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SCIENTIFIC INVESTIGATIONS

Preliminary investigation of interactive associations of sleep and pain with cognition in sedentary middle-aged and older adults

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Study Objectives: The objective of this study was to examine independent and interactive associations between self-reported sleep (sleep efficiency and total sleep time [TST]) and pain with cognition in sedentary middle-aged and older adults.

Methods: Seventy-five sedentary adults at least 50 years of age (M_{age} = 63.24, standard deviation = 8.87) completed 14 daily diaries measuring sleep and pain. Weekly average sleep efficiency, TST, and pain were computed. Participants also completed computerized cognitive tasks: Letter Series (reasoning), *N*-back (working memory), Symbol Digit Modalities Test (processing speed, attention), and Number Copy (processing speed). Multiple regression analyses were conducted to determine independent and interactive (with pain) associations of sleep efficiency and TST with cognition, controlling for age, education, and sex.

Results: Sleep efficiency and pain interacted in their associations with Letter Series performance and *N*-back difference scores (2-back minus 1-back). Specifically, higher sleep efficiency was associated with better reasoning and working memory in those with highest pain but not average or lowest pain. TST and pain also interacted in their associations with Letter Series performance. Specifically, longer TST associated with worse reasoning in those with lowest (not average or highest) pain.

Conclusions: Preliminary results show that in sedentary middle-aged and older adults, pain and sleep interact in their associations with executive function tasks. Higher sleep efficiency may be associated with better reasoning and working memory in those with highest pain. Lower TST may be associated with better reasoning in those with lowest pain. Studies evaluating temporal associations between sleep, pain, and cognition are needed.

Keywords: sleep disturbance; cognitive performance; pain; middle-aged adults; older adults

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Sleep and pain are independently associated with cognition in older adults. However, it is currently unknown whether sleep and pain interact in their association with cognition in middle-aged and older adults living sedentary lifestyles.

Study Impact: Preliminary results suggest sleep and pain interact in their associations with executive functions (reasoning and working memory). In terms of associations with better executive functioning, higher sleep efficiency may be particularly important for those with highest pain, while lower total sleep time may be particularly important for those with lowest pain.

INTRODUCTION

In middle-aged and older adults, sleep[1–3] and pain[4,5] have been shown to be independently associated with cognitive performance. It is also well known that sleep and pain have a reciprocal relationship.[6] There are limited investigations, however, regarding how sleep and pain may interact in their association with cognition. Therefore, in the present study, we sought to preliminarily investigate the interactive associations of sleep and pain with cognitive performance in middle-aged and older adults. These types of examinations are necessary first steps toward establishing the nature of the sleep, pain, and cognition relationship. Such information is important, particularly in vulnerable populations that experience generally more frequent pain, such as sedentary individuals. This will improve understanding of potential modifiable factors associated with cognitive performance and could also facilitate targeted treatments aimed at improving sleep and associated symptoms related to daytime functioning.

Cumulative evidence suggests that poor sleep efficiency (ie, percentage of time spent sleeping while in bed, which is a global measure of how consolidated one's sleep is) impairs cognitive performance in older adults. For instance, poor self-reported sleep efficiency has been associated with worse executive functions such as attentional control,[1] working memory,[7,8] abstract reasoning,[8] and worse global cognition[1,8] and higher scores on dementia rating scales.[9] Despite some exceptions documenting no associations between total sleep time (TST)

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and executive function in older adults,[10] most research findings point to associations between TST and cognitive performance in middle-aged and older adults. For example, some studies suggest that shorter self-reported TST (ie, <6 hours) is associated with worse global cognitive performance.[11] We also previously showed that longer TST (as assessed by actigraphy) was associated with better processing speed and attention in primarily middle-aged and older cardiac patients with implantable cardioverter defibrillators.[12] Although some studies show a curvilinear relationship between TST and cognitive performance (ie, both long and short TST are associated with worse cognition) across a range of tasks,[13,14] another study suggests that the curvilinear relationship between TST and cognition may only be observed in younger and older adults and not in middle-aged adults.[15] Taken together, there are numerous studies evaluating the independent associations between sleep efficiency, TST, and cognition. However, there is a lack of studies that examine other potential interacting variables of this relationship, including poor health factors that are more common with increasing age, such as pain.

