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Research Article

Perceived Fatigability and Objective Physical Activity in Mid- to Late-Life

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Abstract

Background: Fatigability, defined as fatigue in relation to a standardized task, predicts functional decline in older adults independent of reported tiredness or energy level. Although the sensation of fatigue, tiredness, and energy level adversely affect physical activity (PA), the association between fatigability and objectively measured PA is unknown.
Methods: Participants in the Baltimore Longitudinal Study of Aging (n = 557, 50% women, aged 50–97 years) were instructed to wear an Actiheart accelerometer for 7 consecutive days in the free-living environment. Perceived fatigability was assessed using the Borg rating of perceived exertion (RPE) after 5 minutes of treadmill walking at 1.5 mph (0.67 m/s) and categorized as low (6–7 RPE), intermediate (8–9 RPE), and high (10+ RPE) fatigability. Time-of-day PA differences between fatigability groups were assessed using mixed-effects modeling.
Results: Total daily PA was 1.3% lower for every unit increment in perceived fatigability after adjusting for demographic, behavioral, and medical factors (p = .01). In time-of-day analyses, the high fatigability group was less active compared to the low fatigability group throughout the day (8:00 am to 8:00 pm) and the intermediate fatigability group in the morning (8:00 am to 12:00 pm). Patterns of PA within the high fatigability group differed from both the intermediate and low groups in the morning but mirrored the intermediate group in the afternoon and evening.
Discussion: These results suggest that RPE is a bio-marker of fatigability associated with progressively lower PA with aging. Whether the effects of fatigability occurring at the end of the day reflect waning energy levels or a voluntary choice that could be modified remains to be evaluated.

Keywords: Accelerometer, Diurnal patterns, Fatigue, Aging, Circadian rhythms

Fatigue is a common complaint among adults aged 50 years and older, that may affect quality of life and foreshadow the onset of functional decline and disability (1–3). The central response to fatigue—slowing down and/or reducing activity often in subtle ways—not only accelerates deconditioning and the risk of frailty and disability but also complicates recognition of fatigue as persons tend to adjust activity levels to avoid, delay, or diminish fatigue (1–4). Accordingly, an improved understanding of the complex association between fatigue and physical activity is warranted.

The construct of perceived fatigability, defined as perceived fatigue in relation to a standardized task, is a more sensitive predictor of functional decline than traditional subjective measures of fatigue (5–7); whether perceived fatigability provides more insight on differences in levels and patterns of daily physical activity, however, has not been evaluated. Previous research has shown that fatigued older adults have lower levels of physical activity than persons not reporting fatigue, but results vary across studies and are challenging to interpret because fatigue is usually evaluated by self-reported questionnaire and is not standardized to activity level (8–11).

Recent studies have linked higher levels of fatigue and fatigability (eg, self-reported fatigue, energy expenditure, perceived fatigability severity) with lower total objectively measured daily physical activity (8,12–14). These studies suggested that fatigability may affect physical activity especially at specific times during the day. One study illustrated that with aging, physical activity accumulation tended to be lower in the afternoon/evening, suggesting a possible cumulative effect of fatigue (2). This notion is supported by another study that observed adults aged 52–83 years who were less active, had lower energy expenditure in the afternoon and evening than their more active counterparts (13). In contrast, a recent study linked self-reported fatigue to lower physical activity observed only in the mornings among older adults (12), but the subjective nature of self-reported fatigue complicates the interpretation of this finding. Therefore, a more in-depth investigation of the complex association between fatigability and daily physical activity patterns is needed to better understand the ways fatigability may manifest and impact quality of life and opportunities for active pursuits.

This study aims to quantify the association between fatigability and objectively measured dimensions of physical activity including amount, and intensity overall and by time of day in well-functioning older adults. A better understanding of these critical aspects of physical activity is needed to provide insight into the characteristics and context of daily activities in adults in mid-to-late life, and to shed light on the role fatigability may play in the well-established aging related decline in daily physical activity before the onset of functional limitations. We first examined the association between perceived fatigability (reported fatigue level after a standardized slow walking task) and objectively measured daily physical activity. We hypothesized that higher perceived fatigability would be associated with lower total daily physical activity. Next, we evaluated whether the association between perceived fatigability and total daily physical activity varies over the course of the day. We hypothesized that those who report higher levels of fatigability would have lower physical activity in later segments of the day than those with low fatigability.

