Title

Daily Patterns of Accelerometer Activity Predict Changes in Sleep, Cognition, and Mortality in Older Men.

Journal

The Journals of Gerontology Series A, 73(5)

ISSN

1079-5006

Authors

Zeitzer, Jamie M
Blackwell, Terri
Hoffman, Andrew R
et al.

Publication Date

2018-04-17

DOI

10.1093/gerona/glw250

Peer reviewed

THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2018, Vol. 73, No. 5, 682–687
doi:10.1093/gerona/glw250
Advance Access publication February 3, 2017

OXFORD

Research Article

Daily Patterns of Accelerometer Activity Predict Changes in Sleep, Cognition, and Mortality in Older Men

Jamie M. Zeitzer,[1,2,3] Terri Blackwell,[4] Andrew R. Hoffman,[5] Steve Cummings,[4] Sonia Ancoli-Israel,[6,7] and Katie Stone[4] for the Osteoporotic Fractures in Men (MrOS) Study Research Group

[1]Department of Psychiatry and Behavioral Sciences, Stanford University, California. [2]Mental Illness Research, Education, and Clinical Center, VA Palo Alto Health Care System, California. [3]Stanford Center for Sleep Sciences and Medicine, Stanford University, Palo Alto, California. [4]California Pacific Medical Center Research Institute, San Francisco. [5]Department of Medicine, Stanford University, California. [6]Department of Psychiatry and [7]Department of Medicine, University of California, San Diego, La Jolla.

Address correspondence to Jamie M. Zeitzer, PhD, Mental Illness Research, Education, and Clinical Center, VA Palo Alto Health Care System, 3801 Miranda Avenue (151Y), Palo Alto, CA 94304. E-mail: jzeitzer@stanford.edu

Received July 8, 2016; Editorial Decision Date December 1, 2016

Decision Editor: Stephen Kritchevsky, PhD

Abstract

Background: There is growing interest in the area of "wearable tech" and its relationship to health. A common element of many of these devices is a triaxial accelerometer that can yield continuous information on gross motor activity levels; how such data might predict changes in health is less clear.

Methods: We examined accelerometry data from 2,976 older men who were part of the Osteoporotic Fractures in Men (MrOS) study. Using a shape-naive technique, functional principal component analysis, we examined the patterns of motor activity over the course of 4–7 days and determined whether these patterns were associated with changes in polysomnographic-determined sleep and cognitive function (Trail Making Test—Part B [Trails B], Modified Mini-Mental State Examination [3MS]), as well as mortality over 6.5–8 years of follow-up.

Results: In comparing baseline to 6.5 years later, multivariate modeling indicated that low daytime activity at baseline was associated with worsening of sleep efficiency ($p < .05$), more wake after sleep onset ($p < .05$), and a decrease in cognition (Trails B; $p < .001$), as well as a 1.6-fold higher rate of all-cause mortality (hazard ratio = 1.64 [1.34–2.00]). Earlier wake and bed times were associated with a decrease in cognition (3MS; $p < .05$). Having a late afternoon peak in activity was associated with a 1.4-fold higher rate of all-cause mortality (hazard ratio = 1.46 [1.21–1.77]). Those having a longer duration of their daytime activity with a bimodal activity pattern also had over a 1.4-fold higher rate of cardiovascular-related mortality (hazard ratio = 1.42 [1.02–1.98]).

Conclusions: Patterns of daily activity may be useful as predictive biomarkers for changes in clinically relevant outcomes, including mortality and changes in sleep and cognition in older men.

Keywords: Actigraphy—Functional data analysis—Biomarker

The near ubiquitous use of accelerometers in electronic devices ranging from "smartphones" to personal fitness devices provides the biomedical community with a potential wealth of data that could be useful in predicting changes in human health. For more than 25 years, the sleep community has used longitudinal (weeks to months) data from validated, wrist-worn accelerometers to estimate sleep and circadian activity rhythms (1,2), whereas those studying exercise have typically used waist-worn accelerometers to examine amounts of activity (3). It is, however, not known whether these data, independent of their use to impute sleep and exercise amounts, could be used to examine other health-related issues.

