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Research Article

Changes in Objectively Measured Physical Activity Are Associated With Perceived Physical and Mental Fatigability in Older Men

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Abstract

Background: Lower physical activity (PA) is associated with greater perceived fatigability, a person-centered outcome. The association between change in PA and fatigability with advanced age has yet to be established.

Methods: Community-dwelling older men (N = 1 113, age = 84.1 ± 3.9 years at Year 14) had free-living PA assessed using SenseWear Armband prospectively at Year 7 (2007–2009) and Year 14 (2014–2016) of Osteoporotic Fractures in Men Study, a longitudinal cohort established in 2000 (baseline). We categorized percent changes in PA into groups (large decline → large increase) for 4 metrics: step count, light intensity PA (LIPA, metabolic equivalents [METs] >1.5 to <3.0), moderate-to-vigorous PA (MVPA, METs ≥ 3.0), and sedentary behavior (SB, METs ≤ 1.5, excluding sleep). Perceived physical and mental fatigability were measured (Year 14) with the Pittsburgh Fatigability Scale (PFS, higher score = greater fatigability; range = 0–50). Associations between each metric of percent changes in PA and fatigability were examined using linear regression, adjusted for demographics, change in health conditions, and Year 7 step count or total PA (METs > 1.5).

Results: Men declined 2 336 ± 2 546 (34%) steps/d, 24 ± 31 (25%) LIPA min/d, 33 ± 58 (19%) MVPA min/d, and increased 40 ± 107 (6%) SB min/d over 7.2 ± 0.7 years. Compared to large decline (% change less than −50%), those that maintained or increased step count had 3–8 points lower PFS Physical scores; those who maintained or increased LIPA and MVPA had 2–3 and 2–4 points lower PFS Physical scores, respectively (all $p \le .01$). Associations were similar, but smaller, for PFS Mental scores.

Conclusion: Older men who maintained or increased PA had lower fatigability, independent of initial PA. Our findings inform the types and doses of PA that should be targeted to reduce fatigability in older adults.

Keywords: Disablement process, Epidemiology, Exercise, Fatigue

Greater perceived fatigability is common in older adults (1,2), with higher rates in the oldest old as well as those with lower levels of physical activity (PA) (3–6). As a whole-body measure that anchors fatigue to activities of a specific intensity and duration, greater perceived fatigability has been associated with many health conditions, including higher chronic inflammation (7,8), larger cardiovascular burden (9), lower brain volumes (10,11), functional limitations and mobility decline (12–14), frailty (15), and mortality (16). To this end, perceived fatigability has been identified as an early prognostic indicator of phenotypic aging, which may capture impending declines in physical and mental functioning with greater sensitivity (2).

Several studies have found cross-sectional associations between lower levels of objective PA and greater fatigability. Specifically, older adults with lower levels of overall PA (eg, average daily metabolic equivalents [METs], average daily time spent in different PA intensity levels (17,18), or more fragmented PA patterns) tend to have greater perceived fatigability (19,20). However, no studies have examined the associations of longitudinal changes of objective PA and perceived fatigability. Our recent cross-sectional analysis suggested that perceived fatigability is a potential mediator between PA and physical function among older adults with a mean age of about 70 years (21), implying that PA may potentially predict subsequent perceived fatigability but bidirectionality between PA and perceived fatigability exists. Additionally, we showed that perceived fatigability can be improved after an exercise intervention among a small sample of breast cancer survivors (22). Previous studies have also established that greater energy reserve beyond daily physical/cognitive activities was associated with lower fatigability experienced in everyday living (23,24). Therefore, an exploration of changes in PA and perceived fatigability may improve our understanding of intensity and/or amount of activity that is related to lower fatigability in a general population of older men. Ultimately, our current work will inform design of future PA interventions aimed at reducing fatigability in older adults.

Furthermore, PA could influence fatigability *physical* and *mental* subdomains differently. The prevalence of perceived *physical* fatigability has been shown to be of a greater magnitude than the prevalence of perceived *mental* fatigability in older adults (3,4,6). Most studies have focused on PA and physical fatigability (25), perhaps because PA is more aligned with the central response to fatigue identified as muscle fatigue and slowing down in physical performance. However, recent studies have revealed that perceived mental fatigability is also related to PA and physical function (4), yet it is only moderately correlated with physical fatigability (4,26). Studies have revealed that PA benefits cognition and executive functioning in older adults (27,28), which may potentially further influence mental fatigability via these unique mechanistic pathways (4,29). Thus, it is essential to study both subdomains to explore the underlying similarity and differences between perceived physical and mental fatigability.

In this article, we examined the associations between objectively measured longitudinal changes in PA over an average of 7-years follow-up with perceived physical and mental fatigability in ambulatory community-dwelling older men. We first described the changes in PA overall and by fatigability severity strata. Then, we evaluated the associations between changes in PA and perceived physical and mental fatigability separately. We focused on 4 metrics of PA: step count, total time spent in light intensity PA (LIPA, >1.5 to <3.0 METs), time spent in moderate-to-vigorous PA (MVPA, ≥3.0 METs), and time spent in sedentary behavior (≤1.5 METs, excluding sleep). We hypothesized that maintaining or increasing step count and time spent in LIPA and MVPA, or decreasing time spent in sedentary behavior would be associated with lower perceived physical and mental fatigability at follow-up, but the strength of associations would likely be stronger for physical than mental fatigability.

