Moderators and Mediators of Exercise-Induced Objective Sleep Improvements in Midlife and Older Adults With Sleep Complaints

Matthew P. Buman and Eric B. Hekler
Stanford University School of Medicine

Donald L. Bliwise
Emory University School of Medicine

Abby C. King
Stanford University School of Medicine

Objective: Exercise can improve sleep quality, but for whom and by what means remains unclear. We examined moderators and mediators of objective sleep improvements in a 12-month randomized controlled trial among underactive midlife and older adults reporting mild/moderate sleep complaints. ***Methods:*** Participants ($N = 66$, 67% women, 55–79 years) were randomized to moderate-intensity exercise or health education control. Putative moderators were gender, age, physical function, self-reported global sleep quality, and physical activity levels. Putative mediators were changes in BMI, depressive symptoms, and physical function at 6 months. Objective sleep outcomes measured by in-home polysomnography were percent time in Stage I sleep, percent time in Stage II sleep, and number of awakenings during the first third of sleep at 12 months. ***Results:*** Baseline physical function and sleep quality moderated changes in Stage I sleep; individuals with higher initial physical function ($p = .01$) and poorer sleep quality ($p = .03$) had greater improvements. Baseline physical activity level moderated changes in Stage II sleep ($p = .04$) and number of awakenings ($p = .01$); more sedentary individuals had greater improvements. Decreased depressive symptoms (CI:-1.57 to -0.02) mediated change in Stage I sleep. Decreased depressive symptoms (CI:-0.75 to -0.01), decreased BMI (CI:-1.08 to -0.06), and increased physical function (CI: 0.01 to 0.72) mediated change in number of awakenings. ***Conclusions:*** Initially less active individuals with higher initial physical function and poorer sleep quality improved the most. Affective, functional, and metabolic mediators specific to sleep architecture parameters were suggested. These results indicate strategies to more efficiently treat poor sleep through exercise in older adults.

Keywords: objective sleep, exercise, physical activity, multiple mediation, moderation

The majority of Americans over the age of 55 report mild or more serious sleep complaints (National Sleep Foundation, 2003). Even minor sleep complaints can lead to increased risk of accidents, falls, chronic fatigue, and weight gain (Bloom et al., 2009; Patel, Malhotra, White, Gottlieb, & Hu, 2006), while more significant sleep complaints are associated with cognitive decline, reduced immune function, and depression (Krueger & Friedman, 2009; Merlino et al., 2010). Despite the relevance of sleep across the life span, in particular among midlife and older adults, sleep remains one of the least understood health behaviors.

There is growing consensus that regular exercise can improve sleep (Youngstedt, O'Connor, & Dishman, 1997). Cross-sectional studies have consistently found that regular exercise is associated with better sleep (Youngstedt & Kline, 2006) and inversely associated with sleep disorders (Sherrill, Kotchou, & Quan, 1998). Randomized controlled trials (RCTs) of regular exercise that meet national recommendations (Physical Activity Guidelines Advisory Committee, 2008), which is 150 minutes a week of moderate-intensity physical activity, have produced small to moderate improvements in sleep quality in older adults. Self-rated improvements have been reported in global sleep quality, sleep-onset latency, sleep disturbances, and total sleep time (King, Oman, Brassington, Bliwise, & Haskell, 1997; Singh, Clements, & Fiatarone, 1997). Improvements have also been found in objective polysomnographic measures (PSG) of sleep, including decreased percent time in Stage I sleep (transitional sleep between wake and sleep), increased percent time in Stage II sleep (deeper form of sleep characterized by decreased body temperature, heart rate, and muscle tone), and fewer nighttime awakenings during the first third of sleep (King et al., 2008; a marker of sleep disturbance). This paper explores the potential moderators and mediators of the

observed changes in objective sleep originally reported by King et al. (2008).

Why Are Moderators and Mediators of the Exercise-Sleep Relationship Important to Study?

Little is known concerning for whom and by what means exercise-induced sleep changes optimally occur. Exploring moderators (consisting of baseline variables) and mediators (changes in variables related to intervention) is critical to identify the groups of individuals who may benefit most from different treatments (moderators) and the mechanisms underlying effective treatments (mediators; Kraemer, Wilson, Fairburn, & Agras, 2002). Knowledge related to moderator variables could be useful in targeting interventions to appropriate subgroups. Exploring mediation could help to maximize treatment gains by enhancing intervention elements that impact key mechanisms and eliminating elements that do not. These improvements in treatment efficiency could result in larger treatment effects or similar effects at lower cost or risk (Kraemer et al., 2002).

Putative Moderators and Mediators of the Exercise-Sleep Relationship

The current evidence linking exercise to sleep may be underestimated due to ceiling or floor effects for some participant subgroups based on certain individual characteristics (Youngstedt, 2003). For instance, individuals with poor initial sleep quality may benefit more from exercise. Youngstedt (2003) reported that, after controlling for initial poorer sleep, the acute effects observed in exercise studies were similar to those in pharmacological treatment studies for poor sleep. Age itself may be an important moderator as normative sleep is known to decline with age, most notably with respect to sleep architecture (Ancoli-Israel & Cooke, 2005) and circadian rhythms (Hood, Bruck, & Kennedy, 2004). Inactive individuals and those with poorer physical function may benefit more from exercise generally (Physical Activity Guidelines Advisory Committee, 2008). Two randomized controlled trials of sedentary and unfit older individuals reported correlated change between cardiorespiratory fitness and exercise-related sleep improvements (King et al., 1997; Tworoger et al., 2003). Other researchers have reported, however, in meta-analytic reviews of primarily small experimental studies of acute exercise, similar exercise-related benefits among fit and unfit individuals (Youngstedt et al., 1997). Finally, an older meta-analysis reported modestly improved sleep response in women relative to men (Kubitz, Landers, Petruzzello, & Han, 1996). While in the last 10 years women have been better represented in exercise and sleep trials, these more recent studies have not, in general, adequately explored gender as a moderator.

