mail: jennifer.martin@va.gov

DOI: 10.1111/jgs.12622

cognitive recovery after hospital discharge. J Am Geriatr Soc 62:47-53, 2014.

Key words: sleep; cognition; longitudinal change; inpatient hospitalization; older adults

Older adults experience normal declines in cognitive functioning with advanced age, 1,2 but they are at greater risk for decline in cognitive functioning at important points in the health continuum, such as after hospitalization. There is evidence that older adults experience cognitive decline after any hospitalization, 3-6 including those involving a surgical procedure. For example, hospitalization was associated with a 2.4 times greater rate of cognitive decline than change in global cognitive functioning before admission in a longitudinal study of nearly 2,000 older adults.

Identifying predictors of cognitive decline in hospitalized older adults has the potential to affect selection of individuals best suited for elective procedures requiring hospitalization and use of preemptive interventions to lessen the negative effect of hospitalization on late-life cognitive functioning, but little is known about potential predictors of cognitive decline in response to late-life hospitalization. Length of hospital stay, age, and comorbidity severity have been reported to be associated with rate of cognitive decline after hospitalization, 3,6-8 but these factors are not all readily modifiable. The identification of potentially modifiable risk factors is needed to identify those at risk of cognitive decline and to guide the development of interventions.

Sleep is an important factor to be studied in relation to posthospitalization cognitive decline, given the prevalence of sleep disturbance in older adults⁹ and reports that sleep disturbances are associated with cognitive performance.¹⁰ In inpatient settings, older adults have extremely fragmented sleep, short nighttime sleep duration, and more daytime sleeping.^{11–13} Daytime sleep during inpatient hospitalization is associated with less functional

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improvement during and after the rehabilitation stay, which has also been found to predict greater mortality risk 1 year later. 14 Late-life sleep impairment has a known negative relationship with cognitive functioning 10,15–17 and is very malleable well into the last decades of life. 18 Sleep difficulties, specifically daytime sleep, are associated with worse global cognitive functioning in older adults undergoing postacute inpatient rehabilitation, 19 although longitudinal relationships were not evaluated.

To the knowledge of the authors, no prior study has examined the prospective association between sleep habits, as measured using actigraphy, and cognitive function in older adults after hospital discharge. Such an investigation is of importance because of the inherent risks involved in late-life hospitalization, including cognitive decline, functional decline, and mortality, 14 and the modifiable nature of sleep in late life. 18 The current investigation represents a secondary analysis of data derived from two studies. The goal was to examine modifiable predictors of late-life cognitive change after discharge from an inpatient postacute rehabilitation stay. Specifically, the role of changes in objectively assessed daytime and nighttime sleep between a postacute rehabilitation stay and 6-month follow-up and changes in global cognitive functioning over the same time period were examined. These relationships were examined taking into account the effects of age, education, sex, body mass index (BMI), depressive symptoms, pain, and medical comorbidities on initial level of cognitive functioning. It was hypothesized that older adults whose sleep improved after discharge (spent less time awake during the night and less time asleep during the day) would experience positive cognitive changes, whereas those whose sleep worsened after hospital discharge (spent more time asleep during the day and more time awake at night) would experience negative cognitive changes.

METHODS

Participants

Individuals admitted for rehabilitation services who were aged 60 and older were approached for participation in one of two studies. Study 1 was a descriptive study of sleep and health outcomes in older adults undergoing inpatient postacute rehabilitation (n = 85). Study 2 was a behavioral intervention trial to improve sleep during postacute rehabilitation (n = 107). Both studies included individuals admitted to postacute inpatient rehabilitation units at a Veterans Affairs (VA) Medical Center. Inclusion criteria were aged 60 and older and admitted for rehabilitation (receiving physical or occupational therapy). Individuals with profound cognitive impairment (MMSE score <12) were excluded, as were those who had resided in a nursing home before admission; transferred, died, or were discharged within 1 week of admission; could not participate in the study because of a severe medical illness or severe behavioral disturbance; and were unable to communicate verbally in English during the screening process. The same inclusion and exclusion criteria were employed in both studies. The Veterans Affairs Greater

Los Angeles Healthcare System institutional review board reviewed and approved the research methods, and informed consent was obtained from all participants.