Research findings in middle-aged and older adults are generally consistent regarding the negative associations between pain and cognitive functioning. For instance, relative to older adults with no pain, those with chronic lower back pain have been shown to have worse cognitive performance across a range of tasks.[16] Another study found that in middle-aged men, relative to those without chronic pain, those with chronic pain had worse performance on an attention and processing speed task.[17] In community-dwelling older adults (70+ years of age), the degree of pain severity has also been associated with worse performance on tasks measuring executive function, attentional capacity, and verbal memory.[18]

Although limited, there are a few studies that suggest that pain may interact with sleep in the association with cognitive performance. For instance, we recently reported that in older adults, patterns of associations between self-reported sleep and objective cognition differed between older adults with a history or no history of chronic pain.[4] Specifically, we observed that higher wake time after sleep onset was associated with worse attention and processing speed, and worse sleep efficiency was associated with worse verbal memory in older adults with a history of chronic pain, but not in those without a history of chronic pain. These results highlight that sleep and pain may interact and suggest that achieving adequate sleep efficiency may be particularly important for those experiencing chronic pain. Another study that has assessed a model of both sleep and pain in relation to cognition found that in adults with fibromyalgia self-reported sleep quality, but not TST, mediates the association between pain and sustained attention performance, suggesting that improving sleep quality may mitigate the effects of more severe pain on attention.[19] However, this study explored cross-sectional analyses, thus precluding any definitive conclusions regarding temporal cause and effect relationships between sleep, pain, and cognition. We also previously observed that in primarily middle-aged and older adult cardiac patients with implantable cardioverter defibrillators higher sleep efficiency (as assessed by actigraphy) was associated with better attention and processing speed performance, but only in those with more severe pain.[20] These findings show the importance of examining sleep and cognition associations in the context of pain levels. To date there is no research examining the potential interacting role of pain and sleep on cognitive performance in middle-aged and older adults who are sedentary. This type or research is warranted, as it could help answer questions such as who may be the most vulnerable to associations between worse pain and cognition (eg, those with worse sleep efficiency?) or alternatively worse sleep and cognition (eg, those with more severe pain?). Given the reciprocal relationship between sleep and pain and limited research findings in the area of sleep/pain/cognition, proposing a conceptual model at this point with either sleep or pain as a hypothesized mediator to be tested in cross-sectional analyses seems premature. Thus, in the present preliminary study, we sought to examine potential sleep and pain interactive associations with cognition and then examine both sleep and pain as potential moderators. Although not confirmatory, this type of approach will provide further insight into the exact nature of how sleep and pain may influence each other in their association with cognitive performance.

The present preliminary study examined the interactive associations of pain and two self-reported (ie, diary measured) sleep parameters (sleep efficiency and TST) with performance on tasks measuring executive functions (reasoning, working memory), attention and processing speed in middle-aged and older adults who were sedentary. Understanding the factors associated with the sleep and cognition relationship has important clinical implications, as it may identify subgroups of individuals (eg, individuals with high or low pain) that may benefit most from either protective effects of sleep or interventions aimed at improving poor sleep. In the present study, we hypothesized that sleep efficiency and pain would interact in their associations with cognitive performance on tasks measuring executive function (eg, reasoning, working memory) and attention and processing speed function. Specifically, we hypothesized that higher sleep efficiency would be associated with better cognitive function, particularly in participants with higher pain. Given the lack of findings showing the interactive associations between TST and pain on cognition, we did not have specific hypotheses regarding whether the association between TST and performance across cognitive domains (eg, executive function, attention, and processing speed) would interact with pain. However, given the known relationship between TST and cognitive function, we explored these potential sleep/pain interactive associations with cognition in the present sample.

METHODS

Participants

Participants were recruited as part of a larger randomized controlled trial (Active Adults Mentoring Project study) through a university community in the southeastern United States. The Active Adults Mentoring Project study aimed at increasing exercise behaviors in sedentary middle-aged and older adults aged 50 years and older. Full methods are reported elsewhere.[21] Briefly, participants were assigned to either a 16-week Active Lifestyle intervention where they

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received weekly group-based behavioral counseling targeting physical activity or a Healthy Education control group where they received health education related to late-life. The present study used data from the 14 days of baseline, before intervention assignment. Participants were included if they (1) were aged 50 years or older, (2) self-reported a sedentary lifestyle (ie, did not currently meet physical activity guidelines of 150+ min/wk of moderate or vigorous physical activity during the last 6 months[22]), (3) were free from any medical factors (eg, major cardiovascular disease, recent cancer treatment) that would interfere with unsupervised exercise, and (4) did not have cognitive impairment (ie, scored > 27 on the Telephone Interview for Cognitive Status, where the possible values range from 0 to 47 and higher scores represent better global cognitive function). The University of Florida Institutional Review Board approved all study procedures, and all participants provided written informed consent.

Sleep

Each morning on awakening, participants were instructed to complete sleep diaries in a paper format.[23] These were completed for each of the 14 days of baseline. Sleep diaries reported the following values: sleep onset latency (in minutes); total time spent awake (in minutes) after sleep onset; TST (in minutes), total time in bed (in minutes), and sleep efficiency (computed as the ratio of TST to time in bed × 100%). Daily sleep efficiency and TST values were averaged to compute a single weekly value. Baseline weekly values were averaged to compute the sleep efficiency and TST parameters.

Pain

Participants completed daily diaries assessing pain intensity from a scale of 0 (no pain) to 10 (worst pain imaginable). Daily scores were averaged to compute a weekly pain rating. Baseline weekly values were averaged to compute the pain parameter.