The basic mechanisms underlying the exercise-sleep relationship are not fully understood (Buman & King, 2010; Youngstedt, 2005). A number of theories have been posited and three will be discussed and tested here. First, negative affective states, such as depressive symptoms and anxiety, are important contributing factors to poor sleep (Morin et al., 1999). Since exercise is known to have both antidepressant (Dunn, Trivedi, & O'Neal, 2001) and anxiolytic (Stathopoulou, Powers, Berry, Smits, & Otto, 2006) effects, these changes may in turn improve sleep. Second, studies

suggest that exercise is an important contributor overall to energy balance and weight change (Shaw, Gennat, O'Rourke, & Del Mar, 2006), and could therefore improve sleep through weight reduction, perhaps even apart from sleep apnea (Fogelholm et al., 2007). Finally, regular exercise could improve sleep by increasing day-to-day activity levels via enhanced functional status, since poor functional abilities are associated with poor sleep in older adults (Ensrud et al., 2009).

One limitation of the extant literature exploring moderators and mediators is its heavy reliance on meta-analytic reviews of small laboratory-based experimental trials that address only acute exercise effects and often have no or inappropriate control condition(s) (Buman & King, 2010). Randomized controlled trials represent the "gold standard" for evaluating whether regular exercise improves sleep; in addition, they can more explicitly reveal moderators and mediators of the exercise-sleep relationship (Kraemer, Kiernan, Essex, & Kupfer, 2008). To date no studies that we are aware of have examined mediators within an RCT context with appropriate temporal sequencing to suggest a causal relationship. Moreover, given the multidimensional nature of both sleep and exercise and their impacts on nearly every system of the human body, it is unlikely that the effect of exercise on sleep is influenced by only a single baseline characteristic or transmitted by a single mechanism; that is, it is likely that multiple moderators and mediators are operating simultaneously (Buman & King, 2010).

Research Purpose

Using data from a 12-month RCT of moderate-intensity exercise among midlife and older adults with mild to moderate sleep complaints (King et al., 2008), we explored baseline *moderators* (gender, age, and baseline levels of physical activity, rated sleep quality, and physical function) and *mediators* (changes in negative affect, overweight, and physical function) of exercise-induced changes in objective sleep parameters measured by in-home PSG.

Method

Design

The study was a 12-month randomized controlled trial of underactive adults aged 55 years or older with chronic mild to moderate sleep complaints who were recruited from the community at large. The study methods are described in detail elsewhere (King et al., 2008) and summarized here. The primary focus of the exercise program was increasing moderate intensity endurance exercise to a level that met or exceeded public health recommendations (Physical Activity Guidelines Advisory Committee, 2008). Exercise intervention participants were instructed to attend exercise classes 2 days/week for 60 minutes (30–45 minutes of which were aimed at moderate-intensity endurance exercise, including brisk walking and aerobic movement) and home-based exercise an additional 3 days/week for 30 minutes throughout the 12-month intervention period. The endurance exercise was targeted at an intensity of 60% to 85% of treadmill-based peak heart rate and took place during the morning or afternoon. Control arm participants received weekly classes similar to health education classes found in many communities throughout the United States. Both groups received brief printed recommendations for sleep hygiene.

The appropriate university institutional review boards approved the study protocol and this trial was registered at clinicaltrials.gov (#NCT00149747).

Participants

The primary eligibility criteria included (a) age 55 years or older; (b) underactive (defined as <60 minutes/week of moderate or more vigorous physical activity over the previous six months); (c) body mass index ≤35; (d) free of sleep apnea (objectively verified); and (e) mild to moderate sleep complaints (defined by scores ≥ three on at least two of three items of the Sleep Questionnaire and Assessment of Wakefulness (Miles, 1982). Of 201 persons initially responding to the study promotional announcements, 66 individuals were eligible and randomized (36 intervention, 30 control). Eighty-nine percent completed the 12-month trial (exercise = 32/36, or 89%, control = 27/30, or 90%), with no significant differences in dropout rates by study arm ($p > .05$). Class attendance was 74% and 80% for the exercise and control groups, respectively. Home-based participation, through regular participant logs, revealed exercise group participants engaged in 2.1 ($SD = 0.9$) home-based sessions/week for 43.3 ($SD = 19.4$) minutes per session. The exercise group reported greater energy expenditure at 6 and 12 months relative to control. Full adherence data are presented elsewhere (King et al., 2008).

Measurements

Figure 1 depicts the potential moderators and mediators being proposed in the current study. All moderator and mediator variables were selected a priori from the existing literature. Demographic information was self-reported at baseline. All standardized questionnaires and measurements were assessed by trained staff blinded to participant study arm assignment. Moderator variables were assessed at baseline prior to study arm assignment. Mediator variables were assessed at baseline and during the midpoint of the intervention (6 months), and outcome variables were assessed at baseline and at posttest (12 months).

Moderators. Gender and age were self-reported. Baseline physical activity was operationalized as minutes of moderate-intensity or more vigorous physical activity (MVPA) and was measured by the CHAMPS physical activity questionnaire (Stewart et al., 2001). This 47-item self-report questionnaire assesses activities across the intensity spectrum during a typical week over the previous month. Moderate and more vigorous activities were included in the calculations, as defined by metabolic equivalent values ≥3.0 from standards in the field (Ainsworth et al., 2000). The CHAMPS has been found to provide valid and reliable estimates of MVPA in older adults (Harada, Chiu, King, & Stewart, 2001; Stewart et al., 2001). Global sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). The PSQI, a standard measure, is a self-rated measure composed of seven "component" scores (using a 0–3 scale) summed to form a global sleep quality score (range = 0–21; lower score = better sleep quality). The global sleep quality score was used in the current investigation. Baseline physical function was operationalized as upper-body (number of arm curls performed) and lower-body (number of chair stands) function (Rikli & Jones, 2001). These measures are discussed in more detail as mediator variables below.

