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Decreased Daytime Sleeping is Associated with Improved Cognition Following Hospital Discharge in Older Adults

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Abstract

Background/Objectives: The longitudinal association between sleep and cognitive functioning is not well understood in late-life. Examination of the association between a potentially modifiable risk factor such as sleep, and cognitive change in at-risk older adults is of both theoretical and practical importance. We examined the relationship between changes in objectively-assessed sleep and global cognitive functioning from inpatient post-acute rehabilitation to 6-months follow-up.

Design: Secondary analysis of two prospective, longitudinal studies.

Setting: Inpatient rehabilitation units at a VA Medical Center.

Participants: 192 older patients (mean age=73.8±9.4 years) undergoing inpatient rehabilitation.

Measurements: All participants completed 7 nights/days of ambulatory sleep monitoring via wrist actigraphy (yielding an estimate of nighttime wakefulness and daytime sleep) and the Mini-Mental State Examination (MMSE; global cognitive functioning) during a post-acute inpatient rehabilitation stay and 6-months following discharge. The 5-item Geriatric Depression Scale (GDS5), Geriatric Pain Measure (GPM), and Cumulative Illness Rating Scale for Geriatrics were completed during inpatient rehabilitation.

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All authors contributed to the preparation of this manuscript. Joseph M. Dzierzewski: conceptualization, analysis and interpretation of data, and preparation of manuscript; Constance H. Fung: critical review and feedback; Stella Jouldjian: data preparation and feedback; Cathy Alessi: study design, acquisition of subjects, critical review and feedback; Michael R. Irwin: study design, acquisition of subjects, critical review and feedback; Jennifer L Martin: study design, acquisition of subjects, critical review and feedback.

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Results: Growth curve modeling (controlling for baseline age, education, gender, BMI, depression, pain, and comorbidity burden) revealed that individuals whose amount of daytime sleep decreased from inpatient post-acute rehabilitation to 6-month follow-up also experienced improvements in MMSE ($\beta = -0.01$, $t(80) = \beta 3.22$, $p<0.01$). Change in nighttime wakefulness was not a significant predictor of change in MMSE.

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

Keywords

Sleep; Cognition; Longitudinal Change; Inpatient Hospitalization; Older Adults

INTRODUCTION

Older adults experience normative declines in cognitive functioning with advanced age.[1, 2] However, at key points in the health continuum, such as following hospitalization, older adults are at an increased risk for decline in cognitive functioning. Indeed, there is evidence that older adults experience cognitive decline following any hospitalization[3-6] including those involving a surgical procedure.[7, 8] For example, as compared to change in global cognitive functioning prior to admission, hospitalization was associated with a 2.4 fold increased rate of cognitive decline in a longitudinal study of nearly 2,000 older adults.[3]

Identifying predictors of cognitive decline in hospitalized older adults has the potential to impact (a) selection of patients best suited for elective procedures requiring hospitalization, and (b) use of preemptive interventions to lessen the negative impact of hospitalization on late-life cognitive functioning. However, little is known about potential predictors of cognitive decline in response to late-life hospitalization.[7] Length of hospital stay, age, and comorbidity severity have been reported to be associated with rate of cognitive decline following 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 for cognitive decline and to guide the development of interventions.

Sleep represents an important factor to be studied in relation to post-hospital cognitive decline, given the prevalence of sleep disturbance in older adults[9] and reports that sleep disturbances are associated with cognitive performance[10]. In inpatient settings, older adults suffer from extremely fragmented sleep and have short nighttime sleep duration and increased daytime sleeping.[11-13] Further, daytime sleep during inpatient hospitalization is associated with less functional improvement during and following the rehabilitation stay, which has also been found to predict increased mortality risk one year later.[14] Additionally, late-life sleep impairment has known negative relationships to cognitive functioning[10, 15-17] and remains very malleable well into the last decades of life.[18] Indeed, we have also found that sleep difficulties, specifically daytime sleep, is associated with worse global cognitive functioning in older adults undergoing post-acute inpatient rehabilitation,[19] although longitudinal relationships were not evaluated.