Cognitive tasks

A computerized cognitive battery was administered during the first baseline visit of the parent study, which was conducted in the laboratory setting before the 14 days of sleep diary data collection. Cognitive tasks were computerized using the DirectRT experimental generation software[24] and administered through MediaLab software.[25] Tasks were chosen to represent a range of cognitive performance across higher and lower order domains: executive functioning (Letter Series, *N*-back task), attention/processing speed (symbol digit modalities test [SDMT], Number Copy task).

Letter Series

The Letter Series task[26] measures inductive reasoning, an executive function. Participants are presented with a series of letters on the computer screen and instructed to choose the letter (from five possible choices) that would continue the established pattern. Participants were instructed to complete as many of the series as possible in 4 minutes. The total number of correct trials was computed as the outcome measure of interest, where higher scores indicate better performance.

N-*back*

The *N*-back task measures working memory, which is considered an executive function.[27] In this task, participants view a single letter in 48-point font in the center of the computer screen and decide whether that letter matched a target letter present N trials previously, with N varying from 0 to 2 trials. They are instructed to respond as fast and accurately as possible. In the 2-back condition, participants judge whether the current letter matched the letter presented 2 letters previously, indicating their response with designated "yes" and "no" keyboard keys. Letters remained visible until a response was made, with a 1-second interstimulus interval. We examined 2 outcome measures of interest. The first was the total number of correct 2-back trials, with higher scores representing better performance. The second was the difference score between total number correct on the 1-back trials minus the total number correct on the 2-back trials. This difference score more accurately represents effects of added working memory resources needed to perform the 2-back over the 1-back task. In this case, smaller difference scores indicate more working memory resources available to perform the task (ie, better working memory performance).

SDMT

The SDMT[28] measures sustained attention and processing speed.[29] In this task, participants are presented with a legend at the top of the computer screen consisting of 9 digit and symbol pairs. A series of symbols with blank spaces are shown below the legend. Participants are instructed to match the corresponding number (provided in the legend) with each symbol and to complete as many responses as possible within 120 seconds. The number of correct responses entered in the time limit was computed (ie, total items with correct numbers that correspond with the symbol) as the outcome of interest, with higher scores representing better performance.

Number Copy task

The Number Copy task measures processing speed function.[28] Participants are presented with a list of numbers and are instructed to match the same number in a blank space underneath. Participants were to provide as many matching numbers as possible in 120 seconds. The total number of correct answers was computed as the outcome of interest, with higher scores representing better performance.

Statistical analyses

Multiple linear regressions were carried out using the PROCESS macro (model 1)[30] in SPSS (Version 24). Criterion variables included performance on cognitive measures: Letter Series, *N*-back, SDMT, and Number Copy. Sleep parameters were examined as separate independent variables in regression models because of their high degree of correlation (Pearson correlation coefficient = 0.34, $P = .003$). Independent variables included the following: diary reported sleep parameter (sleep efficiency or TST), pain level, and the sleep parameter (sleep efficiency or TST) × pain interaction. Analyses controlled for age, sex, and education. Variables that made up the interaction term (sleep

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parameters and pain) were mean centered (using the PROCESS macro) before analyses. Significant sleep efficiency by pain and TST by pain interactions were clarified in 2 ways. First, we calculated simple slopes of the association between the sleep parameter (sleep efficiency or TST) and cognitive performance for sample-estimated pain values (ie, treating pain as the moderator) characterized as follows. For pain, the simple slopes were calculated at lowest pain (1 standard deviation below mean value: 0.07/10), average pain (mean value of 1.55/10), and highest pain (1 standard deviation above mean value: 3.03/10). We also calculated simple slopes of the association between pain and cognitive performance for sample-estimated sleep values (ie, treating sleep as the moderator) characterized as follows. For sleep efficiency, the simple slopes were calculated at lowest sleep efficiency (1 standard deviation below mean value: 81.25%), average sleep efficiency (mean value of 88.04%), and highest sleep efficiency (1 standard deviation above mean value: 94.83%). Likewise, for TST, the simple slopes were calculated at lowest TST (1 standard deviation below mean value: 380.24 minutes), average TST (mean value of 431.55 minutes), and highest TST (1 standard deviation above mean value: 482.86 minutes).

Second, we examined Johnson-Neyman output in PROCESS[30] to determine (1) more specific points along the pain ratings (when pain was treated as the moderator) where the relationship between the independent variable (sleep efficiency, TST) and criterion variable (cognitive performance) transitions from significant to nonsignificant or (2) more specific points along the sleep variables (when sleep was treated as the moderator) where the relationship between pain and cognitive performance transitions from significant to nonsignificant. Following statistical recommendations,[31] given the paucity of studies regarding pain, sleep, and cognition in middle-aged and older adults, we accepted the false-positive risk in our analyses, and no familywise error correction was applied. All regression results were evaluated at an α level of $P < .05$.