Methods

Study Design and Population

Data for this work come from the Baltimore Longitudinal Study of Aging (BLSA), a continuous enrollment cohort study of normative human aging, established in 1958 and conducted by the National Institute on Aging (NIA) Intramural Research Program. Detailed information about the BLSA sample and enrollment criteria have been previously published (15). Briefly, BLSA participants are community-dwelling volunteers who must be free of cognitive impairment, functional limitations, chronic diseases, and cancer within the past 10 years at the time of enrollment. Once enrolled, participants attend regularly scheduled comprehensive health, cognitive, and functional evaluations over a 3-day visit to the NIA Clinical Research Unit at Harbor Hospital in Baltimore, Maryland every 1–4 years depending on age. Trained and certified study staff administer all assessments following standardized protocols. The National Institute for Environmental Health Sciences Internal Review Board approved the study protocol. Written informed consents were obtained from all participants.

Participants

A total of 770 BLSA participants aged 50–94 years fitted with a chest-worn accelerometer had at least one valid day of data. Participants were excluded if they were unable to walk 400 m to better distinguish fatigability from subclinical disability or disease manifestations (n = 49; mean age of 77.9 ± 12.1 years) or if RPE was not collected (n = 118; mean age of 66.3 ± 15.6 years). The current analysis consists of 557 participants who had a qualifying visit; that is, underwent fatigability assessment and subsequently wore an Actiheart activity monitor for at least 3 valid days (Actiheart, CamNtech, Cambridge, UK) between 2007 and 2015.

Perceived Fatigability

Participants performed a standardized slow-paced walk (0.67 m/s; 1.5 mph) for 5 minutes on a treadmill at 0% grade. Immediately after the walk, participants were instructed to rate their perceived exertion using the Borg rating of perceived exertion (RPE) scale (16). This scale ranges from 6 to 20, where 6 = no exertion at all, 9 = very light, 11 = light, 12 = somewhat hard, and 20 = maximal exertion. The speed of 0.67 m/s has been shown to differentiate frail from nonfrail individuals (17) and requires low enough demand to minimize participant exclusion. Fatigability was examined as a continuous measure from using the RPE from 6 to 20 and as a categorical measure with low fatigability defined as an RPE of 6 or 7, intermediate fatigability as RPE of 8 or 9 and high fatigability as an RPE of 10 or greater (5).

Accelerometer Variables

On the last day of their BLSA clinic visit, participants were fitted with an Actiheart monitor, positioned horizontally on the chest at the third intercostal space using two standard electrocardiogram electrodes, and instructed to wear the monitor continuously for 7 consecutive days. The Actiheart is a light-weight device which utilizes a uniaxial accelerometer and a heart rate monitor to measure physical activity in free-living settings. The Actiheart collects movement in terms of acceleration in units of gravity (g) at a sampling rate of 32 Hz per second and aggregates data into 1-minute activity counts (unit-less quantities of overall movement). At the end of the accelerometer collection period, participants returned the Actiheart to the Clinical Research Unit via express mail and the data were downloaded using Actiheart Software (version 4.0.103).

Minute-level activity counts were averaged across valid days to calculate the average counts per minute for every minute of the day (12:00 am to 11:59 pm). Nonvalid days, defined as greater than 5% of data missing, were excluded from the analysis. For valid days (≤ 5% of data missing), missing values were imputed as the average counts/minute over all available days for each participant (2). Because the distribution of average activity counts/minute is right-skewed at higher intensities, the log of 1 + the mean of activity counts during each minute of the day was calculated (eg, log [1+ mean activity counts from 8:00 am to 8:01 am]). Logged counts were summed across all minutes per participant which normalized the distribution of activity over the sample. For each participant, the transformed activity counts were summed (total logged activity counts [TLAC]) across the full day (12:00 am to 11:59 pm) and by six time-of-day intervals: 12:00 am to 3:59 am, 4:00 am to 7:59 am, 8:00 am to 11:59 am, 12:00 pm to 3:59 pm, 4:00 pm to 7:59 pm, and 8:00 pm to 11:59 pm.