Procedures

Study 1 (descriptive study) and Study 2 (intervention trial) included a baseline and 6-month follow-up assessment. After enrollment, all participants completed a comprehensive baseline assessment including measurement of demographic, comorbidity, sleep, and cognitive data (details below). First, individuals completed the MMSE to establish eligibility and measure global cognitive functioning. Eligible participants then wore a wrist actigraph for 7 nights and days and completed a series of questionnaires administered in interview format by a trained research assistant at the participant's bedside. Six months after hospital discharge, all participants were recontacted for follow-up assessment, which included measurement of global cognitive functioning using the MMSE and repeat wrist actigraphy for 7 nights and days. Participants in Study 1 received no contact from study personnel between the baseline and 6-month assessments. Participants in Study 2 engaged in a behavioral-based treatment aimed at improving sleep (n = 53) or an attention-matched control condition (n = 54) between the baseline and follow-up assessments.

Measures

Demographic Data

Demographic information was recorded at baseline for all participants (age, education (reported years of formal education), and sex).

Comorbidity Data

Baseline depressive symptoms were assessed using the 5-item version of the Geriatric Depression Scale (score range 0–5; scores >2 suggest depression).²⁰ Baseline pain was assessed using an 11-item version of the Geriatric Pain Measure, based on the 24-item Geriatric Pain Measure (score range 0–29; higher scores suggest more pain).²¹ After a medical record review and physical examination by a study physician, a trained research registered nurse completed the Cumulative Illness Rating Scale for Geriatrics, which was used to assess baseline illness severity and comorbidity.^{22,23} BMI was obtained from medical records.

Sleep

Sleep was assessed using 7 consecutive days and nights of wrist actigraphy (Octagonal Sleep Watch-L, Ambulatory Monitoring, Inc, AMI, Ardsley, NY) worn on the dominant arm (unless paralyzed or otherwise limited). Participants reported bedtime and rise time each day, corresponding to the period they intended to sleep the night before. Raw actigraphy data (1-minute epoch length) was reviewed to eliminate technical and situational artifact before scoring sleep using a validated algorithm within commercially available software (ACT software,

AMI). Automatic sleep scoring using time above threshold (default algorithms) was used, based on literature and data comparing actigraphy with standardized observations of sleep and wake in individuals undergoing postacute rehabilitation.^{24–26} At 6-month follow-up, participants again wore wrist actigraphs for 7 days and nights and reported daily bedtime and rise time in a sleep diary, which were again used to define the nighttime and day-time periods for analysis. Actigraphy variables were averaged over recorded nights and days. The current analysis focused on a single indicator of nighttime sleep disturbance (nighttime minutes awake) and a single indicator of daytime sleep (daytime minutes asleep). Change scores for the two sleep variables were calculated as 6-month score minus baseline score.

Global Cognitive Functioning

The MMSE was administered at baseline during postacute rehabilitation and 6-month follow-up. Cognitive assessment during the inpatient postacute rehabilitation stay occurred between 10:00 a.m. and 11:30 a.m. (after breakfast and morning medical appointments but before lunch). The MMSE is a 20-item measure of global cognitive functioning; scores range from 0 to 30, with scores less than 24 suggestive of cognitive impairment.²⁷ MMSE total score was used as a measure of global cognitive functioning and to exclude those with profound cognitive impairment, as described above.

Statistical Analyses

Data were analyzed using SPSS 15.0 (SPSS, Inc., Chicago, IL). A one-way analysis of variance (ANOVA) was used to test for study sample differences between participants in Study 1 and intervention and control participants in Study 2 on all study-related variables of interest (independent and dependent variables). The one-way ANOVA analyses revealed no group differences in variables of interest; thus, the groups were combined for all subsequent analyses and treated as a single group.