RESULTS

Participant characteristics and assumptions of normality

A total of 91 participants completed the baseline portion of the parent study. A total of 76 participants (M_{age} = 63.24, standard deviation = 8.87) had full data available for all independent and outcome variables of interest in the present study. Distributions of continuous independent variables and covariates in this sample were assessed for normality by examining the skewness and kurtosis values.[32,33] Skewness and kurtosis values for sleep efficiency, TST, pain, education, and age were all within acceptable limits according to Tabachnick and Fidell[33] (absolute values < 3 for skewness and < 10 for kurtosis): sleep efficiency (skewness = −2.53, kurtosis = 9.52), TST (skewness = −0.423, kurtosis = 1.11), pain (skewness = 1.21, kurtosis = 1.55), age (skewness = 0.359, kurtosis = −0.434), and education (skewness = −0.103, kurtosis = −0.877). We also evaluated the presence of multivariate outliers by computing Mahalanobis distances and examining whether values differed from expected normal χ^2 distributions with same degrees of freedom ($P < .001$). One multivariate outlier was identified, and this case was removed from the dataset. The distribution normality values of this new dataset (n = 75) were examined. All skewness and kurtosis values remained within acceptable limits: sleep efficiency (skewness = −1.62, kurtosis = 4.11), TST (skewness = 0.05, kurtosis = −0.19), pain (skewness = 1.21, kurtosis = 1.51), age (skewness = 0.34, kurtosis = −0.46), and education (skewness = −0.10, kurtosis = −0.86). Participant demographics and values for sleep, pain, and cognitive measures for the sample included in subsequent regression analyses (n = 75) are provided in **Table 1**.

Multiple regression results: sleep efficiency

Letter Series (reasoning)

For Letter Series, the full regression model was significant and explained approximately 27% of variance in performance (full model $R = 0.52$, full model $R^2 = 0.27$, $P = .001$). As shown in **Table 2**, sleep efficiency and pain were not independently associated with Letter Series performance. However, the sleep efficiency and pain interaction was associated with Letter Series performance, and this interaction explained approximately 5% of the variance in performance (R^2 change = 0.05, $P = .03$).

Pain as a moderator: As shown in **Figure 1**, at the highest levels of pain, greater sleep efficiency was associated with better Letter Series performance ($B = 0.14$, standard error [SE] = 0.07, $P = .04$). Sleep efficiency was not associated with Letter Series performance at average ($B = 0.004$, SE = 0.0,5 $P = .94$) or lowest ($B = −0.13$, SE = 0.09, $P = .17$) pain levels.

Exploration of Johnson-Neyman output revealed 19% (14 individuals) of sample-estimated values fell into the significance range of highest pain, which was estimated at a value of approximately 2.8/10 and higher.

Sleep as a moderator: Additional simple slope analyses examining sleep as a moderator showed that at lowest levels of sleep efficiency, higher pain was associated with worse Letter Series performance ($B = −0.73$, SE = 0.35, $P = .04$). Pain was not associated with Letter Series performance at average ($B = −0.10$, SE = 0.23, $P = .67$) or highest ($B = 0.53$, $SE = 0.38$, $P = .17$) sleep efficiency levels.

Exploration of Johnson-Neyman output revealed 16% (12 individuals) of sample-estimated values fell into the significance range of lowest sleep efficiency, which was estimated at a value of approximately 83% and lower.

N-*back (2-back; working memory)*

For the 2-back task, the full regression model was nonsignificant (full model $R = 0.21$, full model $R^2 = 0.04$, $P = .79$). As shown in **Table 2**, performance on the 2-back task was not associated with any of the examined independent variables.

N-*back difference scores (1-back minus 2-back; additional working memory resources needed)*

For the *N*-back difference score, the full regression model was significant and explained approximately 23% of variation in performance (full model $R = 0.48$, full model $R^2 = 0.23$,

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Table 1—Demographics, cognition, pain, and sleep outcomes of study sample of sedentary older adults (n = 75).

Variable	Mean (SD)	Range
Age	63.24 (8.87)	50.00–87.00
Sex (% male)	17% male	—
Race		
Caucasian (n, %)	68 (91%)	—
African American (n, %)	3 (4%)	—
Asian (n, %)	1 (1%)	—
Biracial (n, %)	1 (1%)	—
Other (n, %)	2 (3%)	—
Education	16.19 (2.20)	12.00–20.00
TICS score	37.75 (.44)	28.00–47.00
Pain level	1.55 (1.48)	0.00–7.00
Sleep measures		
Sleep efficiency (%)	88.04 (6.79)	58.77–97.98
Total sleep time (minutes)	431.55 (51.31)	320.83–548.29
Cognitive measures		
Letter Series (total correct)	6.74 (3.10)	1.00–14.00
N-back (2-back; total correct)	89.65 (13.94)	2.00–100.00
N-back difference score (total correct of 1-back minus 2-back)	6.15 (8.58)	−31.00 to 28.00
SDMT (total correct)	23.01 (4.78)	1.00–30.00
Number copy (total correct)	41.80 (6.38)	1.00–50.00

SDMT = symbol digit modalities test, TICS = telephone interview for cognitive status, — = not applicable.