Studies of 24-hour activity patterns often use "actigraphs," which are wrist-worn devices that use triaxial accelerometers to determine the amount and timing of gross motor movement (1). These data can be analyzed in a variety of ways and are often mathematically modeled using cosinor (ie, based on the mathematical formula of

a cosine wave) or modified cosinor analyses that yield information concerning the amplitude of activity, the timing of "peak" activity, and the goodness-of-fit (how close pattern is to cosine wave) (1). Although this is often quite useful in young adults with robust activity patterns, these analyses assume the presence of a particular shape of activity (ie, a predictable pattern, such as a cosine waveform) that may not be present in individuals with physical or psychological impairments, such as those associated with aging. One technique that is helpful to quantify nonstandard activity patterns is a shape-naive modeling approach, functional principal component analysis (fPCA) (4). In one use of fPCA, we observed that a specific pattern of daily activity (bimodal peak activity with large midday decline) was associated with a clinical diagnosis of apathy in individuals with Alzheimer's disease (5). Using more traditional methods, such as cosinor-fitting, other aspects of health have been associated with daily patterns of activity, most notably cognitive impairment among older adults (6–10) and mortality (11,12). In Paudel and colleagues (11), an extended cosinor analysis of diurnal patterns of actigraphy was used to search for associations with future mortality. In that study, the goodness-of-fit of the cosinor analysis was the best predictor of mortality, especially from cardiovascular disease (CVD). Thus, individuals whose patterns of activity were most divergent from the assumed cosine waveform were the most likely to die within the next 3.5 years. This type of finding exemplifies the need to examine whether specific shapes of activity, not necessarily of a cosinor variety, are associated with specific medical outcomes. We therefore analyzed data from a longitudinal study of a large cohort of community-dwelling older men in an effort to determine whether specific patterns of activity were associated with changes in sleep and cognition as well as mortality rates.

Materials and Methods

All data are presented as mean ± *SD*.

Participants

All participants were enrolled in the Osteoporotic Fractures in Men (MrOS) study, a large (n = 5,994) cohort of community-dwelling men aged 65 and older, recruited from March 2000 to April 2002 from clinical centers in Birmingham, AL; Minneapolis, MN; Palo Alto, CA; the Monongahela Valley near Pittsburgh, PA; Portland, OR; and San Diego, CA. Full details of the study methodology are published (13,14). Written consent was obtained from all participants prior to engaging in research, and all methods conform to the principles laid out in the Declaration of Helsinki.

Surviving and active participants were invited to participate in the ancillary MrOS Sleep study (n = 3,135), on average 3.4 ± 0.5 years (range 1.9–4.9 years) after initial recruitment into the MrOS study (Figure 1). All participants who remained active in the study and had acceptable polysomnograph (PSG) and actigraphy data from the initial sleep visit were eligible to be contacted to participate in a second sleep visit 6.5 ± 0.68 years (range 4.9–7.9 years) later. Participants were contacted in random order for enrollment until the study recruitment goal (N = 1,000) was met. In this manuscript, we report on four analytic subgroups: suitable actigraphy data for fPCA analysis (n = 2,976), data on mortality (n = 2,943, 8.0 ± 2.3 years of follow-up), data on change in objective sleep measures from PSG from Sleep Visits 1 to 2 (n = 1,004), and data on change in cognition from two different cognitive tests administered during Sleep Visits 1 and 2 (n = 968; Figure 1).

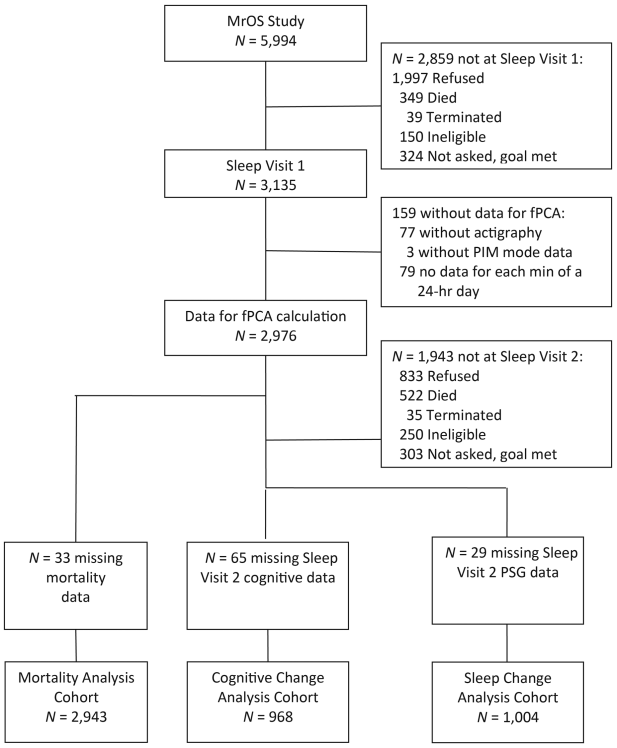

Figure 1. Participant flow chart.

fPCA Predictor

For at least five consecutive days at the time of the first sleep visit, participants had their activity patterns monitored using a wrist-worn accelerometer (Octagonal SleepWatch-O; Ambulatory Monitoring Inc., Ardsley, NY; an "actigraph") placed on the nondominant wrist. An actigraph is a small device that contains a three-dimensional accelerometer that monitors and records general arm movement. It is commonly used in sleep research as the data adequately estimate general sleep and wake patterns (1). Data in this study were acquired during 1-minute epochs in proportional integration mode, which provides an estimate of the magnitude of movement.