Covariates

Covariates including age, sex, race, currently working for pay, self-rated general health, and falls in the past 12 months (eg, falling and landing on the ground or the floor) were self-reported via an interview questionnaire. Body mass index (BMI) was calculated from measured weight and height (kg/m^2). Usual gait speed was measured over a 6-m course, with the faster of two trials used for analysis. Participants reported whether they were ever told by a doctor or other health professional that they had any of the following conditions: cardiovascular disease including angina, myocardial infarction, congestive heart failure, peripheral arterial disease, and vascular-related procedures; hypertension or high blood pressure; diabetes, glucose intolerance, or high blood sugar; cerebrovascular disease including stroke and transient ischemic attack; chronic bronchitis, emphysema, chronic obstructive pulmonary disease, or asthma; arthritis or osteoarthritis. Responses were summed and categorized into a comorbidity index score (0, 1, and 2+ morbid conditions).

Statistical Analysis

Differences in participant characteristics by fatigability group were tested using analysis of variance for continuous variables and the chi-squared test for categorical variables. Linear regression models were constructed to examine the association between average daily TLAC and perceived fatigability (as both a continuous and categorical variable). To unpack this association within the 24-hour cycle, the smoothed median of unadjusted activity counts at each minute was calculated for each fatigability group to visualize the diurnal patterns of physical activity. Because activity accumulated in the earlier in the day may correlate with activity accrued later in the day, we used multiple linear mixed effects modeling to detect fatigability group differences across six different time periods of the day (4-hour intervals from 12:00 am to 11:59 pm). To account for within-participant clustering, time intervals (random effect) were treated as repeated measures within each participant. Then, the interaction between time intervals by fatigability group was tested to examine whether daily TLAC differed across the time-of-day intervals for each group of fatigability (time by fatigability group interaction). If the interaction term was significant, a priori contrast statements were used to test TLAC differences between fatigability groups within each time interval. All models were successively adjusted for demographic, behavioral, and medical history covariates. Statistical significance was determined using two-tailed hypothesis testing with an alpha level = 0.05. All statistical analyses were performed using Stata software (version 14.2; Stata Corporation, College Station, TX).

Results

Table 1 describes participant characteristics by perceived fatigability group. Of the 557 participants in the analytic sample, the mean age was 71 (*SD* = 9.8) years, 50% were women, 25% were African American, and mean BMI was 27 (4.5) kg/m^2. The prevalence of intermediate and high fatigability was 28% and 25%, respectively. Across fatigability groups, average age and history of stroke or transient ischemic attack and hypertension tended to be higher in higher fatigability groups. In contrast, employment and usual gait speed tended to be lower across higher fatigability groups. In addition, the daily average of cumulative activity counts and TLAC tended to be lower among those with higher fatigability. Those missing valid accelerometer data did not differ greatly by perceived fatigability (mean RPE of 8.3 (2.5) and 8.5 (2.2) for those with nonvalid and valid accelerometer data, respectively; p = .38).

Table 2 describes the linear association between daily TLAC and perceived fatigability—as either continuous RPE or categorical fatigability groups—and the influence of successive covariate adjustment on this association. In continuous analyses, we observed a significant negative association between TLAC and fatigability rating (p < .001)