To our knowledge, no prior study has examined the prospective association between sleep habits, as measured by actigraphy, and cognitive function in older adults following hospital discharge. Such an investigation is of importance due to the inherent risks involved in late-life hospitalization, which include: 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. We sought to examine modifiable predictors of late-life cognitive change following discharge from an inpatient post-acute rehabilitation stay. Specifically, we examined the role of changes in objectively assessed daytime and nighttime sleep between a post-acute rehabilitation stay and 6-month follow-up, and changes in global cognitive functioning over the same time period. These relationships were examined taking into account the effects of age, education, gender, body mass index (BMI), depressive symptoms, pain, and medical comorbidities on initial level of cognitive functioning. We hypothesized that older adults whose sleep improved following discharge (i.e., spent less time awake during the night and less time asleep during the day) would experience positive cognitive changes, while older adults whose sleep worsened following hospital discharge (i.e., spent increased time asleep during the day and more time awake at night) would experience negative cognitive changes.

METHODS

Participants

Patients admitted for rehabilitation services who were over age 60 years were approached for participation in one of two studies. The first study (Study 1) was a descriptive study of sleep and health outcomes in older adults undergoing inpatient post-acute rehabilitation (n=85). The second study (Study 2) was a behavioral intervention trial to improve sleep during post-acute rehabilitation (n=107). Both studies included patients admitted to post-acute inpatient rehabilitation units at a VA Medical Center. Inclusion criteria were: 1) aged 60 years or older; and 2) admitted for rehabilitation (i.e., receiving physical or occupational therapy). Individuals with profound cognitive impairment (defined by MMSE<12) were excluded. We also excluded those who 1) resided in a nursing home prior to admission, 2) transferred, died, or were discharged within one week of admission, 3) could not participate in the study due to a severe medical illness or severe behavioral disturbance, and 4) were unable to communicate verbally in English during the screening process. The same inclusion/exclusion criteria were employed in both studies. Research methods were reviewed and approved by the Veterans Administration Greater Los Angeles Healthcare System Institutional Review Board, and informed consent was obtained from all participants.

Procedures

Both 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. At 6-months following hospital discharge, all participants were re-contacted for follow-up assessment. Follow-up assessment included measurement of global cognitive functioning with the MMSE and repeat wrist actigraphy for 7 nights and days. Participants in Study 1 received no contact from study personnel in-between baseline and 6-month assessments. Participants in Study 2 engaged in either a behavioral-based treatment aimed at improving sleep (n=53) or an attention-matched control condition (n=54) in-between baseline and follow-up assessments.

Measures

Demographic Data—Demographic information was recorded at baseline for all participants, including age (calculated as years since birth), education (measured in reported years of formal education), and gender.

Comorbidity Data—Baseline depressive symptoms were assessed with 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] The Cumulative Illness Rating Scale for Geriatrics was completed by a trained research registered nurse following a medical record review and physical examination by a study physician, and was used to assess baseline illness severity/comorbidity.[22, 23] BMI was obtained from medical records.

Sleep—Sleep was assessed by seven 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 "bed time" and "rise time" each morning, 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, prior to scoring sleep using a validated algorithm within commercially-available software (ACT software, AMI). Automatic sleep scoring using time above threshold (TAT; default algorithms) was employed, based on literature and our data comparing actigraphy with standardized observations of sleep/wake in post-acute rehabilitation patients.[24-26] At 6-month follow-up, participants again wore wrist actigraphs for 7 days/nights and reported daily "bed time" and "rise time" on a sleep diary, which were again used to define the nighttime and daytime periods for analysis. Actigraphy variables were averaged over recorded nights/days. The current analysis focused on a single indicator of nighttime sleep disturbance (i.e., total nighttime wake minutes) and a single indicator of daytime sleep (i.e., daytime minutes asleep). Change scores for the two sleep variables were calculated as 6-month score – baseline score.