In a subset of 2,976 participants, we were able generate an "average day" of actigraph data by averaging each minute of the day across days of collection. This set of 1,440 points (one for each minute) from the 2,976 participants (ie, 4,285,440 data points) was subjected to fPCA (5,15), which is similar to PCA except that it is applied to semicontinuous data rather than discrete data. In this iteration of fPCA, each individual's data was fit with a nine-Fourier-based function, thereby generating a set of 2,976 Fourier functions (one for each participant). Functional data analysis then determined the equations that explained the greatest amount of variance in the Fourier functions (4). We calculated the first four components of the fPCA as these typically explain the majority of the variance, with subsequent components yielding diminishing returns (5,16). Each participant was then assigned an eigenvalue for each of the four components, representing how closely an individual's activity data followed a specific pattern uncovered by the fPCA. These eigenvalues (four per participant—one for each of the four fPCA components) were then subjected to parametric statistics. The first four fPCA components were separately calculated for each of the three analysis cohorts (cognition, sleep, mortality).

Change in Sleep

Of the 2,976 men with actigraphy data, a subset of 1,004 had sleep recorded by PSG during the two sessions that were 6.5 ± 0.68 years apart. In-home sleep studies were completed using unattended, portable polysomnography at both Sleep Visits 1 and 2 (Safiro; Compumedics, Melbourne, Australia), using procedures similar to those used in the Sleep Heart Health Study (17). PSG data were obtained from C_3/A_2 and C_4/A_1 electroencephalograms, bilateral electrooculograms, and bipolar submental electromyogram. Data were downloaded to the Central Sleep Reading Center and scored by certified research polysomnologists using standard criteria (18,19). For the purposes of these analyses, we calculated total sleep time (time scored as sleep during the sleep period), wake after sleep onset (WASO; time scored as wake occurring after the initiation of sleep and before the final awakening), and sleep efficiency (total sleep time divided by time of the sleep period). The change in the measurements between the two time points was calculated as Sleep Visit 2 – Sleep Visit 1.

Change in Cognition

Two tests of cognitive function were administered at both sleep visits by trained staff: Trail Making Test—Part B (Trails B) and Modified Mini-Mental State examination (3MS). Of the 2,976 men with actigraphy data, a subset of 968 had both 3MS and Trails B scores obtained during the two sleep visits.

Trails B is a timed (300 seconds) test that measures attention, sequencing, visual scanning, and executive function. Trails B requires the participant to continuously scan a page to identify numbers and letters in a specified sequence while shifting from number to letter sets (20). A shorter completion time represents better cognitive functioning. A positive increase in completion time (took longer to complete the test at Sleep Visit 2) represents cognitive decline.

The 3MS is a global measurement of cognitive function, with components for orientation, concentration, language, praxis, and immediate and delayed memory (21). Scores range from 0 to 100, with higher scores representing better cognitive functioning. A decrease in 3MS score (ie, lower at Sleep Visit 2) represents cognitive decline.

Mortality

Participants were contacted every 4 months to ascertain vital status. During a follow-up of 8.0 ± 2.3 years, over 99% of these contacts were completed. Deaths were confirmed with death certificates and cause of death was adjudicated to be due to CVD, cancer or other cause by central physician review of death certificates and medical records. Cause of death was broadly categorized by International Classification of Disease-9 codes as cardiovascular (codes 394.9–443.9, 785.51, 966.71), cancer (codes 141.9–208.0), and other causes (codes not in previous categories). The most common cause of death in the "other" category was dementia (either senile dementia unspecified or Alzheimer's disease, $n = 61$).

Other Measurements

During Sleep Visit 1, participants completed questionnaires including items about self-reported health status and demographics (age, race, highest year of schooling completed, body mass index). For the purposes of this analysis, race was coded as White and non-White. Education was coded as less than high school education, high school education, and some college or graduate school. Body mass index was calculated as weight (kilogram) per the square of height (square meter). Also assessed were social status (MacArthur Subjective Status Scale [MSSS] range: 1–10, higher scores equating to perceived elevated social status (22)), sleep (Pittsburgh Sleep Quality Index [PSQI] range: 0–21, scores > 5 are associated with disrupted sleep (23)), daytime sleepiness (Epworth Sleepiness Scale [ESS] range: 0–24, higher scores associated with greater subjective sleepiness and scores > 10 considered clinically significant (24)), depressive symptomatology (Geriatric Depression Scale-Short Form [GDS] range: 0–15, designed for the assessment of depressive symptoms in older adults, scores > 5 associated with depression (25)), and anxiety (Goldberg Anxiety Scale [GAS] range: 0–9, higher scores associated with greater anxiety and scores > 4 associated with clinically relevant anxiety (26)).