Table 1. Participant Characteristics by Perceived Fatigability Categories

	Low (RPE 6–7; *n* = 261)	Intermediate (RPE 8–9; *n* = 156)	High (RPE 10+; *n* = 140)	*p* Value
Age (years), mean (*SD*)	67.7 (9.1)	73.1 (9.2)	75.6 (9.1)	<.001
Female, *n* (%)	127 (48.7)	77 (49.4)	76 (54.3)	.542
Black or African American, *n* (%)	67 (25.7)	36 (23.1)	38 (27.1)	.512
Currently employed, *n* (%)	133 (51.0)	41 (26.3)	30 (27.1)	<.001
Body mass index (kg/cm^2), mean (*SD*)	27.0 (4.2)	27.2 (4.5)	27.9 (4.9)	.169
Self-reported good/very good/excellent health, *n* (%)	253 (96.9)	154 (98.7)	134 (95.7)	.452
Usual gait speed (m/s), mean (*SD*)	1.2 (0.2)	1.2 (0.2)	1.0 (0.2)	<.001
Fell in the past 12 mo, *n* (%)	51 (19.5)	41 (26.3)	30 (21.4)	.270
Two or more comorbidities, *n* (%)	184 (70.5)	124 (79.5)	110 (78.6)	.065
MI/CHF/angina/vascular procedure/PAD, *n* (%)	23 (8.8)	21 (13.5)	22 (15.7)	.096
Hypertension, *n* (%)	106 (40.6)	82 (52.6)	77 (55.0)	.008
Hyperlipidemia, *n* (%)	164 (62.8)	111 (71.2)	81 (57.9)	.052
Stroke/TIA, *n* (%)	11 (4.2)	7 (4.5)	14 (10.0)	.044
Pulmonary disease, *n* (%)	38 (14.6)	21 (13.5)	17 (12.1)	.795
Diabetes, *n* (%)	53 (20.3)	33 (21.2)	26 (18.6)	.853
Cancer, *n* (%)	75 (28.7)	51 (32.7)	55 (39.3)	.099
Osteoarthritis, *n* (%)	134 (51.3)	84 (53.9)	86 (61.4)	.151
Activity counts/day, mean (*SD*)	41,067.5 (21,872.5)	30,534.2 (16,088.0)	26,516.4 (13,694.3)	<.001
TLAC/day, mean (*SD*)	1,941.5 (471.4)	1,739.0 (440.0)	1,691.4 (464.7)	<.001
Accelerometer days, mean (*SD*)	5.2 (1.1)	5.3 (1.1)	5.2 (1.1)	.741

Note: Fatigability based on Borg's Rate of Perceived Exertion score during a 1.5 mph standardized treadmill walk. CHF = congestive heart failure; MI = Myocardial infarction; PAD = peripheral arterial disease; RPE = Rating of perceived exertion; TIA = Transient ischemic attack; TLAC = Total logged activity counts.

Table 2. Association Between Total Logged Activity Counts (TLAC) and Perceived Fatigability as a Continuous or Categorical Variable

	Model 1	Model 2	Model 3	Model 4
		TLAC Beta Coefficient (*SE*)		
	Continuous analysis			
RPE during 5-min 0.6 m/s treadmill walk	−54.8 (8.8)***	−30.7 (9.0)**	−24.3 (9.2)**	−24.5 (9.3)**
	Categorical analysis			
Low fatigability group	Reference	Reference	Reference	Reference
Intermediate fatigability group	−202.5 (46.7)***	−113.8 (45.3)*	−91.6 (45.3)*	−91.8 (45.4)*
High fatigability group	−250.1 (48.3)***	−130.2 (48.3)**	−92.6 (49.5)	−93.3 (49.6)

Note: Model 1: Unadjusted model.
Model 2: Model 1 adjusted for age, sex, and race.
Model 3: Model 2 + employment, body mass index (kg/m^2), self-reported health, and gait speed (m/s).
Model 4: Model 3 + fall in the past 12 months and two or more comorbidities.
*p < .05; **p < .01; ***p < .001.

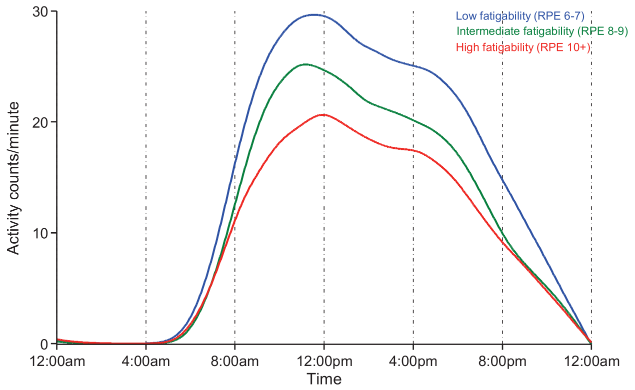

Figure 1. Smoothed 24-hour median activity counts per minute for each fatigability group in adults 50+ years of age. RPE = Rate of perceived exertion.

in the unadjusted linear regression model. As demographics, behavioral factors, and number of medical conditions were progressively added as covariates, the magnitude of the association between TLAC and fatigability rating was attenuated towards the null, but remained significant in the fully-adjusted model (p = .008). In categorical analyses, the intermediate (RPE 8–9) and high (RPE 10+) fatigability groups both exhibited lower TLAC compared to the low (RPE 6–7) fatigability group (p < .001 for both) in unadjusted models. After full covariate adjustment, the intermediate fatigability group had lower TLAC than the low fatigability group (p = .04) but the high fatigability group did not (p = .06).