P = .005). As shown in **Table 2**, sleep efficiency and pain were not independently associated with performance. However, the sleep efficiency and pain interaction was associated with *N*-back difference scores, and this interaction explained approximately 8% of the variance in performance (R^2 change = 0.08, P = .009).

Pain as a moderator: As shown in **Figure 2** (for comparison across tasks/figures, *y*-axis values reverse coded so that higher values represent lower difference scores), at highest levels of pain, greater sleep efficiency was associated with lower (ie, better working memory) *N*-back difference scores (B = −0.62, SE = 0.19, P = .002). Sleep efficiency was not associated with *N*-back difference scores at average (B = −0.16, SE = 0.15, P = .27) or lowest (B = 0.29, SE = 0.26, P = .26) pain levels.

Exploration of Johnson-Neyman output revealed 35% (26 individuals) of sample-estimated values fell into the significance range of highest pain, which was estimated at a value of approximately 2.0/10 and higher.

Sleep as a moderator: Additional simple slope analyses examining sleep as a moderator showed that at highest levels of sleep efficiency, increased pain was associated with lower (ie, better working memory) *N*-back difference scores (B = −2.74, SE = 1.07, P = .01). Pain was not associated with *N*-back difference scores at average (B = −0.60, SE = 0.65, P = .36) or lowest (B = 1.55, SE = 0.97, P = .12) sleep efficiency levels.

Exploration of Johnson-Neyman output revealed two regions of significance at sample-estimated sleep efficiency values. Results showed 37% (28 individuals) of sample-estimated values fell into the significance range of highest sleep efficiency, which was estimated at a value of approximately 91% or higher. An additional region of significance along the sleep efficiency moderator was identified, with 9% (7 individuals) of sample-estimated sleep efficiency values of 78% and lower showing positive associations. That is, higher pain was associated with larger *N*-back difference scores (ie, worse working memory performance).

SDMT (attention and processing speed)

For SDMT, the full regression model was significant and explained approximately 34% of variation in performance (full model R = 0.58, full model R^2 = 0.34, P < .001). As shown in **Table 2**, for SDMT, sleep efficiency and pain were not independently associated with performance. Additionally, sleep efficiency did not interact with pain in its association with SDMT performance.

Number Copy (processing speed)

For the Number Copy task, the full regression model was significant, and explained approximately 27% of variation in performance (full model R = 0.52, full model R^2 = 0.27, P = .001). As shown in **Table 2**, sleep efficiency and pain were not independently associated with Number Copy performance. The interaction between sleep efficiency and pain was also not associated with Number Copy performance.

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Table 2—Multiple regression results of sleep efficiency, pain, and physical activity predicting cognitive performance (n = 75).

Cognitive Task	*B*	SE	*t*	*P*
Letter Series				
Sleep efficiency	0.004	0.05	0.07	.94
Pain level	−0.10	0.23	−0.44	.66
Sleep efficiency × pain	0.09	0.04	2.19	.03
Age	−0.14	0.04	−3.78	.00
Sex	−0.50	0.84	−0.60	.55
Education	0.28	0.15	1.86	.07
N-back (2back)				
Sleep efficiency	0.02	0.27	0.06	.95
Pain level	−1.32	1.18	−1.12	.27
Sleep efficiency × pain	0.03	0.21	0.12	.90
Age	−0.12	0.19	−0.63	.53
Sex	−4.56	4.34	−1.05	.30
Education	0.24	0.77	0.31	.76
N-back (1-back minus 2-back)				
Sleep efficiency	−0.16	0.15	−1.11	.27
Pain level	−0.62	0.65	−0.95	.34
Sleep efficiency × pain	−0.31	0.12	−2.67	.009
Age	0.27	0.10	2.64	.01
Sex	1.57	2.40	0.66	.51
Education	−0.18	0.43	−0.41	.68
SDMT				
Sleep efficiency	0.11	0.08	1.47	.15
Pain level	−0.25	0.34	−0.74	.46
Sleep efficiency × pain	0.02	0.06	0.32	.75
Age	−0.26	0.05	−4.92	.00
Sex	−2.70	1.24	−2.18	.03
Education	0.29	0.22	1.32	.19
Number Copy				
Sleep efficiency	−0.01	0.11	−0.05	.96
Pain level	−0.87	0.47	−1.86	.07
Sleep efficiency × pain	0.10	0.08	1.16	.25
Age	−0.32	0.07	−4.28	.00
Sex	−0.91	1.73	−0.52	.60
Education	0.21	0.31	0.70	.49

SDMT = symbol digit modalities test, SE = standard error.

Multiple regression results: total sleep time

Letter Series (reasoning)

For Letter Series, the full regression model was significant and explained approximately 29% of variation in performance (full model $R = 0.54$, full model $R^2 = 0.29$, $P < .001$). As shown in **Table 3**, TST and pain were not independently associated with performance. However, the interaction between TST and pain was associated with Letter Series performance, explaining 9% of variation in performance (R^2 change = 0.09, $P = .005$).