Statistical Analysis

Using four independent multivariable linear regression models, we examined the relationship of each of the four fPCA components with a variety of psychiatric status and demographics variables that might be associated with daily activity patterns, including education, socioeconomic status (MSSS), self-rated health, age, mental status (3MS), race, anxiety (GAS), depression (GDS), sleepiness (ESS), and history of sleep disruption (PSQI). Results are presented as beta coefficients (B) and their 95% confidence intervals along with p values. To assess the association of fPCA with the outcomes of change in sleep, change in cognition, and mortality, fPCA predictors were expressed in quartiles in adjusted models. In these models, all four fPCA predictors were included in the same model for each outcome. Missing data from covariates (0.1%) were replaced with median values in these models. Linear regression models were used to assess the relationship of fPCA to change in sleep and change in cognition. Results are presented as adjusted means (95% confidence intervals), the p value for the test for linear trend across quartiles, and B (95% confidence intervals) and p value. All models were minimally adjusted for age and race. Models for the three sleep outcomes (change in WASO, sleep efficiency, total sleep time) were further adjusted for education, socioeconomic status, mental status, anxiety, depression, daytime sleepiness, history of sleep disruption, and baseline value for the outcome measure (eg, minutes of WASO at Sleep Visit 1 for the regression analysis examining the change in WASO). The models for the two cognitive outcomes (change in Trails B test time, change in 3MS score) were further adjusted for education, socioeconomic status, self-rated health, anxiety, depression, sleepiness, history of sleep disruption, and baseline value for the outcome measure. Cox proportional hazards models were used to estimate the association of fPCA with all-cause and cause-specific mortality outcomes. The Schoenfeld residuals and the interaction between fPCA predictor and log-(time) were examined to verify the proportionality assumption. The hazard ratios and 95% confidence intervals for each outcome were calculated across quartiles of fPCA. Quartile 4 served as the referent group for fPCA1, whereas Quartile 1 served as the referent group for fPCA2–fPCA4. Tests for trend were performed by including fPCA measure (ordinal variable, four levels) as an independent variable in models. Men who were lost to follow-up ($n = 125$) were censored after date of last follow-up contact. In cause-specific mortality analyses, men who died of another cause were censored at the time of death. All models for the outcome of mortality were minimally adjusted for age and race, then further adjusted for depression, anxiety, social status, education, daytime sleepiness, self-reported sleep quality, baseline cognitive function (3MS), and self-reported health status.

Results

Participant Population

There were 2,976 men in the MrOS Sleep cohort who had sufficient actigraphy data to perform fPCA (Figure 1). As with the overall cohort, these men were older (76.4 ± 5.53 years), predominantly White (90%), had a relatively high self-rated social status (MSSS = 7.0 ± 1.7), had good self-rated health (87% rating "good" or "excellent"), and were well educated (79% had at least some college education). At Sleep Visit 1, the men were cognitively normal (3MS: 92.7 ± 6.01) and had relatively low rates of clinically relevant depressive symptomatology (6.7% with GDS ≥ 6) or anxiety (9% with GAS ≥ 5). Nearly half reported problems with sleep (44% with PSQI > 5), but fewer exhibited symptoms of daytime sleepiness (13% with ESS > 10).

Variance in Activity Patterns Was Explained Using fPCA

In computing the fPCA of the diurnal motor patterns in older men (n = 2,976), the first component of the fPCA (fPCA1) explained 50% of the variance and could be described as the amplitude such that the higher the fPCA1 values, the greater the overall daytime activity (Figure 2A). fPCA2 explained variance (23%) associated with the timing of sleep, with lower values associated with an earlier wake and bed time and a greater morning peak of activity (Figure 2B). fPCA3 explained variance (9.1%) associated with a bimodal pattern, with higher values associated with a greater midday dip in activity and a slightly later bed and earlier wake time (Figure 2C). fPCA4 explained variance (6.0%) associated with shifts in peak activity, with higher values associated with greater evening activity and lower values associated with greater morning activity (Figure 2D). In total, the four fPCA components accounted for 88% of the variability in the diurnal motor activity pattern. This technique also produced orthogonality within the fPCA components, with nonsignificant Pearson correlations among the four fPCA components ($|r|$'s < .025, p's > .20), indicating that each of the four components can be thought of as an independent descriptor of the variance of the activity data.