Global Cognitive Functioning—We administered the Mini-Mental State Examination (MMSE) at both baseline during post-acute rehabilitation and 6-month follow-up. Cognitive assessment during the inpatient post-acute rehabilitation stay occurred between 10:00AM and 11:30AM (following breakfast and morning medical appointments, but prior to lunch). The MMSE is a 20-item measure of global cognitive functioning; scores range from 0-30, with scores <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 with 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 (i.e., 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 (i.e., 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 (HLM[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}), gender (β_{03}), BMI (β_{04}), depressive symptoms (β_{05}), pain (β_{06}), comorbidity severity (β_{07})], Δ daytime sleeping (β_{07}), Δ nighttime sleeping (β_{08}), Δ daytime sleeping*linear time (β_{20}), Δ nighttime sleeping*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: $\text{Cognition}_{it} = \beta_{00} + \beta_{10}(\text{Time}) + \beta_{01}(\text{Age}_i) + \beta_{02}(\text{Education}_i) + \beta_{03}(\text{Gender}_i) + \beta_{04}(\text{BMI}_i) + \beta_{05}(\text{Depression}_i) + \beta_{06}(\text{Pain}_i) + \beta_{07}(\text{Comorbidity}_i) + \beta_{08}(\Delta\ \text{Daytime Sleep}_i) + \beta_{09}(\Delta\ \text{Nighttime Sleep}_i) + \beta_{20}(\Delta\ \text{Daytime Sleep*Time}) + \beta_{30}(\Delta\ \text{Nighttime Sleep*Time}) + r_{1i}(\text{Time}) + r_{oi} + e_{it}$

All variables were evaluated based on their significance levels and their effects on intercept and residual-related variance estimates.[28, 29] While 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) we re-estimated the final MLM described above selecting only two of our three potential sources of participants (i.e., 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 (i.e., 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 to the fully combined original model.

RESULTS

Sample Characteristics

A total of 192 participants provided baseline data. Rates of follow-up were: 78% provided at least partial follow-up data, 6% were deceased, and 16% either refused follow-up, relocated out of the area and thus were unable to participate, or were unable to be contacted. The participants had a mean age of 73.8 ± 9.7 years, 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. 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 stratified by intervention allocation (n=107).

Growth Curve Model

Prior to estimating the growth curve model, we plotted the raw MMSE scores obtained during post-acute rehabilitation and 6-months follow-up for a random subset of participants. This was done to visually inspect change in global cognitive functioning from inpatient hospitalization to 6-months follow-up. Visual inspection suggested differing trajectories of change among study participants, suggesting 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, $\beta = -0.09$, SE = 0.03, $t(80) = -2.58$, $p < .05$, 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 linear time*change in daytime sleep interaction, $\beta = -0.01$, SE = 0.003, $t(80.00) = -3.22$, $p < .01$, 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 by 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 (i.e., study 1 and intervention and control conditions of study 2) was identical to those of the combined model reported above. As such, our results do not appear to be influenced by variance due to study design differences between our sources of participants. Only the combined model is reported here.

In order 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 a hypothetical individual whose amount of daytime sleeping: (a) decreased following hospital discharge (i.e., sleep improved), and (b) increased following hospital discharge (i.e., sleep worsened) (see Figure 1). There was a positive trajectory of 6-month change in global cognitive functioning for an individual

whose amount of daytime sleep decreased following hospital discharge and a negative trajectory of 6-month change in global cognitive functioning for an individual whose amount of daytime sleep increased following hospital discharge.

DISCUSSION

The current study examined the relationships between changes in sleep and changes in cognitive function following an inpatient post-acute rehabilitation stay in older adults. We discovered that older adults whose amount of daytime sleep decreased between their rehabilitation stay and 6-months follow-up experienced positive changes in global cognitive functioning. However, older adults whose amount of daytime sleep increased between their rehabilitation stay and 6-months 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.