Mediators. Negative affect change measures included the 10-item short version of the Center for Epidemiological Studies - Depression Scale (CES-D) to measure depressive symptoms (Andresen, Malmgren, Carter, & Patrick, 1994) and the 40-item State–Trait Anxiety Inventory (STAI) to measure state and trait anxiety (Spielberger, Gorsuch, & Lushene, 1983). Change in overweight was assessed by measuring body weight (kg) and height (meters) using standard procedures to obtain BMI (kg/m2; King, Haskell, Taylor, Kraemer, & DeBusk, 1991). Chair stands and arm curls
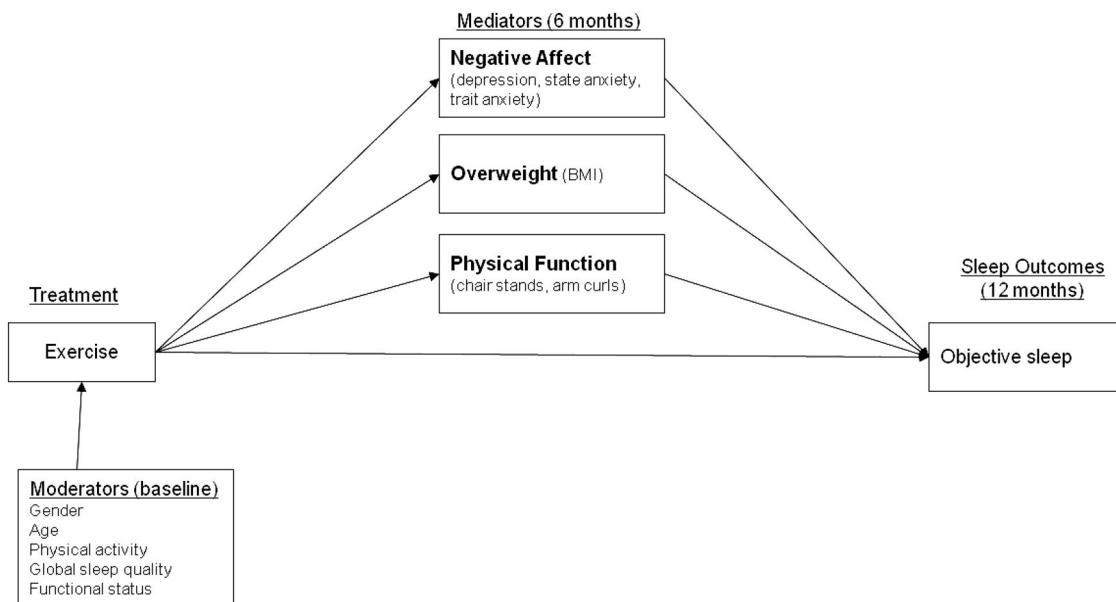

Figure 1. Potential moderators and mediators of exercise-induced sleep outcomes.

were used as measures of lower- and upper-body physical function, respectively, as these are standard, field-based measures commonly used for older adults to measure physical function. These tasks were performed following standard procedures (Rikli & Jones, 2001). Finally, cardiorespiratory fitness (VO_2peak) data were collected through a standard treadmill-based test. There were notable amounts of missing data ($n = 13$) in the sample due to participants refusing or clinical staff deciding that it was not safe to initiate and/or complete the test. Preliminary analyses found that data were not missing at random and, therefore, the VO_2peak variable was dropped from further analysis.

Objective sleep.   Sleep was measured via in-home PSG. Nine-channel PSG was measured for three nights at baseline and two nights at 12 months using the Oxford Medilog MR95 digital recording system (Oxford Instruments, Oxford, U.K.). Polysomnographic data were collected and scored following standard procedures—a full description of these methods are published elsewhere (King et al., 2008). Results indicated that at 12 months, exercisers showed (a) significantly less percent total sleep time in Stage I sleep (group difference = 2.3%; effect size = 0.66); (b) significantly greater percent time in Stage II sleep (group difference = 3.2%; effect size = 0.41); and (c) significantly fewer awakenings during the first third of the sleep period (group difference = 1.0 awakening; effect size = 0.50) relative to controls. These results informed our decision to explore moderators and mediators of these outcomes.

Statistical Analyses

Three separate hierarchical regression models, one for each objective sleep outcome (percent time in Stage I, percent time in Stage II, number of awakenings), were used to examine whether the proposed moderators (see Figure 1) impacted intervention effects. Each baseline objective sleep value and study arm assignment was entered at Step 1. Main effects for all proposed moderators were entered at Step 2. The proposed moderators were mean centered and a Group assignment × Moderator interaction term was entered for each proposed moderator in Step 3 simultaneously (Aiken & West, 1991). Effect sizes were calculated for moderation effects using Cohen's d formula: $d = 2t/\sqrt{df}$ (Rosenthal & Rosnow, 1991).

Analysis of covariance (ANCOVA) was used (with baseline values as covariates) to evaluate whether the exercise intervention produced significant changes in the proposed mediators (see Figure 1) at 6 months. Variables that met this criterion were included in the formal tests of mediation. Intent-to-treat principles were used such that baseline values were carried forward when data were missing. Prior to entry in the mediation models, mediator and outcome variables were converted to residualized change scores such that values were centered at 0 and reflected change from baseline (Lance, 1988).

Mediation analyses were performed using methods described by Preacher and Hayes with the accompanying SAS macro (Preacher & Hayes, 2008). This procedure provides total and specific indirect effects (through the proposed mediator[s]) of the predictor (study arm assignment: exercise or control) on outcomes (objective sleep outcomes). Separate statistical models were run for percent time in Stage I, percent time in Stage II, and number of awakenings during the first third of sleep. Multiple mediator models have a number of advantages relative to single mediator models. Multiple mediator analyses allow inferences regarding the overall mediational effect of a set of mediators (i.e., total indirect effects) as well as unique effects of each mediator (i.e., specific indirect effects), holding constant the effects of all other mediators in the model. Pairwise contrasts can also be estimated to assess the relative magnitudes of any two mediators, allowing comparisons to be made regarding competing mechanisms (Preacher & Hayes, 2008). The product-of-coefficients method (Sobel, 1986), most commonly used to assess mediation models, relies upon the assumption that indirect effects are normally distributed; however, this is likely not the case except in very large samples (MacKinnon, Krull, & Lockwood, 2000). Bootstrapping, a nonparametric sampling procedure, has been advocated as a more powerful alternative whereby percentile-based confidence limits are obtained (MacKinnon, Lockwood, & Williams, 2004). We use this bootstrapping procedure here, with 1,000 bootstrap samples with bias-corrected and accelerated intervals (Preacher & Hayes, 2008), to make inferences. We also present product-of-coefficient standard errors and Z for comparison, recognizing their limitations due to our limited sample size.