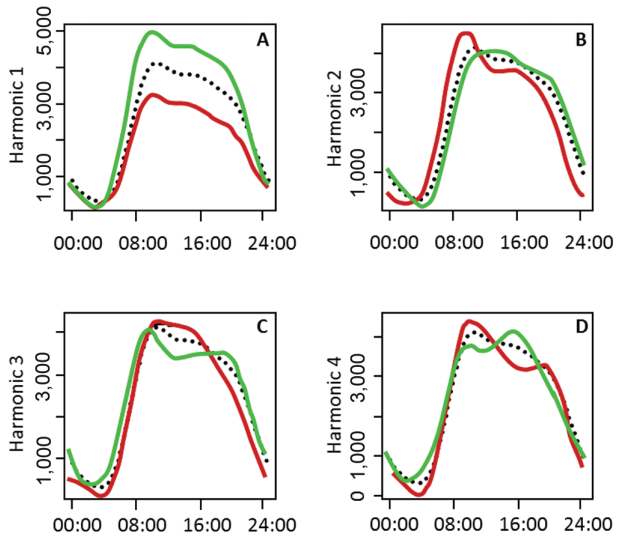

Figure 2. The first four components of the functional principal component analysis (fPCA) of actigraphy data from older men (n = 2,976). Plotted against clock time are the average pattern (black, dotted) and curves showing the pattern of activity in individuals with the average eigenvalue of positive fPCA scores (grey) or negative scores (solid black) added to the average activity pattern (note that the activity is described in a unitless measure). The first component (fPCA1, **A**) represents high (high eigenvalues) and low (low eigenvalues) overall amplitude. The second component (fPCA2, **B**) represents later (high eigenvalues) and earlier (low eigenvalues) rise and bed times. The third component (fPCA3, **C**) represents longer, biphasic (high eigenvalues) and shorter, more monophasic (low eigenvalues) activity patterns. The fourth component (fPCA4, **D**) represents morning (low eigenvalues) and evening (high eigenvalues) peaks in activity.

Diurnal Activity Patterns, Demographics, and Psychiatric Status

At Sleep Visit 1, greater activity (higher fPCA1) was associated with younger age, better self-rated health, better cognitive function, more anxiety, less depression, and less sleep disruption (Supplementary Table 1). Later activity (higher fPCA2) was associated with more depression, less daytime sleepiness, higher self-rated social status, and being non-White (Supplementary Table 1). A larger midday dip (higher fPCA3) was associated with older age, more depression, worse cognitive function, being non-White, and more daytime sleepiness (Supplementary Table 1). An evening peak activity (higher fPCA4) was associated with more sleep disruption and less education (Supplementary Table 1). The different descriptors of the overall diurnal activity pattern were, therefore, differentially influenced by a variety of factors that must be considered when examining the relationship between diurnal activity patterns and other outcome measures.

fPCA Components of Diurnal Activity Predicted Changes in Sleep

We examined whether any of the four fPCA patterns of diurnal activity that occurred at Sleep Visit 1 could predict changes in PSG-measured sleep at Sleep Visit 2. At Sleep Visit 1, participants had 107 ± 61.3 minutes of WASO, 359 ± 63.1 minutes of total sleep time, and a sleep efficiency of 77.6% ± 11.1%. By Sleep Visit 2, 6.5 years later, sleep worsened as WASO increased 16.2 ± 78.1 minutes, total sleep time decreased 16.2 ± 81.9 minutes, and sleep efficiency decreased 3.62% ± 14.1%. Although results were not significant in minimally adjusted models, when the four fPCA components were entered into the same multivariable adjusted model for predicting either change in total sleep time, WASO, or sleep efficiency, with adjustment for covariates, the amplitude of activity (fPCA1) at baseline was associated with changes in both WASO and sleep efficiency (Supplementary Table 2A–C), such that individuals who had less daily activity (lower fPCA1) at Sleep Visit 1 were more likely to have a greater increase in WASO (p trend = .002) and worse sleep efficiency (p trend = .02) 6.5 years later. fPCA component 2, the timing of sleep, was associated to changes in WASO and sleep efficiency in minimally adjusted models, but not after further adjustment. fPCA components 3 and 4 at Sleep Visit 1 were not associated with changes in WASO, sleep efficiency, or total sleep time.

fPCA Components of Diurnal Activity Predicted Changes in Cognitive Function

We examined whether the pattern of diurnal activity could predict changes in cognitive function. 3MS started at 94.2 ± 4.43 and declined 1.29 ± 4.92 between the two visits, 6.5 years apart. When the four fPCA components were entered into the same model for predicting change in 3MS scores, with adjustment for covariates, the

timing of sleep (fPCA2) at Sleep Visit 1 was associated with changes in 3MS scores (Supplementary Table 3A) such that men who had an earlier activity schedule (lower fPCA2) were more likely to have a larger decline in 3MS scores at Sleep Visit 2, 6.5 years later (p trend = .01).