To explore associations between changes in sleep and changes in global cognitive functioning in participants, a conditional growth model (a growth curve model including substantive predictors of change across time) was parameterized through a multilevel model (MLM) framework.²⁸ MLM, also referred to as mixed-effects modeling or hierarchical linear modeling,²⁹ is an extension of the general linear model and does not require observations to be independent. Model specification resulted in a model that predicted change in global cognitive functioning with average level of cognitive functioning (β_{00}), linear time (β_{10}) , demographic and comorbidity variables (age (β_{01}) , education (β_{02}), sex (β_{03}), BMI (β_{04}), depressive symptoms (β_{05}) , pain (β_{06}) , comorbidity severity (β_{07}) , change in daytime sleeping (β_{07}), change in nighttime sleeping (β_{08}) , change in daytime sleeping by linear time (β_{20}) , change in nighttime sleeping by linear time (β_{30}), random coefficient of linear time (r_{1i}) , random error term (e_{it}) , and random residual component (r_{oi}) . The final model equation was:

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\begin{split} \operatorname{Cognition}_{it} = & \beta_{00} + \beta_{10}(\operatorname{time}) + \beta_{01}(\operatorname{age}_i) + \beta_{02}(\operatorname{education}_i) \\ & + \beta_{03}(\operatorname{sex}_i) + \beta_{04}(\operatorname{BMI}_i) + \beta_{05}(\operatorname{depression}_i) \\ & + \beta_{06}(\operatorname{pain}_i) + \beta_{07}(\operatorname{comorbidity}_i) \\ & + \beta_{08}(\Delta \operatorname{daytime sleep}_i) + \beta_{09}(\Delta \operatorname{nighttime sleep}_i) \\ & + \beta_{20}(\Delta \operatorname{daytime sleep} \times \operatorname{time}) \\ & + \beta_{30}(\Delta \operatorname{nighttime sleep} \times \operatorname{time}) + r_{1i}(\operatorname{time}) + r_{0i} \end{split}
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All variables were evaluated based on their significance and their effects on intercept and residual-related variance estimates. Although missing data can be problematic in longitudinal studies, multilevel modeling uses all available data and is valid for making inferences to the population of origin when data are missing at random.29 To further examine any potential effects of combining participants from different studies (one of which was an intervention trial), the final MLM described above was reestimated, selecting only two of the three potential sources of participants (observational participants from Study 1, intervention participants from Study 2, and control participants from Study 2). This process resulted in the estimation of three additional MLMs (Study 1 + Study 2 intervention, Study 1 + Study 2 control, Study 2 intervention + Study 2 control). These models were examined for differing patterns of results between each other and in comparison with the fully combined original model.

RESULTS

Sample Characteristics

One hundred ninety-two participants provided baseline data, 78% of whom provided at least partial follow-up data; 6% who died; and 16% who refused follow-up, relocated out of the area and thus were unable to participate, or were unable to be contacted. Participants had a mean age of 73.8 ± 9.7 , were 97% male, had an average level of education of 13.8 ± 3.0 years, and had an average BMI of 27.3 ± 7.0 kg/m². Table 1 provides means and standard deviations for variables of interest for the study participants, along with comparisons between the groups of participants in Study 1 (n = 85) and Study 2 (n = 107) stratified according to intervention allocation.

Growth Curve Model

Before estimating the growth curve model, raw MMSE scores obtained during postacute rehabilitation and at 6-month follow-up were plotted for a random subset of participants to visually inspect change in global cognitive functioning from inpatient hospitalization to 6-month follow-up. Visual inspection suggested differing trajectories of change of study participants, indicating that the examination of factors related to change may yield fruitful information.