Results

Moderation Effects

Table 1 displays baseline descriptive statistics for the proposed moderators by group assignment. Both exercise and control study

Table 1
Descriptive Statistics by Study Arm for Proposed Moderators

Moderator	Control	Exercise	Total
N	30	36	66
Female gender (%)	66%	66%	66%
Age, yr (SD)	60.90 (7.19)	61.86 (6.33)	61.42 (6.70)
MVPA, min · wk^{-1} (SD)	280.50 (403.0)	211.70 (204.70)	242.95 (310.18)
+ Global sleep quality (SD)	7.70 (2.84)	8.47 (3.61)	8.12 (3.28)
Chair stands (SD)	15.20 (4.79)	14.56 (3.42)	14.85 (4.08)
Arm curls (SD)	18.60 (6.61)	16.92 (4.25)	17.68 (5.47)

Note. MVPA = moderate-vigorous or greater physical activity.
+ 0–21 scale: lower score = better sleep quality. There were no statistically significant between-arm baseline differences (p values > .10)

arms were similar in terms of each moderator under study. As reported previously (King et al., 2008), there were also no baseline group differences for other demographic variables, including educational status, race/ethnicity, marital status, employment status, and over-the-counter sleep medication use (p values >0.10). Global sleep quality results indicated that the sample, on average, was comprised of "poor sleepers" as defined by PSQI global scores >5 (Buysse et al., 1989). For chair stands and arm curls, the sample fell within the normal range (within the middle 50%) for age, according to a national sample (Rikli & Jones, 1999). Chair stands and arm curls were found to be collinear ($r = .58$, $p < .0001$). The chair stand variable was included in the moderator analyses given the importance of lower-body function in delaying onset of disability in older adults (Pahor et al., 2006).

No significant main effects were observed in the moderation models. For percent time in Stage I, baseline chair stands, $t(55) = 2.83$, $p = .006$, $\beta = .33$, $d = .76$ and global sleep quality, $t(55) = 3.04$, $p = .003$, $\beta = .37$, $d = .82$ were significant moderators. Figure 2 (Panels A and B for chairs stands and global sleep quality,

respectively) displays values graphically, indicating that individuals with better baseline lower-body physical function as measured via the chair stands and worse global sleep quality improved the most (less percent time in Stage I sleep = better). For percent time in Stage II sleep, baseline MVPA was a significant moderator, $t(55) = 2.43$, $p = .02$, $\beta = .35$, $d = .66$. Figure 2 (C) indicates that less active individuals at baseline improved the most (more percent time in Stage II sleep = better). For number of awakenings in the first third of sleep, baseline MVPA was a significant moderator, $t(55) = 2.61$, $p = .01$, $\beta = .37$, $d = .70$. Figure 2 (D) indicates that less active individuals at baseline improved the most (fewer awakenings = better). Age and gender were not significant moderators.

Mediator Effects

ANOVA tests were conducted to identify which of the proposed mediators significantly improved during the first 6 months of the intervention (see Table 2). Depressive symptoms
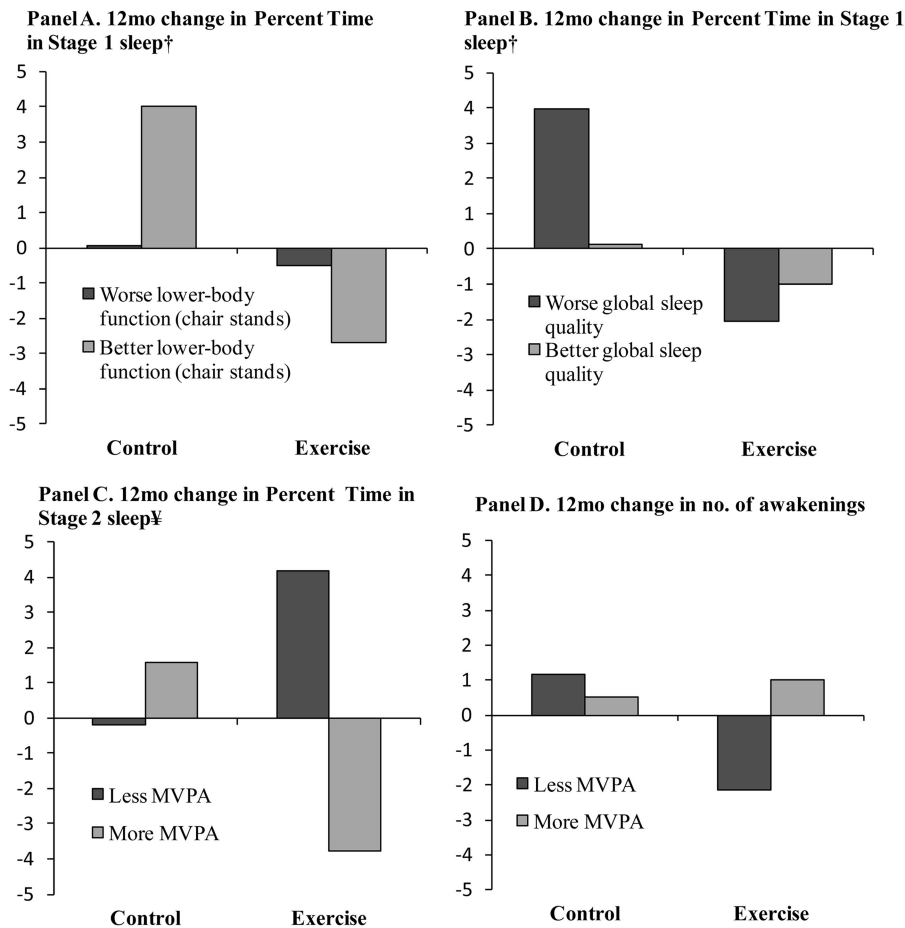
Figure 2. Moderator effects of exercise on objective sleep outcomes by baseline lower-body physical function (chair stands), global sleep quality, and moderate-intensity and more vigorous physical activity (MVPA). Notes: Predicted values derived from the regression equation in which "high" and "low" values for moderators were specified as one standard deviation above and below the mean; Models are adjusted for main effects and interactions for gender, age, MVPA, global sleep quality, and chair stands. †Percent time in Stage I sleep: less = better; ¥ Percent time in Stage II sleep: more = better.