Trails B completion time started at 105 ± 39.6 seconds and increased 23.4 ± 57.1 seconds between the two visits. When the four fPCA components were entered into the same model for predicting change in Trails B time, with adjustment for covariates, activity amplitude (fPCA1) at Sleep Visit 1 was associated with changes in Trails B time (Supplementary Table 3B), such that men who had less daily activity (lower fPCA1) were more likely to have a larger increase in Trails B completion time at Sleep Visit 2, 6.5 years later (p trend = .001).

fPCA Components of Diurnal Activity Predicted Mortality

Among the 882 (30.0%) deaths, 302 were attributed to CVD, 230 to cancer, and 349 to non-CVD/noncancer causes. fPCA1 and fPCA4 were both associated with a higher rate of death (Figure 3, Supplementary Table 4A). After adjustment for multiple factors that could covary with activity, men with less activity (quartile 1, fPCA1) had over a 1.6-fold higher rate of all-cause mortality (hazard ratio 1.64 [1.34–2.00], p trend < .0001). Men with an evening peak in activity (quartile 4, fPCA4) had over a 1.4-fold higher rate of all-cause mortality (hazard ratio 1.46 [1.21–1.77], p trend < .0001). No associations were seen with fPCA2 or fCPA3 and rate of all-cause mortality.

The association between both fPCA1 and fPCA4 and a higher rate of all-cause mortality appeared to be primarily related to increased risks of CVD and non-CVD/noncancer deaths among men in the higher risk category (Supplementary Table 4B). Although fPCA3 was not related to all-cause mortality, it was related to cardiovascular death (Supplementary Table 4B). No associations were seen with fPCA and cancer deaths.

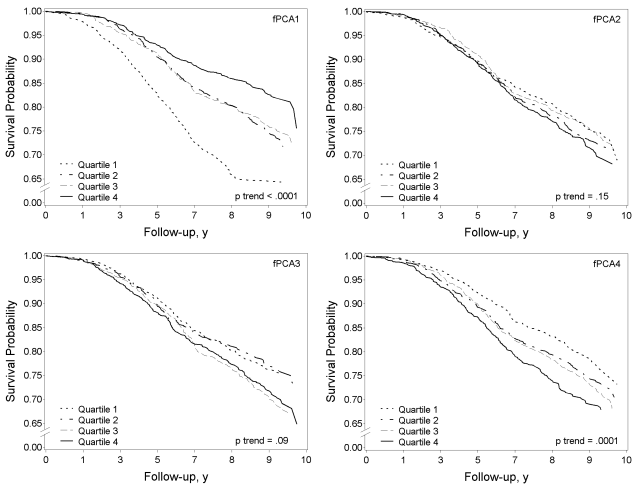

Figure 3. All-cause mortality adjusted survival plots for fPCA1 (upper left), fPCA2 (upper right), fPCA3 (lower left), and fPCA4 (lower right). Survival curves are adjusted for age, race, depression, anxiety, social status, education, daytime sleepiness, self-reported sleep quality, baseline cognitive function (Modified Mini-Mental State Examination [3MS]), and self-reported health status. Missing data (0.1%) were replaced with median values.

Discussion

In older, community-dwelling men, specifiable daily patterns of activity were associated with future worsening of sleep and decreased cognition, as well as with shorter survival. Lower overall activity levels at baseline were associated with a future worsening of sleep (both WASO and sleep efficiency), diminished frontal lobe activity (Trails), and greater overall and cardiovascular-related mortality. Both overall and cardiovascular-related mortality were also related to a late afternoon activity peak and a bimodal activity pattern with an expansion of the time spent active. We also found that those with earlier bed and rise times with a peak of activity in the morning were more likely to have diminished overall cognitive function (3MS).