Method

Study Population

The Osteoporotic Fractures in Men Study (MrOS) is a prospective longitudinal cohort study of ambulatory community-dwelling men aged 65 and older at enrollment (30,31). Briefly, at baseline (2000–2002), 5 994 men without a history of bilateral hip replacement and able to walk without the assistance of another person were recruited from population-based listings across 6 study sites in the United States: Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Pittsburgh, PA; Portland, OR; and San Diego, CA.

The current study used data from Year 7 (Visit 3, March 2007 through March 2009) and Year 14 (Visit 4, May 2014 through May 2016) of MrOS. There were 4 681 men who completed Year 7, of which 3 071 men had valid activity monitor data (90% of activity monitor wear time with <5 days) (32). Among the 3 071 men, 1 860 men completed Year 14, of which 1 150 men had valid activity monitor data for Year 14 (the same definition for valid data as used in Year 7). Of these, 1 113 completed the questionnaires about perceived fatigability and other covariates, ending in the final analytical sample (Figure 1). The average follow-up was 7.2 ± 0.6 years. Overall, those who had valid activity monitor data at Year 7, but were not included in the analytical sample, were older, less educated, and had similar body mass index (BMI) but more multimorbidities, less time spent in LIPA and MVPA, but longer time spent in sedentary behavior at Year 7 and greater perceived fatigability at Year 14 (data not shown).

Objectively Measured PA

At Year 7 and Year 14, participants were instructed to wear the activity monitor (SenseWear Pro3 Armband; BodyMedia, Inc., Pittsburgh, PA) for 24 hours a day, including while sleeping, over

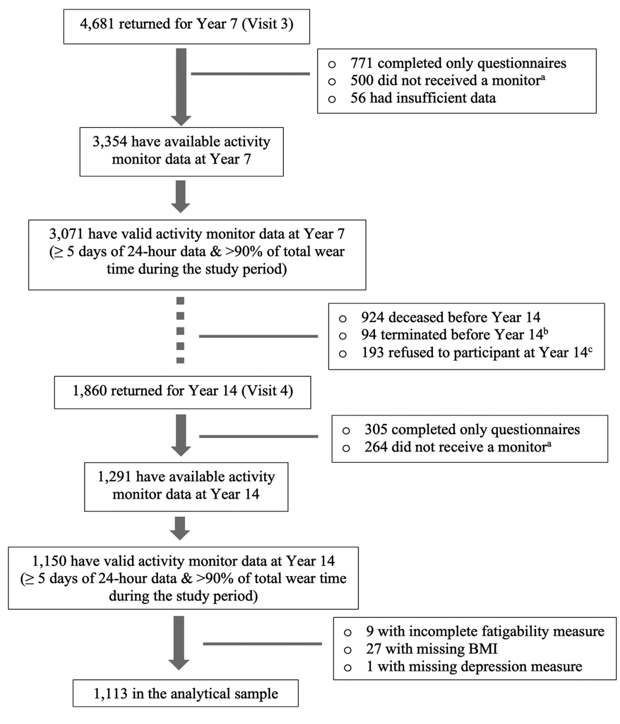

Figure 1. Participants flow chart for inclusion in the current analyses of changes in physical activity and perceived fatigability in the Osteoporotic Fractures in Men Study. BMI = body mass index. [a]Reasons included cognitive impairment, physical/medical problem, oxygen use, right arm disability/amputation, no device available/schedule problem, or others. [b]Reasons for termination included: participant requested change, participant unable to participate, unable to locate participant, participant refuses to complete, participant withdrew consent, or others. [c]Reasons for refusal included: not interested/too busy, health problems, out of area, caregiver responsibilities, postcard only status, or others.

the right triceps for a 7-day period and to remove it only for brief periods of bathing and water activities. Valid data were defined as 90% of activity monitor wear time with <5 days (32). The SenseWear Pro3 Armband (SWA) incorporates a variety of measured parameters (accelerometry, head flux, galvanic skin response, skin temperature, and near-body temperature) and demographic characteristics (age, height, weight, handedness, and smoking status) into proprietary algorithms to estimate energy expenditure (33,34). The SWA has been validated against doubly labeled water in older adults, which showed excellent levels of agreement for energy expenditure (35). METs were calculated as energy expenditure divided by the constant value of 1 kcal/kg per hour (36,37). Four metrics of PA were calculated for each participant: (a) daily step count; (b) average total time spent in LIPA (METs >1.5 to <3.0); (c) average total time spent in MVPA (METs ≥ 3.0); and (d) average total time spent in sedentary behavior (excluding sleep; METs ≤ 1.5) (38). Additionally, total time spent in all PA at Year 7 (METs > 1.5) was also derived for each participant as a covariate in the models for the LIPA, MVPA, and sedentary behavior models.