Our study expands on previous studies which have examined habitual sleep difficulties and global cognitive functioning in community-dwelling older adults[16, 17] in several substantive ways. First, our sample was comprised of older adults who were enrolled during an inpatient stay, where hospitalized older adults represent an at-risk group for many unwanted negative outcomes.[3, 7] Second, instead of using static indicators of sleep as predictors of long-term cognitive changes,[16, 17] we used change in sleep following hospital discharge to predict change in cognitive functioning following 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. Futhermore, 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 following hospitalization.[3, 6-8] We have added to the literature on predictors of cognitive response to hospitalization in older adults. Importantly, we have identified predictors of cognitive response to hospitalization, namely nighttime sleep disturbance and daytime sleep, that is ripe for interventional work. Cognitive-behavioral treatment for insomnia (CBTi) is an evidence-based treatment in older adults.[32] While 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 impactful for hospitalized older adults. Our results suggest that during and following hospital discharge older adults could likely 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 sleeping,[33] and 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 patient population), light exposure following hospital discharge, and circadian factors on daytime sleeping and cognitive functioning in older adults.

This works adds evidence to our current understanding of the mechanisms through which hospitalization may impact late-life cognitive functioning (and subsequent independence). Previous research has reported that surgery can result in inflammation and cognitive impairment.[35] Additionally, sickness behavior following acute illness is also characterized by both systemic inflammation and cognitive decrements.[36] Both postoperative and posthospital inflammation are normative responses to physical insult; however, these inflammation responses are thought to be relatively short lived, without concomitant long lasting negative consequences. Current understanding suggests that both 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 inflammtion and cytokine levels.[38, 39] As such, following 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/insult that could produce both disturbed sleep/wake patterns and cognitive decline. Future research that longitudinally assesses sleep, inflammation, and cognitive functioning in older adults following hospitalization is needed to further clarify these relationships. Additionally, as sleep and physical activity are related in older adults[40], and physical activity is related to cognitive functioning[41] – future investigations would be well suited to 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. Our study was conducted within a VA setting, and our sample is therefore primarily male. Our results may not generalize to older women. Our analysis did not include information on sleep disorders, such as sleep apnea, which may have associations with daytime sleepiness and cognitive functioning. Additionally, we assessed sleep habits through wrist actigraphy. While actigraphy has been well validated for measurement of nighttime sleep,[24, 25] comparatively little data 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, caution must be had in restricting the daytime sleep of hospitalized older adults, due to potential iatrogenic effects.

In summary, we identified an association between changes in objectively measured daytime sleep and changes in global cognitive functioning following a post-acute rehabilitation stay in older adults. This relationship was observed after accounting for age, education, gender, BMI, comorbidity severity/burden, depression, and pain. Such a relationship extends previous work on sleep and cognition in late-life and could inform theoretical accounts of postoperative and post-hospital cognitive decline to include sleep as a mediator of prolonged inflammation. Results could also inform interventional work aimed at decreasing negative changes following hospitalization in late-life.

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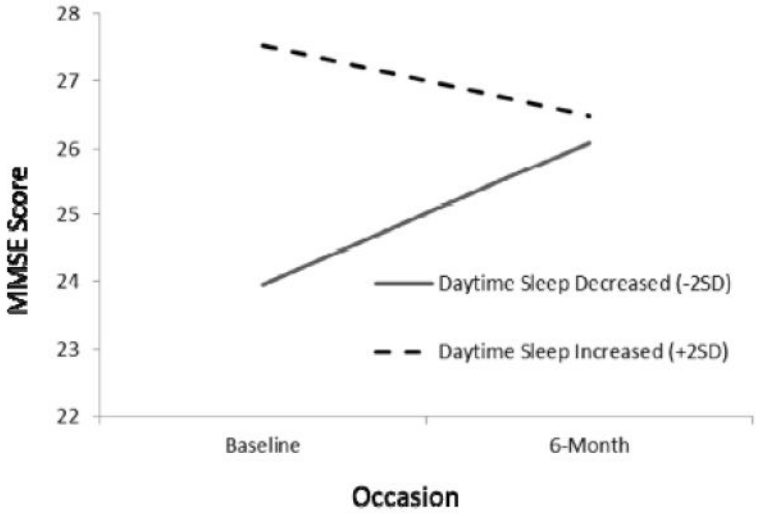

Figure 1. Change in Daytime Sleep and Change in MMSE Scores

Change in daytime sleep was analyzed as a continuous variable, but is graphed dichotomously to easily depict the nature of the results. Two levels of hypothetical change in daytime sleep (i.e., daytime sleep amount reduced and daytime sleep amount increased), defined as 2 standard deviations below and 2 standard deviations above the average amount of change in daytime sleep are shown for illustrative purposes. Note that the Y-axis spans 6 points on the 30 point MMSE scale.