Predictor estimates, significance levels, and model parameters for the conditional growth model predicting 6-month change in MMSE score after discharge are presented in Table 2. Age ($\beta = -0.09$, standard error

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Table 1. Demographic and Descriptive Variables According to Group

			Study 2, n = 107				
Variable	Total Sample, n = 192	Study 1, n = 85	Intervention, n = 53	Control, n = 54	F	df	<i>P</i> -Value
Age, mean \pm SD	73.8 ± 9.4	75.0 ± 8.5	73.3 ± 10.7	72.6 ± 9.5	1.16	2,189	.32
Education, years, mean \pm SD	13.8 ± 2.3	13.6 ± 3.4	13.7 ± 3.0	14.2 ± 2.6	0.63	2,160	.53
Male,%	97.4	98.8	96.2	96.3	_	_	_
Body mass index, kg/m 2 , mean \pm SD	27.3 ± 7.0	27.8 ± 8.9	27.465 ± 5.4	26.4 ± 4.6	0.60	2,181	.55
Geriatric Depression Scale score, mean \pm SD	1.43 ± 1.37	1.57 ± 1.49	1.19 ± 1.27	1.47 ± 1.27	1.54	2,178	.22
Geriatric Pain Measure score, mean \pm SD	49.0 ± 28.3	47.1 ± 28.7	52.2 ± 28.8	48.5 ± 27.6	1.25	2,186	.29
Comorbidity Illness Rating Scale total score, mean \pm SD	22.3 ± 5.4	22.7 ± 5.6	21.2 ± 5.9	22.9 ± 4.3	0.52	2,179	.6
Δ daytime sleep, minutes, mean \pm SD	-11.1 ± 90.4	-10.8 ± 127.5	0.06 ± 77.31	-23.0 ± 75.5	0.56	289	.57
Δ nighttime wake, minutes, mean \pm SD	2.0 ± 104.0	13.4 ± 132.2	9.4 ± 71.5	-13.2 ± 113.5	0.58	289	.56
Δ Mini-Mental State Examination score, mean \pm SD	0.23 ± 2.90	0.39 ± 2.38	0.43 ± 2.63	-0.10 ± 3.50	0.41	2,114	.66

 Δ scores = 6-month follow-up minus baseline. There were no differences between the groups on any study-related variables of interest. SD = Standard Deviation.

Table 2. Conditional Growth Models for 6-Month Change in Mini-Mental State Examination Score (n = 192)

Fixed-Effects Predictor Variables	β	SE	т
Occasion	0.44	0.28	1.56
Age	-0.09	0.03	-2.58^{a}
Education	0.03	0.06	0.70
Sex	1.80	1.55	1.16
Body mass index	0.02	0.05	0.45
Geriatric Depression Scale score	-0.17	0.22	-0.78
Geriatric Pain Measure score	-0.01	0.01	-0.69
Comorbidity Illness Rating Scale score	-0.06	0.06	-0.87
Δ daytime sleep, minutes	0.02	0.01	3.70 ^c
Δ nighttime sleep, minutes	0.001	0.01	0.16
Linear time by Δ daytime sleep	-0.01	0.003	-3.22^{b}
Linear time by Δ nighttime sleep	-0.0005	0.003	-0.16

 Δ scores = 6-month follow-up minus baseline. The model also included a random effect for occasion, but the variance was too small to be estimated, and the final Hessian matrix is not positive definite, although all convergence criteria are satisfied. The test statistic and confidence interval cannot be computed. Within pseudo coefficient of variation (R^2) = 26%; between pseudo R^2 = 46%.

(SE) = 0.03, t(80) = -2.58, P = .01) and change in daytime sleep ($\beta = 0.02$, SE = 0.01, t(141.97) = 3.70, P < .001) were the only significant between-person predictors, suggesting that younger individuals and those whose daytime sleep changed more from baseline to 6-month follow-up had higher-than-average MMSE scores. At the within-person level, the interaction between linear time and change in daytime sleep ($\beta = -0.01$, SE = 0.003, t(80.00) = -3.22, P = .002) was the only significant predictor of 6-month change in MMSE performance, suggesting that older individuals whose amount of daytime sleep decreased between hospitalization and 6-month follow-up experienced improvements in global cognitive functioning as assessed according to the MMSE. The model explained

26% of the within-person variance and 46% of the between-person variance in MMSE scores. The pattern of predictor estimates, significance levels, and model parameters for the conditional growth models estimated to examine the influence of the differing sources of participants (Study 1 and intervention and control conditions of Study 2) was identical to those of the combined model reported above. As such, variance due to study design differences between sources of participants do not appear to have influenced the results. Only the combined model is reported here.