Table 2

Mean (SD) of Proposed Mediators at Baseline and Six Months by Study Arm (N = 66)

Variable	Control (n = 30)	Exercise (n = 36)	Cohen's d
Depressive symptoms			
Baseline	7.03 (4.44)	8.17 (5.06)	
6 months	8.30 (5.58)	7.06 (6.04)*	.50
Trait anxiety[†]			
Baseline	35.69 (9.09)	35.94 (12.19)	
6 months	37.07 (10.44)	34.94 (11.71)	.43
State anxiety[†]			
Baseline	33.76 (9.91)	33.66 (12.98)	
6 months	36.62 (11.30)	35.43 (14.02)	.16
Body mass index			
Baseline	27.18 (3.92)	27.86 (4.06)	
6 months	27.49 (3.78)	27.55 (4.03)**	.71
Chair stands			
Baseline	15.20 (4.79)	14.56 (3.42)	
6 months	16.60 (5.47)	16.78 (4.50)	.22
Arm curls			
Baseline	18.60 (6.61)	16.92 (4.25)	
6 months	19.27 (6.32)	19.53 (5.20)*	.57

[†] Two individuals (1 exercise, 1 control) did not have complete baseline scores. * Between-arm difference (ANCOVA), p < .05, two-tailed. ** Between-arm difference (ANCOVA), $p < .01$, two-tailed.

were marginally reduced in the exercise arm relative to the control arm (*M diff* = −2.16, 95% CI: −4.35 to 0.03, p = .05). Trait and state anxiety were not reduced. Body mass index was significantly reduced in the exercise arm relative to the control arm (*M diff* = −0.60, 95% CI: −1.02 to −0.17, p = .006). Chair stands were not significantly improved, yet arm curls were (*M diff* = 1.76, 95% CI: 0.21 to 3.31, p = .03). Changes in depressive symptoms, BMI, and arm curls were therefore included in the mediator models.

Mediation results are displayed in Table 3. For percent time in Stage I sleep, the total indirect effect of the variables in combination did not mediate the effects of the intervention. Specific indirect effects indicated that decreased depressive symptoms mediated changes in percent time in Stage I sleep. For percent time in Stage II sleep, total and specific indirect effects were not significant. Finally, for number of awakenings, the total indirect effect was not significant. However, specific indirect effects indicated that decreased depressive symptoms, decreased BMI, and in-

Table 3

Mediation of the Effect of Exercise on 12-Month Polysomnographic Sleep Outcomes Through Depressive Symptoms, BMI, and Physical Function

Variable	Point estimate	Product-of-coefficents method		Bootstrapped BCa 95% CI	
		SE	Z	Lower	Upper
Percent time in Stage 1 Sleep					
Total	−0.30	0.48	−0.63	−1.58	0.49
Depressive symptoms	−0.41*	0.28	−1.45	−1.57	−0.02*
BMI	0.28	0.29	0.98	−0.22	0.98
Arm curls	−0.18	0.23	−0.79	−0.88	0.17
Percent time in Stage 2 Sleep					
Total	0.29	1.05	0.27	−2.46	2.44
Depressive symptoms	0.18	0.48	0.36	−0.60	1.56
BMI	0.59	0.71	0.83	−0.58	2.47
Arm curls	−0.48	0.58	−0.83	−2.47	0.55
Number of awakenings: 1st third of sleep period[†]					
Total	0.41	0.35	1.16	−0.33	1.22
Depressive symptoms	−0.26*	0.18	−1.44	−0.75	−0.01*
BMI	−0.41*	0.23	−1.78	−1.08	−0.06*
Arm curls	0.36*	0.18	1.44	0.01	0.72*

[†] Significant contrasts: BMI > Depressive symptoms, Depressive symptoms > Arm curls. * denotes CI does not include zero, point estimate represents unstandardized beta coefficient. Bca = bias corrected and accelerated, 1,000 bootstrap samples.

creased arm curls mediated changes in number of awakenings. Pairwise contrasts revealed that among the significant mediators for number of awakenings, BMI change was the best mediator, following by changes in depressive symptoms and arm curls, respectively.

Discussion

Understanding for whom and by what means exercise impacts sleep is critical to optimize exercise interventions for midlife and older adults. Moderator results suggested that initially less active individuals with higher initial physical function and poorer sleep quality had the greatest objective sleep improvements. Mediation results suggest that the observed exercise-induced improvements in sleep at 12 months were at least partially due to decreased depressive symptoms, decreased weight, and improvements in physical function at 6 months. Results also indicated that moderators and mediators differed for each parameter of sleep architecture.