Table 1

Patient Demographics and Descriptive Variables across Groups.

	Total Sample (n=192)		Study 1 (n=85)		Study 2 (n=107)						
					Intervention (n=53)		Control (n=54)				
	Mean (SD)		Mean (SD)		Mean (SD)		Mean (SD)		*F*	*df*	*P*
Age (years)	73.8	(9.4)	75.0	(8.5)	73.3	(10.7)	72.6	(9.5)	1.16	2,189	0.32
Education (years)	13.8	(2.3)	13.6	(3.4)	13.7	(3.0)	14.2	(2.6)	0.63	2,160	0.53
Gender (% male)	97.4	--	98.8	--	96.2	--	96.3	--	--	--	--
BMI	27.32	(7.00)	27.79	(8.91)	27.46	(5.39)	26.44	(4.57)	0.60	2,181	0.55
GDS Score	1.43	(1.37)	1.57	(1.49)	1.19	(1.27)	1.47	(1.27)	1.54	2,178	0.22
GPM Score	49.00	(28.34)	47.13	(28.70)	52.23	(28.76)	48.51	(27.62)	1.25	2,186	0.29
CIRS Total Score	22.34	(5.39)	22.69	(5.62)	21.17	(5.95)	22.88	(4.32)	0.52	2,179	0.6
Δ Daytime Sleep (minutes)	−11.06	(90.42)	−10.81	(127.53)	0.06	(77.31)	−23.01	(75.50)	0.56	2,89	0.57
Δ Nighttime Wake (minutes)	2.00	(103.99)	13.37	(132.21)	9.39	(71.51)	−13.17	(113.53)	0.58	2,89	0.56
Δ MMSE Score	0.23	(2.90)	0.39	(2.38)	0.43	(2.63)	−0.10	(3.50)	0.41	2,114	0.66

Notes: BMI=Body Mass Index; GDS=Geriatric Depression Scale; GPM=Geriatric Pain Measure; CIRS=Cormorbidity Illness Rating Scale; Δ Scores represent 6-month follow-up minus baseline; There were no differences between the groups on any study-related variables of interest.

Table 2

Conditional Growth Models for 6-Month Change in MMSE (n=192).

	Fixed Effects		
Predictor Variable	***B***	***SE***	***t***
Occasion	0.44	0.28	1.56
Age	−0.09	0.03	−2.58*
Education	0.03	0.06	0.70
Gender	1.80	1.55	1.16
BMI	0.02	0.05	0.45
GDS Score	−0.17	0.22	−0.78
GPM Score	−0.01	0.01	−0.69
CIRS Score	−0.06	0.06	−0.87
Δ Daytime Sleep	0.02	0.01	3.70**
Δ Nighttime Sleep	0.001	0.01	0.16
Linear Time * Δ Daytime Sleep	−0.01	0.003	−3.22***
Linear Time * Δ Nighttime Sleep	−0.0005	0.003	−0.16
	Random Effects		
Covariance parameter estimate	*B*	*SE*	*Z*
Occasion	0.00	0.00	-- [a]
	Within Pseudo R^2		26%
	Between Pseudo R^2		46%

Notes: BMI=Body Mass Index; GDS=Geriatric Depression Scale; GPM=Geriatric Pain Measure; CIRS=Cormorbidity Illness Rating Scale; Daytime Sleep measured as minutes spent asleep during the day; Nighttime Sleep measured as minutes spent asleep at night; Δ Scores represent 6-month follow-up minus baseline; .

*** Predictor is significant at .001 level;

** Predictor is significant at the .01 level;

* Predictor is significant at the .05 level.

[a] Variance too small to be estimated. The final Hessian matrix is not positive definite although all convergence criteria are satisfied. The test statistic and confidence interval cannot be computed.