Although it is tempting to associate causality between specific patterns and outcome measures, our study does not directly address such. It may be that the activity patterns, especially fPCA1, could be manipulated to change outcomes (eg, increasing overall activity to improve sleep (27)). It is possible, however, that the associations we observe between activity patterns and these outcome measures are epiphenomenal in that the patterns may reflect compensatory mechanisms related to a proximally related cause of the decline (eg, those who will die from CVD may not have the cardiovascular capacity to have elevated activity levels, but the lower activity did not cause the increased deaths related to CVD). Likewise, the association between a higher risk of death from CVD and a bimodal (fPCA3) pattern of activity may represent an increase in daytime napping in these individuals that is secondary to the CVD (ie, the CVD does not allow them to maintain a consolidated period of wakefulness). The association of elevated evening pattern of activity and increased all-cause mortality might be evidence of the increased activity associated with a dichotomy between desired and actual bedtimes, which has been linked to more rapid progression of breast cancer in women (28). The lack of direct association between patterns and outcomes does not diminish the utility of using activity pattern recognition to potentially identify risk factors in older men, but may limit interpretation of these data for prediction of response targets.

Two previous studies of this same cohort have reported associations between mortality and diurnal activity rhythms, notably a lower amplitude and elevated minimum of a cosinor fit to the data (11,29). We found multiple patterns of activity that were associated with an increased rate of mortality, especially those resulting from CVD. Individuals with less overall activity (low fPCA1), a longer activity period that is bimodal (high fPCA3), and a late afternoon peak in activity (high fPCA4) are all associated with increased mortality from CVD (Figure 3). The previous studies in the same cohort were unable to find graded associations between mortality from CVD and most metrics derived from cosinor analysis (including measures of activity such as mesor and amplitude). The association of these fPCA-derived activity patterns with mortality, and the failure of traditional shape-specific methods of data fitting, highlight the importance of using a shape-naive approach in examining activity data from a population that might have a non-"normal" pattern of activity (eg, older individuals).

These data were collected from a group of relatively healthy, older community-dwelling men at two time points. Collection at multiple time points would have been useful to examine the nature of the trajectory of changes in cognition and sleep, and the relative importance of these activity patterns in predicting these trajectories. Whether the same patterns occur in unhealthy individuals, in women, or in men or women of different ages remains to be

discovered. One of the benefits of this technique, however, is that there is no predefined shape of the activity—individual shapes can be defined in populations of interest. Most previous research has been cross-sectional and depended on a priori assumptions about the shape of the activity. Although the quality and availability of movement data obtainable from current forms of wearable technology are unknown, at this point, however, the ability to detect patterns of activity that might be associated with clinically meaningful outcomes, such as changes in cognitive function and mortality, and the plethora of such data from personal activity monitors and mobile phones make this technique a potentially important part of the clinical toolbox in the years to come.

Supplementary Material

Supplementary data are available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

Funding

This work was supported by the National Institute on Aging, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Center for Advancing Translational Sciences, National Heart, Lung, and Blood Institute, and NIH Roadmap for Medical Research under the following grant numbers: U01AG027810, U01AG042124, U01AG042139, U01AG042140, U01AG042143, U01AG042145, U01AG042168, U01AR066160, UL1TR000128, R01HL071194, R01HL070848, R01HL070847, R01HL070842, R01HL070841, R01HL070837, R01HL070838, and R01 HL070839. This analysis project was supported by the VA Sierra Pacific Mental Illness Research, Education, and Clinical Center.