Pain as a moderator: As shown in **Figure 3**, simple slope analyses revealed that higher (ie, longer) TST was associated with worse Letter Series performance only in individuals with lowest pain ($B = -0.03$, SE = 0.01, $P = .008$). TST was not associated with Letter Series performance in those with average ($B = -0.01$, SE = 0.01, $P = .26$) or highest ($B = 0.01$, SE = 0.01 $P = .16$) pain.

Exploration of Johnson-Neyman output revealed 47% (35 individuals) of sample-estimated values fell into the significance range of lowest pain, which was estimated at a value of approximately 1.0/10 and lower. Johnson-Neyman output also showed an

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Figure 1—Association between subjective sleep efficiency and Letter Series performance, at varying levels of self-reported pain in middle-aged and older sedentary adults.

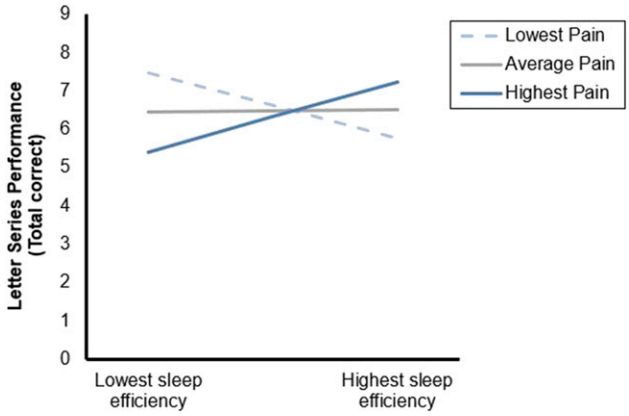
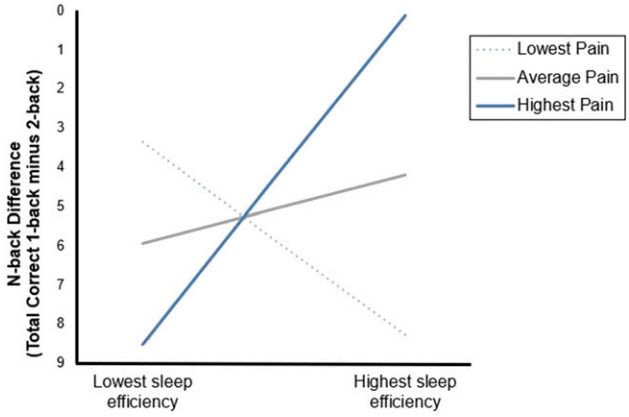


Figure 2—Association between subjective sleep efficiency and N-back difference score performance, at varying levels of self-reported pain in middle-aged and older sedentary adults.



For comparison across tasks/figures, *y*-axis values reverse coded so that higher values represent lower difference scores (ie, better working memory performance).

additional region of significance for the pain moderator, revealing 9% (7 individuals) of sample-estimated pain values of 3.8/10 and higher showed a positive association between TST and Letter Series performance.

Sleep as a moderator: Additional simple slope analyses revealed that higher pain was associated with worse Letter Series performance only in individuals with lowest TST ($B = -0.73$, SE = 0.27, $P = .01$). Pain was not associated with Letter Series performance in those with average ($B = -0.03$, SE = 0.23, $P = .88$) or highest ($B = 0.66$, SE = 0.37, $P = .08$) TST.

Exploration of Johnson-Neyman output revealed 2 regions of significance at sample-estimated TST values. Specifically, 28% (21 individuals) of sample-estimated values fell into the significance range of lowest TST, which was estimated at a value of approximately 400 minutes and lower. An additional region of significance showed that 9% (7 individuals) of sample-estimated TST values of 497 minutes and higher showed a positive association between pain and Letter Series performance.

Table 3—Multiple regression results of total sleep time, pain, and physical activity predicting cognitive performance (n = 75).

Cognitive Task	*B*	SE	*t*	*P*
Letter Series				
TST	−0.007	0.007	−1.14	.26
Pain level	−0.04	0.23	−0.16	.88
TST × pain	0.01	0.005	2.93	.005
Age	−0.12	0.04	−3.32	.002
Sex	−0.38	0.85	−0.45	.66
Education	0.39	0.15	2.70	.009
N-back (2-back)				
TST	0.03	0.03	1.03	.31
Pain level	−1.10	1.17	−0.94	.35
TST × pain	0.01	0.02	0.34	.73
Age	−0.16	0.19	−0.84	.40
Sex	−5.36	4.37	−1.23	.22
Education	0.30	0.75	0.40	.70
N-back (1-back minus 2-back)				
TST	−0.03	0.02	−1.37	.17
Pain level	−0.24	0.69	−0.34	.73
TST × pain	−0.01	0.01	−0.43	.67
Age	0.33	0.11	2.93	.005
Sex	2.10	2.58	0.81	.42
Education	−0.53	0.44	−1.19	.24
SDMT				
TST	−0.002	0.01	−0.32	.75
Pain level	−0.37	0.34	−1.09	.28
TST × pain	0.004	0.01	0.61	.54
Age	−0.27	0.06	−4.86	.00
Sex	−2.48	1.28	−1.94	.06
Education	0.35	0.22	1.58	.11
Number Copy				
TST	0.004	0.01	0.27	.79
Pain level	−0.86	0.47	−1.82	.07
TST × pain	0.01	0.01	0.70	.48
Age	−0.33	0.08	−4.29	.00
Sex	−1.01	1.77	−0.57	.57
Education	0.32	0.30	1.07	.29

SDMT = symbol digit modalities test, SE = standard error, TST = total sleep time.