Moderator Results

Initial level of physical activity was the strongest and most consistent moderator of sleep. This was observed despite excluding individuals reporting >60 minutes of moderate-intensity exercise in a typical week at baseline, suggesting that those almost completely inactive were likely to benefit more from the intervention relative to those reporting greater, yet still insufficient, amounts of exercise. It should also be noted that these effects were observed for a sleep parameter that reflects more consolidated sleep patterns (number of awakenings). This is an important finding given shifts in circadian rhythms with age that may lead to more fragmented sleep (Ancoli-Israel & Cooke, 2005; Hood et al., 2004). Individuals with poorer self-rated global sleep quality at baseline had greater improvements in percent time in Stage I sleep. This result was present despite study eligibility criteria targeting only participants reporting mild to moderate sleep complaints (participants with diagnosed sleep disorders and those without sleep complaints were excluded). At least for percent time in Stage I sleep, this indicates that exercise is beneficial for the large number of midlife and older adults in the mild to moderate sleep complaint range, with individuals at the more serious end of this range appearing to benefit most.

We also observed that individuals with higher levels of lower-body physical function had greater improvements in percent time in Stage I sleep. This suggests that higher functioning participants may have had greater overall exercise volume during the intervention. The exercise intensity prescription given was based on relative intensity (60–85% peak heart rate), and, therefore, individuals with higher physical function were likely able to exercise at higher levels of absolute intensity relative to lower functioning individuals. This would result in an increased overall volume of exercise, suggesting a dose-response effect for exercise. A dose-response effect has previously been reported in an exercise RCT (Singh et al., 2005). Additionally, higher functioning individuals in our sample may have participated in more resistance training activities as part of the intervention. Unfortunately, our adherence measures did not assess physical activity modality at this level of detail to formally explore this hypothesis.

It should be noted that the significant percent time in Stage I sleep moderator results for chair stands (Figure 2, Panel A) and global sleep quality (Figure 2, Panel B) were likely partially driven by increases in percent time in Stage I sleep in control group participants with better lower-body function and worse global sleep quality. While these were not expected effects, this may reflect (a) individuals with better physical function may require at least modest levels of physical activity to maintain sleep quality; and (b) poorer sleepers, in the absence of physical activity and with the expectation that their sleep would improve, may have adopted maladaptive strategies to enhance sleep (i.e., spending extra time in bed to achieve sleep) that had the opposite effect. Additionally, we also acknowledge because these findings were not found consistently across all sleep outcomes and our sample size was small, it may be that these findings are not replicable and should be interpreted with caution.

Gender and age were not significant moderators in any models. For gender, our results are in contrast with conclusions from an older meta-analysis that indicated women improved more in response to exercise than men (Kubitz et al., 1996). Women generally were underrepresented in the studies used in this meta-analysis. Our sample was more evenly distributed (66% women) and, therefore, may reflect a more accurate assessment of this effect. Age also was not a significant moderator, which was not surprising given that we only sampled older adults (55–79 years of age). Age-related variations were likely related to differences in rated sleep quality and therefore were likely more accurately captured in the rated sleep quality moderator variable discussed above. Exercise-induced sleep changes may still be amplified or attenuated among younger (or older) age cohorts not included in our sample.

Mediator Results

Depressive symptoms, as measured by a screening tool for depression, were found to mediate both percent time in Stage I sleep and number of awakenings. This result is in line with the Singh et al.(1997) study, where improvements in depressive symptoms co-occurred with improvements in subjective sleep-onset latency and sleep disturbances following 10 weeks of high intensity progressive resistance training in depressed older adults. Our results extend these results in three ways: (a) our sample as a whole did not appear to be clinically depressed, as indicated by baseline levels on the CESD measure, suggesting reasonably modest improvements in a nonclinical sample may be large enough to lead to improved sleep; (b) our sleep results were based on objective as opposed to subjective measures; and (c) the temporal sequence of our measures (depressive symptoms at 6 months preceded sleep outcome at 12 months) suggest that shorter-term improvements in depressive symptoms drive longer-term sleep improvements, although the effects may be bidirectional. There are a number of plausible mechanisms by which depressive symptoms may mediate sleep improvements, including reductions in general hyper-arousal (Morin et al., 1999) and improved autonomic control (Youngstedt, 2005).

Despite excluding participants with substantial levels of sleep apnea (King et al., 2008), the small, yet significant reductions in body weight mediated number of awakenings during the first third of sleep. It is possible that the reduction of such awakenings might

have reflected small changes in whatever residual levels of sleep disordered breathing that persisted in our sample, despite careful screening. Unfortunately, our PSG montage did not include recordings of sleep disordered breathing as outcomes. Additionally, evidence is now accruing that body weight and sleep quality could be associated, even apart from sleep apnea (Fogelholm et al., 2007), which leaves open yet another path of mediation. Such an effect would be compatible with the known link between sleep integrity and successful thermoregulation (Shaw, 2005), a process that may be optimized by even modest levels of physical activity (Levine, Eberhardt, & Jensen, 1999).

Poor sleep is associated with greater risk for falls and functional disability in older adults (Ensrud et al., 2009), along with a number of other health-related quality of life outcomes (e.g., cognitive function, chronic pain). While researchers primarily have discussed how sleep problems lead to these impairments, our results suggest that improved physical function may also lead to improved sleep, specifically number of awakenings during the first third of sleep. Changes in upper-body physical function, as measured in the current study through arm curls (a commonly used measure among older adults), may reflect overall improvements in functional capacity (Rikli & Jones, 2001). These results are similar to studies that have observed correlated change between fitness measures and sleep improvements (King et al., 1997; Tworoger et al., 2003). Our results strengthen these conclusions by establishing temporal order of these effects.

Two important caveats are worth noting in regard to the mediation outcomes. First, none of the proposed mediators explained changes in percent time in Stage II sleep. This was likely due to the relatively small exercise-induced effect that was observed for Stage II sleep. We likely did not have sufficient statistical power to account for such a small effect via our mediators. Second, the mediators tested in this study represent only three potential mechanisms through which exercise may impact sleep. Other mechanisms are also plausible that were not measured in this study, most notably thermoregulatory effects (Van Someren, 2000; Youngstedt, 2005), proinflammatory cytokines such as IL-1, IL-6, and TNF-α (Santos, Tufik, & De Mello, 2007), and brain neuropeptides and neurotransmitters (Buman & King, 2010). This is one likely explanation for why the sleep outcomes were only partially mediated by the set of proposed mediators. Future RCT studies should explore these additional mechanisms.