To further explicate the effects of changes in daytime sleep on level and rate of change in global cognitive functioning and to make these effects fully apparent, the model predicted values were plotted separately for hypothetical individuals whose amount of daytime sleeping decreased after hospital discharge (sleep improved) and increased after hospital discharge (sleep worsened) (Figure 1). There was a positive trajectory of 6-month change in global cognitive functioning for an individual whose amount of daytime sleep decreased after hospital discharge and a negative trajectory of 6-month change in global cognitive functioning for an individual whose amount of daytime sleep increased after hospital discharge.

DISCUSSION

The current study examined the relationships between changes in sleep and changes in cognitive function after an inpatient postacute rehabilitation stay in older adults. It was discovered that older adults whose amount of daytime sleep decreased between their rehabilitation stay and 6-month follow-up experienced positive changes in global cognitive functioning and that older adults whose amount of daytime sleep increased between their rehabilitation stay and 6-month follow-up experienced negative changes in global cognitive functioning. Such results are congruent with, and extend, previous research that demonstrated negative consequences of poor sleep on changes in cognitive functioning in late life.

 $^{^{}a}P < .05, \, ^{b}P < .01, \, ^{c}P < .001.$

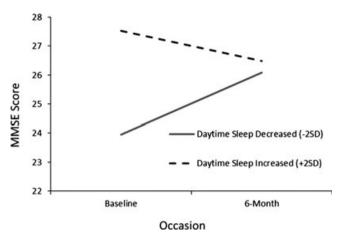


Figure 1. Change in daytime sleep and change in Mini-Mental State Examination (MMSE) scores. Change in daytime sleep was analyzed as a continuous variable but is graphed dichotomously to depict the nature of the results easily. Two levels of hypothetical change in daytime sleep (daytime sleep amount reduced and daytime sleep amount increased), defined as 2 standard deviations (SDs) below and 2 SDs above the average amount of change in daytime sleep are shown for illustrative purposes. The y-axis spans 6 points on the 30-point MMSE scale.

The current study expands on previous studies that have examined habitual sleep difficulties and global cognitive functioning in community-dwelling older adults 16,17 in several substantive ways. First, the current sample comprised hospitalized older adults, who are at risk for many unwanted negative outcomes.^{3,7} Second, instead of using static indicators of sleep as predictors of long-term cognitive changes, 16,17 the study used change in sleep after hospital discharge to predict change in cognitive functioning after hospital discharge. Research has shown that the sleep of older adults is highly inconsistent from night to night, 30,31 suggesting that single, aggregate indicators may be unreliable predictors. Furthermore, the sleep of older adults remains highly plastic well into late life, 18 and examination of coupled change between sleep and cognition could yield important theoretical and practical implications.

Length of hospital stay, age, and comorbidity severity have been reported to be associated with rate of cognitive decline after hospitalization.^{3,6–8} The current study has added to the literature on predictors of cognitive response to hospitalization in older adults and has identified predictors of cognitive response to hospitalization, namely nighttime sleep disturbance and daytime sleep, that are good candidates for interventional work. Cognitive-behavioral treatment for insomnia (CBTi) is an evidence-based treatment in older adults.³² Although the present study did not focus on older adults with insomnia, common components of treatment that focus on reducing daytime sleep and improving nighttime sleep^{18,32} may be useful for hospitalized older adults. The results of the current study suggest that, during and after hospital discharge, older adults could benefit from CBTi-based recommendations, specifically recommendations to avoid daytime sleep. Interventional work with institutionalized older adults has shown

that decreasing time in bed during the day and increasing daytime light exposure reduces daytime sleeping³³ and that there is a relationship between circadian rhythms and cognitive functioning in older adults.³⁴ Future interventional work is needed to determine the effects of CBTi-based recommendations (including its safety within this population), light exposure after hospital discharge, and circadian factors on daytime sleeping and cognitive functioning in older adults.