N-*back (2-back; working memory)*

For the 2-back task, the full regression model was nonsignificant (full model $R = 0.25$, full model $R^2 = 0.06$, $P = .62$). As shown in **Table 3**, TST and pain were not independently

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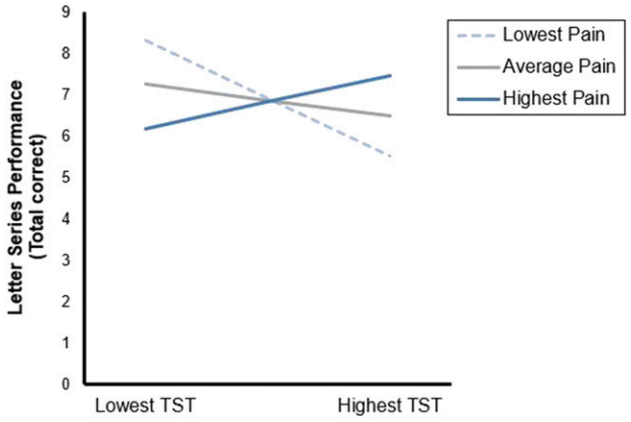
Figure 3—Association between subjective total sleep time and Letter Series performance, at varying levels of self-reported pain in middle-aged and older sedentary adults.



associated with 2-back performance. Additionally, the interaction between TST and pain was not associated with performance.

N-*back difference scores (1-back minus 2-back; additional working memory resources needed)*

For the *N*-back difference scores, the full regression model was nonsignificant (full model $R = 0.36$, full model $R^2 = 0.13$, $P = .12$). As shown in **Table 3**, TST and pain were not associated with 2-back performance. Additionally, the interaction between TST and pain was not associated with performance.

SDMT (attention and processing speed)

For SDMT, the full regression model was significant and explained approximately 32% of variation in performance (full model $R = 0.56$, full model $R^2 = 0.32$, $P < .001$). However, as shown in **Table 3**, TST was not associated with performance, and the interaction between TST and pain was also not associated with performance. The significance of the overall regression model was driven by associations of older age and worse SDMT performance.

Number Copy (processing speed)

For Number Copy, the full regression model was significant and explained approximately 26% of variation in performance (full model $R = 0.51$, full model $R^2 = 0.26$, $P = .002$). However, TST was not associated with performance, and the interaction between TST and pain was not associated with performance. The significance of the overall regression model was driven by associations of older age and worse Number Copy performance.

DISCUSSION

The present study assessed whether self-reported sleep efficiency or TST interacted with pain in their associations with cognitive performance in sedentary community dwelling middle-aged and older adults. Findings revealed that sleep efficiency and TST interacted with pain in their associations with performance on tasks measuring executive function. Specifically, we found interactive associations of sleep efficiency and pain with reasoning and working memory, as well as interactive associations of TST and pain with reasoning.

Our hypothesis that higher sleep efficiency would be associated with better performance on cognitive tasks measuring executive function, attention, and processing speed, particularly in participants with higher pain, was partially supported. We observed the expected association on both a reasoning measure (ie, Letter Series) and working memory measure (ie, *N*-back difference scores), but unlike our previous results in cardiac patients,[20] we found no such associations for attention and processing speed measures. We also observed a largely similar pattern of results when alternatively examining sleep as a moderator of the pain and cognition relationship. That is, it was only at the lowest sleep efficiency levels that worse pain was associated with worse reasoning (shown in both the simple slope and Johnson-Neyman analyses) and working memory (shown only in the Johnson-Neyman analyses). Given that objective sleep efficiency has been associated with frontal executive functioning in cognitively intact community-dwelling older adults,[34] and the known overlap of brain regions involved in pain and executive function (eg, dorsolateral prefrontal cortex[35,36]), it is possible that in individuals with highest pain, not achieving adequate sleep efficiency is associated with exacerbation of reasoning and working memory disruption. In other words, it is conceivable that individuals with higher pain who cannot sleep through their pain may experience more negative effects on executive function. It should be noted that the qualification of highest pain (approximately 3/10) in our sample was not typical of a high pain rating (usually these are greater than 5/10), and thus this may have contributed to the null findings for attention and processing speed tasks. In sum, results suggest that in sedentary middle-aged and older adults with higher pain, it is important to achieve adequate sleep efficiency to potentially minimize disrupted executive functioning underlying reasoning and working memory performance.