Figure 1 illustrates unadjusted diurnal activity patterns for each fatigability group across 24 hours. Table 3 shows that, after adjusting for demographics, behavioral factors, and medical conditions, the low fatigability group was consistently more active from 8:00 am to 8:00 pm. An overall significant interaction effect was detected between TLAC and fatigability groups across time-of-day intervals (p = .02), showing that differences between the intermediate or high fatigability diminished over time. Overall, differences in physical activity between fatigability groups increased progressively in the morning, reached maximum around noon and then were maintained constant until 4:00 pm, although the difference between high and intermediate fatigability groups was no longer statistically significant (p = .22 between 12:00 pm and 4:00 pm). Afterword, the difference between intermediate and high fatigability group was progressively reduced, with the low fatigability group remaining more active than the other two groups until 8:00 pm. For the rest of the day, the low fatigability group remained more active than only the intermediate fatigability group (8:00 pm to 12:00 am; p = .02) but not the high fatigability group (high versus low fatigability group p value = 0.10).

Discussion

In well-functioning adults aged 50 years and older, higher perceived fatigability was associated not only with lower overall daily physical activity, but also lower activity levels between 8:00 am and midnight. Although the lower overall level was expected based on previous research (8,12–14), the significantly lower levels of activity late in the day among persons with high fatigability and comparable levels in those with intermediate fatigability are novel observations. This diurnal downshifting in physical activity was associated with perceived fatigability and independent of various demographic, behavioral, and medical history factors, supporting our hypotheses, and accentuating the importance of assessing fatigability in older adults.

In the continuous analysis, we observed that for every one unit higher perceived fatigability, total daily physical activity was 1.3% lower. Our findings are supported by a previous study which found a similar association between perceived fatigability and accelerometry-derived physical activity in a small sample of older adults that operationalized fatigability using change in reported energy before and after a standardized 10-minute walk (14). The categorical analysis showed that differences in total daily physical activity were only observed between the intermediate and low fatigability groups where the intermediate group accumulated 2.7% less total physical activity when compared to the low group. Even though the magnitude of the difference in total daily activity between the low and high fatigability groups was comparable, it did not retain statistical significance after adjusting for behavioral and medical history factors. This suggests a possible shared progression between fatigability and manifestations of functional impairment, disability, and disease; where high fatigability no longer reflects adaptation to total daily activity but rather represents response to onset and progression of disability (6,18) and disease (19–21). Over time, as fatigability increases with advancing age, this may contribute to substantial declines in daily physical activity but further research is needed to understand the temporal pathway that perceived fatigability may share with latent progression of morbid conditions.

The diurnal shape of daily physical activity is similar to other published studies using accelerometer data (2,12,13,22), where participants start with little to no activity at 12:00 am, reach peak

Table 3. Interaction Effect of 4 h Time-of-day Intervals and Fatigability Categories on Transformed Total Daily Activity, Mean (*SE*)

	12:00 am to 4:00 am	4:00 am to 8:00 am	8:00 am to 12:00 pm	12:00 pm to 4:00 pm	4:00 pm to 8:00 pm	8:00 pm to 12:00 am
Low	58.7 (6.4)	171.8 (6.6)	487.5 (7.0)	476.7 (7.4)	440.0 (7.8)	254.8 (8.3)
Intermediate	60.6 (8.1)	154.5 (8.5)	475.2 (8.9)	458.3 (9.4)	399.7 (10.0)***	224.1 (10.6)***
High	76.5 (8.8)	173.0 (9.1)	438.9 (9.5)*,**	441.5 (10.1)*	389.5 (10.7)*	231.5 (11.3)

Note: Mixed effects estimates adjusted for age, sex, race, employment, body mass index (kg/m^2), self-reported health, gait speed (m/s), falls in the past 12 months and two or more comorbidities.

**p* < .05 for the difference between high and low fatigability. ***p* < .05 for the difference between high and intermediate fatigability. ****p* < .05 for the difference between intermediate and low fatigability.

activity around midday, and then decrease activity throughout the afternoon and evening. Adding to the current knowledge, we observed that the accumulation of physical activity throughout waking hours was reduced in those reporting fatigability above a "low" threshold (RPE 6–7). Specifically, the diurnal pattern of the intermediate fatigability group followed the low fatigability group pattern more closely in the morning intervals, but then reduced to mirror the high fatigability diurnal pattern after 12:00 pm and converging later in the evening (Figure 1). This finding suggests that fatigability has a greater negative impact on afternoon activity and further supports the identification of individuals who are transitioning to high fatigability as a possible intervention target. Finally, the high fatigability group never reached the same peak intensity of the low or intermediate fatigability groups from 8:00 am to 8:00 pm; a possible indicator of future risk of functional limitations, disability, comorbidities, and eventual mortality (6,23,24).