This study adds evidence to the current understanding of the mechanisms through which hospitalization may affect late-life cognitive functioning (and subsequent independence). Previous research has reported that surgery can result in inflammation and cognitive impairment, 35 and systemic inflammation and cognitive decrements also characterize sickness behavior after acute illness.³⁶ Postoperative and posthospital inflammation are normative responses to physical insult, but these inflammation responses are thought to be short lived, without concomitant long-lasting negative consequences. Current understanding suggests that age and underlying systemic dysfunction may result in a state of prolonged inflammation, resulting in long-term negative cognitive consequences.³⁷ The current study supports this model by elucidating the potential role of disrupted sleep on 6-month changes in global cognitive functioning. Negative changes in sleep have been found to be associated with changes in inflammation and cytokine levels. 38,39 As such, after hospitalization, older adults whose sleep worsens may be promoting prolonged inflammation, increasing their likelihood of experiencing negative long-term consequences. Alternatively, poor sleep may be a marker of neurological vulnerability or insult that could produce disturbed sleep-wake patterns and cognitive decline. Future research that longitudinally assesses sleep, inflammation, and cognitive functioning in older adults after hospitalization is needed to clarify these relationships further. Additionally, because sleep and physical activity are related in older adults, ⁴⁰ and physical activity is related to cognitive functioning, ⁴¹ future investigations should examine the combined effects of sleep and physical activity on cognitive functioning in older adults.

This study has several limitations that need to be acknowledged. It was conducted within a VA setting, and the sample was therefore primarily male. The results may not generalize to older women. The analysis did not include information on sleep disorders, such as sleep apnea, which may have associations with daytime sleepiness and cognitive functioning. Additionally, sleep habits were assessed using wrist actigraphy. Although actigraphy has been well validated for measurement of nighttime sleep, 24,25 comparatively little information exists on the validation of actigraphy for daytime sleep, especially in hospitalized older adults. A final limitation of the current study is the lack of explanation for the significant daytime sleep. As noted above, care must be taken in restricting the daytime sleep of hospitalized older adults because of potential iatrogenic effects.

In summary, an association was found between changes in objectively measured daytime sleep and changes in global cognitive functioning after a postacute rehabilitation stay in older adults. This relationship was observed 52 DZIERZEWSKI ET AL. JANUARY 2014–VOL. 62, NO. 1 JAGS

after accounting for age, education, sex, BMI, comorbidity severity and burden, depression, and pain. Such a finding extends previous work on sleep and cognition in late life and could inform theoretical accounts of postoperative and posthospital cognitive decline to include sleep as a mediator of prolonged inflammation. Results could also inform interventional work aimed at decreasing negative changes after hospitalization in late life.

ACKNOWLEDGMENTS

Conflict of Interest: None of the authors have declared a conflict of interest with a commercial entity.

This work was supported by the National Institute on Aging (K23 AG028452; PI Martin), University of California at Los Angeles (UCLA) Claude D. Pepper Older Americans Independence Center (NIA 5P30 AG028748, Career Development Award and Pilot Award, Martin; Inflammatory Biology Core, Irwin), UCLA Cousins Center for Psychoneuroimmunology, VA Health Services Research & Development (IIR 04–321–3, Alessi), VA Advanced Geriatrics Fellowship Program (Dzierzewski and Fung), American Sleep Medicine Foundation (Physician Scientist Training Award, Fung), and VA Greater Los Angeles Healthcare System Geriatric Research, Education and Clinical Center.

Author Contributions: Dzierzewski: conceptualization, analysis and interpretation of data, preparation of manuscript. Fung: critical review, feedback. Jouldjian: data preparation, feedback. Alessi: study design, acquisition of subjects, critical review, feedback. Irwin: study design, acquisition of subjects, critical review, feedback. Martin: study design, acquisition of subjects, critical review, feedback.

Sponsor's Role: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Aging, the University of California at Los Angeles, or the Greater Los Angeles VA, nor were the funding institutions responsible for the design, methods, subject recruitment, data collection, analysis, or preparation of paper.

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