Our results for TST indicated that sleep and pain interact in their association with reasoning (ie, Letter Series) performance. Longer TST was associated with worse reasoning in participants reporting lowest pain. One potential explanation for this finding is related to the range of TST, which was approximately 5–9 hours in our sample (**Table 1**). Given that sleep duration recommendations[37] for older adults is approximately 7–8 hours per night, we speculate that in participants with lowest pain, oversleeping is associated with worse reasoning. In those with higher levels of pain, increasing sleep duration may not impact reasoning because this extra sleep is needed to compensate for increased pain experienced during the day. Taken from another perspective (examining sleep as a moderator), we found that higher pain was only associated with worse reasoning in those with lowest TST, again suggesting the potential need for adequate sleep duration to mitigate negative associations with reasoning performance. As the present results are considered preliminary, more work is needed in samples of middle-aged and older adults with larger ranges of pain and across additional measures of executive function to fully explore these potential

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explanations and to determine temporal precedence of the TST and pain interactive associations with cognitive function.

Our finding of a lack of independent associations between sleep efficiency, TST, and pain with cognitive performance (reasoning, working memory, attention, and processing speed) is generally inconsistent with findings in other populations (eg, healthy older adults, middle-aged and older adult cardiac patients).[1,2,4,5,12] These prior studies have generally showed better sleep efficiency, both long and short sleep duration, and less pain, are associated with better cognitive performance, typically in executive functions. However, it is possible that in middle-aged and older adults who are sedentary, sleep efficiency and TST are only associated with cognition in the context of other poor health factors such as pain (or vice versa), underscoring the need to examine these factors in such investigations. It is also possible that the independent sleep and pain associations could be observed in other cognitive tasks not measured in this study, and thus future work should continue to explore other cognitive measures of executive function, attention, and processing speed.

The present study has several limitations. First, as stated earlier, given the low average pain level (**Table 1**), results may not necessarily generalize to middle-aged and older adults with higher levels of pain. Second, given that sleep was measured by self-reported sleep diaries, it will be important for future work to examine whether similar patterns of associations exist between objective sleep (eg, measured by actigraphy or polysomnography), pain, and cognitive performance. Third, a potential limitation concerns the timing of the cognitive and sleep assessments. That is, the cognitive battery was administered before the sleep diary assessments. It may be important for future work to investigate current findings in the context of more closely matched cognition and sleep assessments, such as cognitive performance during a point within the timeframe of the sleep assessments (eg, beginning of week 2). Finally, although we adhered to the general rule of thumb in regression analyses of examination of 1 independent variable per every 10 cases,[38] investigation of these variables in larger samples would strengthen reliability of our findings. It should also be noted that, although there are no strict guidelines on the minimum number of cases required in the regions of significant to interpret findings using the Johnson-Neyman output of the PROCESS macro,[39] our findings showed a relatively small sample of participants included in each region of significance. For instance, for analyses examining sleep efficiency, the number of individuals estimated to fall within the highest pain category for Letter Series and *N*-back tasks (and thus exhibit the association between sleep and cognitive performance) were 14 and 26, respectively. Similarly, for analyses examining TST and Letter Series performance, approximately 35 individuals were estimated to fall within the significance region of lowest pain and 7 individuals within the additional regions of significance for highest pain (and thus exhibit the positive association between sleep and cognitive performance). Although the estimated numbers of individuals in the critical regions could be considered small, given the large percentage (25–35%[40]) of sedentary middle-aged and older adults in the United States, it is important when interpreting the present results to consider the scaling up of the estimated subgroup numbers in larger populations. Although the present findings are considered preliminary, future results contributing to this line of work will help identify subgroups of middle-aged and older adults (eg, those with higher pain) who may benefit most from better sleep in terms of associations with cognitive performance. This type of research has clinical merit as it has the potential to facilitate the tailoring of clinical recommendations for improving cognitive performance in these age groups and ultimately inform personalized medicine.

The present preliminary study showed that in sedentary adults aged 50 and older, the association between self-reported sleep and cognitive performance interacts with pain, and this is limited to executive function tasks. Results show that pain interacts with sleep efficiency in the associations with reasoning and working memory, as well as with TST in the association with reasoning. Although our results are preliminary, this line of work has several clinical implications. For instance, findings suggest that self-reported sleep is potentially a modifiable factor to be targeted in behavioral interventions but may be most important in certain subgroups. For instance, in those sedentary middle-aged and older adults with more severe pain, improving sleep efficiency may be a target of behavioral sleep therapies (eg, cognitive behavioral therapy for insomnia) to maximize improvements in executive functioning. Additionally, TST may be important to monitor in those with more pain, because too much sleep may be associated with worse reasoning. Taken together, pain should be considered in the understanding of how self-reported sleep is associated with daytime functioning in sedentary middle-aged and older adults. Prospective analyses in larger samples are encouraged to uncover the temporal order of sleep and pain associations with cognitive performance in this population.

ABBREVIATIONS

SDMT, Symbol Digit Modalities Test
TST, total sleep time

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