Strengths and Limitations

The primary strengths of this study are the testing of multiple moderators and mediators within a single RCT, the appropriate temporal order of treatment, mediator, and outcome variables, and the use of objective parameters of sleep architecture. Past conclusions regarding moderators and mediators of exercise-induced sleep improvements have been limited primarily to meta-analytic results of experimental studies addressing acute exercise effects that rely on cross-sectional associations to establish moderation and mediation evidence. We chose potential moderators and mediators, guided by this limited evidence, to formally test moderation and mediation within an RCT and within recommended temporal conditions (Kraemer et al., 2008).

Our findings are also limited by an inability to control for light exposure. This is a shared limitation with virtually all other RCTs

exploring exercise effects on sleep. Our intervention included two weekly indoor group-based exercise sessions supplemented with several home-based exercise bouts—with many participants choosing to walk outdoors. We viewed this exercise prescription as a necessary "trade-off" to maintain high levels of adherence, a sufficient volume of exercise to optimize health effects, and strong external validity of our program.

Conclusion

Our results suggest older adults with poor initial sleep quality who are physically inactive and are relatively higher functioning are most likely to receive sleep benefits from moderate-intensity physical activity. Interventions should target these subgroups for maximal benefit. It also appears that these sleep-related benefits may have been conferred through reductions in depressive symptoms as measured by a screening tool for depression, decreased weight, and improved physical function. Intervention strategies aimed at optimally impacting these specific outcomes are recommended to improve treatment efficiency.

References

Aiken, L. S., & West, S. G. (1991). *Multiple regression: Testing and interpreting interactions.* Newbury Park, CA: Sage.

Ainsworth, B., Haskell, W. L., Whitt, M. C., Irwin, M. L., Swartz, A. M., Strath, S. J., . . . Leon, A. S. (2000). Compendium of physical activities: An update on activity codes and MET intensities. *Medicine & Science in Sports & Exercise, 32,* S498–S516.

Ancoli-Israel, S., & Cooke, J. R. (2005). Prevalence and comorbidity of insomnia and effect on functioning in elderly populations. *Journal of the American Geriatrics Society, 53,* S264–S271.

Andresen, E. M., Malmgren, J. A., Carter, W. B., & Patrick, D. L. (1994). Screening for depression in well older adults—Evaluation of a short-form of the CES-D. *American Journal of Preventive Medicine, 10,* 77–84.

Bloom, H. G., Ahmed, I., Alessi, C. A., Ancoli-Israel, S., Buysse, D. J., Kryger, M. H., . . . Zee, P. C. (2009). Evidence-based recommendations for the assessment and management of sleep disorders in older persons. *Journal of the American Geriatrics Society, 57,* 761–789.

Buman, M. P., & King, A. C. (in press). Exercise as treatment to enhance sleep. *American Journal of Lifestyle Medicine.*

Buysse, D. J., Reynolds, C. F., 3rd, Monk, T. H., Berman, S. R., & Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Research, 28,* 193–213.

Dunn, A. L., Trivedi, M. H., & O'Neal, H. A. (2001). Physical activity dose-response effects on outcomes of depression and anxiety. *Medicine & Science in Sports & Exercise, 33,* S587–S597.

Ensrud, K. E., Blackwell, T. L., Redline, S., Ancoli-Israel, S., Paudel, M. L., Cawthon, P. M., . . . Stone, K. L. (2009). Sleep disturbances and frailty status in older community-dwelling men. *Journal of the American Geriatrics Society, 57,* 2085–2093.

Fogelholm, M., Kronholm, E., Kukkonen-Harjula, K., Partonen, T., Partinen, M., & Harma, M. (2007). Sleep-related disturbances and physical inactivity are independently associated with obesity in adults. *International Journal of Obesity, 31,* 1713–1721.

Harada, N. D., Chiu, V., King, A. C., & Stewart, A. L. (2001). An evaluation of three self-report physical activity instruments for older adults. *Medicine & Science in Sports & Exercise, 33,* 962–970.

Hood, B., Bruck, D., & Kennedy, G. (2004). Determinants of sleep quality in the healthy aged: The role of physical, psychological, circadian and naturalistic light variables. *Age and Ageing, 33,* 159–165.

King, A. C., Haskell, W. L., Taylor, C. B., Kraemer, H. C., & DeBusk,

R. F. (1991). Group- vs. home-based exercise training in healthy older men and women. A community-based clinical trial. *Journal of the American Medical Association, 266,* 1535–1542.

King, A. C., Oman, R. F., Brassington, G. S., Bliwise, D. L., & Haskell, W. L. (1997). Moderate-intensity exercise and self-rated quality of sleep in older adults. A randomized controlled trial. *Journal of the American Medical Association, 277,* 32–37.

King, A. C., Pruitt, L. A., Woo, S., Castro, C. M., Ahn, D. K., Vitiello, M. V., . . . Bliwise, D. L. (2008). Effects of moderate-intensity exercise on polysomnographic and subjective sleep quality in older adults with mild to moderate sleep complaints. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences, 63,* 997–1004.

Kraemer, H., Kiernan, M., Essex, M., & Kupfer, D. J. (2008). How and why criteria defining moderators and mediators differ between the Baron & Kenny and Macarthur approaches. *Health Psychology, 27,* S101–S108.

Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry, 59,* 877–883.

Krueger, P. M., & Friedman, E. M. (2009). Sleep duration in the United States: A cross-sectional population-based study. *American Journal of Epidemiology, 169,* 1052–1063.

Kubitz, K. A., Landers, D. M., Petruzzello, S. J., & Han, N. W. (1996). The effects of acute and chronic exercise on sleep—A meta-analytic review. *Sports Medicine, 21,* 277–291.

Lance, C. E. (1988). Residual centering, exploratory and confirmatory moderator analysis, and decomposition of effects in path models containing interactions. *Applied Psychological Measurement, 12,* 163–175.