References

1. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep*. 2003;26:342–392.
2. Morgenthaler TI, Lee-Chiong T, Alessi C, et al.; Standards of Practice Committee of the American Academy of Sleep Medicine. Practice parameters for the clinical evaluation and treatment of circadian rhythm sleep disorders. An American Academy of Sleep Medicine report. *Sleep*. 2007;30:1445–1459.
3. Yang CC, Hsu YL. A review of accelerometry-based wearable motion detectors for physical activity monitoring. *Sensors (Basel)*. 2010;10:7772–7788. doi:10.3390/s100807772.
4. Ramsay JO, Silverman BW. *Functional Data Analysis*. 2nd ed. New York, NY: Springer; 2005. doi:10.1007/978-1-4757-7107-7
5. Zeitzer JM, David R, Friedman L, et al. Phenotyping apathy in individuals with Alzheimer disease using functional principal component analysis. *Am J Geriatr Psychiatry*. 2013;21:391–397. doi:10.1016/j.jagp.2012.12.012
6. Cochrane A, Robertson IH, Coogan AN. Association between circadian rhythms, sleep and cognitive impairment in healthy older adults: an actigraphic study. *J Neural Transm*. 2012;119:1233–1239. doi:10.1007/s00702-012-0802-2
7. James BD, Boyle PA, Bennett DA, Buchman AS. Total daily activity measured with actigraphy and motor function in community-dwelling older persons with and without dementia. *Alzheimer Dis Assoc Disord*. 2012;26:238–245. doi:10.1097/WAD.0b013e31822fc3cb
8. Buchman AS, Boyle PA, Yu L, Shah RC, Wilson RS, Bennett DA. Total daily physical activity and the risk of AD and cognitive decline in older adults. *Neurology*. 2012;78:1323–1329. doi:10.1212/WNL.0b013e3182535d35
9. Barnes DE, Blackwell T, Stone KL, Goldman SE, Hillier T, Yaffe K. Cognition in older women: the importance of daytime movement. *J Am Geriatr Soc*. 2008;56:1658–1664. doi:10.1111/j.15325415.2008.01841.x
10. Tranah GJ, Blackwell T, Stone KL, et al. Circadian activity rhythms and risk of incident dementia and mild cognitive impairment in older women. *Ann Neurol*. 2011;70:722–732. doi:10.1002/ana.22468
11. Paudel ML, Taylor BC, Ancoli-Israel S, et al. Rest/activity rhythms and mortality rates in older men: MrOS Sleep study. *Chronobiol Int*. 2010;27:363–377. doi:10.3109/07420520903419157
12. Buchman AS, Yu L, Boyle PA, Shah RC, Bennett DA. Total daily physical activity and longevity in old age. *Arch Intern Med*. 2012;172:444–446. doi:10.1001/archinternmed.2011.1477
13. Orwoll E, Blank JB, Barrett-Connor E, et al. Design and baseline characteristics of the osteoporotic fractures in men (MrOS) study—a large observational study of the determinants of fracture in older men. *Contemp Clin Trials*. 2005;26:569–585. doi:10.1016/j.cct.2005.05.006
14. Blank JB, Cawthon PM, Carrion-Petersen ML, et al. Overview of recruitment for the osteoporotic fractures in men study (MrOS). *Contemp Clin Trials*. 2005;26:557–568. doi:10.1016/j.cct.2005.05.005
15. Ding J, Symanzik J, Sharif A, Wang J, Duntley S, Shannon WD. Powerful actigraphy data through functional data representation. *Chance*. 2011;24:30–36. doi:10.1007/s00144-011-0027-4
16. Gershon A, Ram N, Johnson SL, Harvey AG, Zeitzer JM. Daily actigraphy profiles distinguish depressive and interepisode states in bipolar disorder. *Clin Psychol Sci*. 2016;4:641–650. doi:10.1177/2167702615604613
17. Redline S, Sanders MH, Lind BK, et al. Methods for obtaining and analyzing unattended polysomnography data for a multicenter study. Sleep Heart Health Research Group. *Sleep*. 1998;21:759–767.
18. Rechtschaffen A, Kales A. *A Manual of Standardized Terminology, Techniques and Scoring System for Sleep Stages of Human Subjects*. Washington, DC: US Department of Health, Education, and Welfare, Government Printing Office; 1968.
19. American Sleep Disorders Association. EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep*. 1992;15:173–184.
20. Reitan R. Validity of the Trail Making Test as an indicator of organic brain damage. *Percept Mot Skills*. 1958;8:271–276. doi:10.2466/pms.1958.8.3.271
21. Teng EL, Chui HC. The Modified Mini-Mental State (3MS) examination. *J Clin Psychiatry*. 1987;48:314–318.
22. Adler NE, Epel ES, Castellazzo G, Ickovics JR. Relationship of subjective and objective social status with psychological and physiological functioning: preliminary data in healthy white women. *Health Psychol*. 2000;19:586–592. doi:10.1037//0278-6133.19.6.586
23. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28:193–213. doi:10.1016/0165-1781(89)90047-4
24. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep*. 1992;15:376–381.
25. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. In: Brink TL, ed. *Clinical Gerontology: A Guide to Assessment and Intervention*. New York, NY: The Haworth Press; 1986:165–173. doi:10.1300/j018v05n01_09
26. Goldberg D, Bridges K, Duncan-Jones P, Grayson D. Detecting anxiety and depression in general medical settings. *BMJ*. 1988;297:897–899. doi:10.1136/bmj.297.6653.897
27. Montgomery P, Dennis J. Physical exercise for sleep problems in adults aged 60+. *Cochrane Database Syst Rev*. 2002;CD003404. doi:10.1002/14651858.CD003404
28. Hahm BJ, Jo B, Dhabhar FS, et al. Bedtime misalignment and progression of breast cancer. *Chronobiol Int*. 2014;31:214–221. doi:10.3109/07420528.2013.842575
29. Paudel ML, Taylor BC, Ancoli-Israel S, et al. Rest/activity rhythms and cardiovascular disease in older men. *Chronobiol Int*. 2011;28:258–266. doi:10.3109/07420528.2011.553016