This study included both middle-aged and older participants to better understand the association between fatigability and physical activity across the age spectrum and to account for rising subclinical disease and inflammatory processes and age-related changes in energy regulation that often begin to manifest in midlife (23,25–27). By categorizing the sample into three fatigability groups we distinguished an intermediate fatigability group (prevalence of 28%) of mid-to-late life individuals who appear to be transitioning to high fatigability, and may thus be at greater risk of functional decline and mobility impairment over time (6). Early detection of intermediate fatigability and lower physical activity in such persons is essential to identifying individuals at risk for further declines in physical activity who may benefit substantially from intervention efforts.

Sleep may also play a role in the relationship between fatigability and physical activity. During the 8:00 pm to 12:00 am period, we observed that intermediate, but not high fatigability groups, accumulated significantly lower physical activity when compared to the low fatigability group. This may suggest that the high fatigability individuals accrue activity during the later hours of the day, potentially leading to delays in sleep onset that limit total sleep time or to alterations in the sleep/wake cycle. This is important because, when measured by actigraphy, shorter sleep has been linked to poorer performance on a measure of global cognition and to a greater odds of functional decline (28,29). Moreover, "phase delayed" circadian rest/activity rhythms have been linked to a greater risk of both poor cognitive outcomes and mortality in older women (30,31). Although beyond the scope of this manuscript, further study of associations of fatigability with sleep disturbances and sleep/wake patterns is needed.

The BLSA is healthier than the general population, thus likely understating the true association between fatigability and physical activity in middle- and older-aged adults. Further, in our study, we excluded persons who did not complete the 400 m walk, limiting generalizability to those without mobility limitation. Although this may be a limitation, it also reduces the potential for confounding by disease burden. Moreover, excluding 400 m walk noncompleters more clearly elucidates the association between fatigability and disability. Replication of this research is needed in less healthy middle-aged and older populations with greater chronic disease burden and mobility impairments.

This study is cross-sectional which limits the ability to determine the temporal association between fatigability and physical activity (eg, whether fatigability decreases physical activity or reduced physical activity exacerbates fatigability). Future longitudinal analyses are warranted to better understand the direction/reciprocal nature of this association. Lastly, accelerometer data was collected using a chest-worn device, and comparisons with other accelerometer studies must be made with caution as accelerometry is typically collected either on the hip or the wrist in older adults (32).

This study benefits from a well characterized, large sample of adults aged 50 years and older who wore an accelerometer for 3 or more days in the free-living environment. Moreover, these data were collected over multiple 24-hour cycles, providing the unique opportunity to characterize diurnal patterns of physical activity. Although our choice of comparing daily physical activity in 4-hour intervals throughout the day between fatigability groups was somewhat arbitrary, it was designed to follow trends of morning, afternoon, evening, and overnight. Additionally, perceived fatigability was standardized to a slow-paced walk, increasing specificity towards the construct of fatigue.

In conclusion, higher fatigability is associated with lower physical activity, overall and at particular times of day, in a well-functioning cohort of middle-aged and older adults. Diurnal patterns of physical activity among those with intermediate fatigability appear to simulate those with high fatigability later in the day and may provide a target for future interventions to avoid potentially irreversible trajectories toward functional limitations and subsequent disability. Identification of fatigability types may be possible among adults who have not quite reached the later stages in life and who may be more compliant to lifestyle modification. Though development of fatigability may occur earlier in the aging process, further work is needed to understand the underlying biological mechanisms driving fatigability and influencing physical activity throughout the 24-hour cycle.

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Conflict of Interest

A.P.S. has agreed to serve as a consultant to Awarables, Inc. in support of an NIH grant. E.M.S., S.S., L.F., and J.A.S. currently serve on the editorial board for the Journal of Gerontology: Medical Sciences. All other authors have no conflicts of interest to disclose.

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