Levine, J. A., Eberhardt, N. L., & Jensen, M. D. (1999). Role of nonexercise activity thermogenesis in resistance to fat gain in humans. *Science, 283,* 212–214.

MacKinnon, D. P., Krull, J. L., & Lockwood, C. M. (2000). Equivalence of the mediation, confounding and suppression effect. *Prevention Science, 1,* 173–181.

MacKinnon, D. P., Lockwood, C. M., & Williams, J. (2004). Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate Behavioral Research, 39,* 99–128.

Merlino, G., Piani, A., Gigli, G. L., Cancelli, I., Rinaldi, A., Baroselli, A., . . . Valente, M. (2010). Daytime sleepiness is associated with dementia and cognitive decline in older Italian adults: A population-based study. *Sleep Medicine, 11,* 372–377.

Miles, L. E. (1982). A sleep questionnaire. In C. Guilleminault (Ed.), *Sleeping and waking disorders: Indications and techniques.* Menlo Park, CA: Addison Wesley.

Morin, C. M., Hauri, P. J., Espie, C. A., Spielman, A. J., Buysse, D. J., & Bootzin, R. R. (1999). Nonpharmacologic treatment of chronic insomnia. *Sleep, 22,* 1134–1156.

National Sleep Foundation. (2003). *2003 Sleep in America poll.* Washington, DC: National Sleep Foundation.

Pahor, M., Blair, S. N., Espeland, M., Fielding, R., Gill, T. M., Guralnik, J. M., . . . Studenski, S. (2006). Effects of a physical activity intervention on measures of physical performance: Results of the lifestyle interventions and independence for elders pilot (LIFE-P) study. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences, 61,* 1157–1165.

Patel, S. R., Malhotra, A., White, D. P., Gottlieb, D. J., & Hu, F. B. (2006). Association between reduced sleep and weight gain in women. *American Journal of Epidemiology, 164,* 947–954.

Physical Activity Guidelines Advisory Committee. (2008). *Physical activity guidelines advisory committee report.* Washington, DC: U.S. Department of Health and Human Services.

Preacher, K., & Hayes, A. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods, 40,* 879–891.

Rikli, R. E., & Jones, C. J. (1999). Functional fitness normative scores for community-residing older adults, ages 60–94. *Journal of Aging and Physical Activity, 7,* 162–181.

Rikli, R. E., & Jones, C. J. (2001). *Senior fitness test manual.* Champaign, IL: Human Kinetics.

Rosenthal, R., & Rosnow, R. L. (1991). *Essentials of behavioral research: Methods and data analysis* (2nd ed.). New York: McGraw-Hill.

Santos, R. V. T., Tufik, S., & De Mello, M. T. (2007). Exercise, sleep and cytokines: Is there a relation? *Sleep Medicine Reviews, 11,* 231–239.

Shaw, K., Gennat, H., O'Rourke, P., & Del Mar, C. (2006). Exercise for overweight or obesity. *Cochrane Database of Systematic Reviews, 4,* 1–104.

Shaw, P. J. (2005). Thermoregulatory changes. In C. A. Kushida (Ed.), *Sleep deprivation: Basic science, physiology, and behavior* (pp. 319–338). New York: Marcel Dekker.

Sherrill, D. L., Kotchou, K., & Quan, S. F. (1998). Association of physical activity and human sleep disorders. *Archives of Internal Medicine, 158,* 1894–1898.

Singh, N. A., Clements, K. M., & Fiatarone, M. A. (1997). Sleep, sleep deprivation, and daytime activities—A randomized controlled trial of the effect of exercise on sleep. *Sleep, 20,* 95–101.

Singh, N. A., Stavrinos, T. M., Scarbek, Y., Galambos, G., Liber, C., & Fiatarone Singh, M. A. (2005). A randomized controlled trial of high versus low intensity weight training versus general practitioner care for clinical depression in older adults. *Journals of Gerontology Series A-Biological Sciences & Medical Sciences, 60,* 768–776.

Sobel, M. E. (1986). Some new results on indirect effects and their standard errors in covariance structure models. In S. Leinhart (Ed.), *Sociological methodology 1982* (pp. 290–312). San Francisco: Jossey-Bass.

Spielberger, C., Gorsuch, R., & Lushene, R. (1983). *The State Trait Anxiety Inventory (STAI) test manual.* Palo Alto, CA: Consulting Psychologists Press.

Stathopoulou, G., Powers, M. B., Berry, A. C., Smits, J. A. J., & Otto, M. W. (2006). Exercise interventions for mental health: A quantitative and qualitative review. *Clinical Psychology-Science and Practice, 13,* 179–193.

Stewart, A. L., Mills, K. M., King, A. C., Haskell, W. L., Gillis, D., & Ritter, P. L. (2001). CHAMPS physical activity questionnaire for older adults: Outcomes for interventions. *Medicine & Science in Sports & Exercise, 33,* 1126–1141.

Tworoger, S. S., Yasui, Y., Vitiello, M. V., Schwartz, R. S., Ulrich, C. M., Aiello, E. J., . . . McTiernan, A. (2003). Effects of a yearlong moderate-intensity exercise and a stretching intervention on sleep quality in postmenopausal women. *Sleep, 26,* 830–836.

Van Someren, E. J. W. (2000). More than a marker: Interaction between the circadian regulation of temperature and sleep, age-related changes, and treatment possibilities. *Chronobiology International, 17,* 313–354.

Youngstedt, S. D. (2003). Ceiling and floor effects in sleep research. *Sleep Medicine Reviews, 7,* 351–365.

Youngstedt, S. D. (2005). Effects of exercise on sleep. *Clinics in Sports Medicine, 24,* 355–365.

Youngstedt, S. D., & Kline, C. E. (2006). Epidemiology of exercise and sleep. *Sleep & Biological Rhythms, 4,* 215–221.

Youngstedt, S. D., O'Connor, P. J., & Dishman, R. K. (1997). The effects of acute exercise on sleep: A quantitative synthesis. *Sleep, 20,* 203–214.