Percent changes in PA were calculated as the differences between PA at Year 14 and PA at Year 7 divided by PA at Year 7. To obtain meaningful comparisons, men were categorized into 5 groups (selected based on distribution of percent changes in PA) for each of the PA metrics separately: large decline (% change < −50%), moderate decline (% change ≥ −50% and < −10%), maintained (% change ≥ −10% and ≤ +10%), moderate increase (% change > +10% and ≤ +30%), and large increase (% change > +30%). Since the distribution of change in sedentary behavior had a narrower range, we categorized men into 4 groups: declined (% change < −10%), maintained (% change ≥ −10% and ≤ +10%), moderate increase (% change > +10% and ≤ +30%), and large increase (% change > +30%).

Perceived Fatigability

Perceived physical and mental fatigability were measured using the Pittsburgh Fatigability Scale (PFS)—a validated, self-administered 10-item scale for older adults (5). The PFS was collected for the first time in MrOS at Year 14. Participants rated on a scale (0 "no fatigue"–5 "extreme fatigue") how much fatigue "they expected or imagined to feel immediately after completing each task/activity" on 2 subscales—physical and mental. Scores of all responses were added to generate physical and mental fatigability subscale scores, with higher PFS score indicating greater perceived fatigability (range from 0 to 50). The PFS activities included: leisurely walk for 30 minutes, brisk or fast walk for 1 hour, light household activity for 1 hour, heavy gardening or outdoor work for 1 hour, watching television for 2 hours, sitting quietly for 1 hour, moderate- to high-intensity strength training for 30 minutes, participating in a social activity for 1 hour, hosting a social event for 1 hour, and high-intensity activity for 30 minutes. Severity strata were derived to describe participants' characteristics according to established thresholds (PFS Physical score: 0–4 [least severe fatigability], 5–9, 10–14, 15–19, 20–24, ≥25 [most severe fatigability] (2,6); PFS Mental score: 0–3 [least severe fatigability], 4–7, 8–12, 13–15, 16–19, ≥20 [most severe fatigability]) (4).

Covariate Measures

Participants were asked about their date of birth, race/ethnicity, and education level at baseline. At Year 14, height and weight were assessed at the clinic visit to calculate BMI (kg/m^2). Participants self-reported their physician diagnoses of several medical conditions both at Year 7 and Year 14 (including diabetes, hypertension, congestive heart failure, heart attack, coronary or myocardial infarction, stroke, peripheral vascular disease, and chronic obstructive lung disease [COPD]) and fall history in the past 12 months. Participants were also evaluated for depression using Geriatric Depression Scale (range 0–15, score >6 indicates depressive symptoms) (39), and poor sleep quality using the Pittsburgh Sleep Quality Index (range 0–21, score >5 indicates poor sleep quality) (40). The seasonality of SWA measures was coded as winter (January–March), spring (April–June), summer (July–September), and fall (October–December).

Statistical Analysis

Descriptive characteristics of participants were reported as mean ± standard deviation (*SD*) or frequencies (*n*, percentages) for the overall sample and across the perceived fatigability severity strata at Year 14. Trends in characteristics by perceived fatigability severity strata were examined using univariate linear regression. Alpha was set to 0.05 and, after accounting for multiple comparisons using Bonferroni method, 2-sided *p* values smaller than .0125 were considered significant for all analyses. All analyses were performed using Stata version 16 (StataCorp, College Station, TX).

First, each metric of PA and perceived fatigability was modeled separately with multiple linear regression, with per *SD* of changes in PA entered into the model as a continuous variable. Then, we generated similar models with percent changes of PA entered as a categorical variable (5 groups) as described earlier. The referent category was the large decline group (% change > −50%). Progressive covariate adjustments were applied to account for established and potential confounders based on prior literature (3,4,41). Model 1 was adjusted for age at Year 14 and study site. Model 2 was further adjusted for education (≤high school, some college/college degree, and some graduate/graduate degree), BMI (kg/m^2), change in number of self-reported medical conditions between Year 7 and Year 14 (including diabetes, hypertension, congestive heart failure, heart attack, coronary or myocardial infarction, stroke, peripheral vascular disease, COPD, and fall history), depression, poor sleep quality, and seasonality of SWA measures. Finally, Model 3 further adjusted for step count at Year 7 for the step count related models and total time spent in all PA (METs > 1.5) at Year 7 for LIPA, MVPA, and sedentary behavior related models. We checked the variance inflation for all models, all VIFs ≤ 2.0. In addition, we examined the linear trend of the effect sizes across percent changes in PA groups in the final adjusted Model 3.

Results

Overall, the men in our sample were 84.1 ± 3.9 years old at Year 14, 92% White and had a mean BMI of 26.9 ± 3.7 kg/m^2 (Table 1). The mean PFS Physical and Mental scores at Year 14 were 15.8 ± 9.3 points and 7.3 ± 7.9 points, respectively (Table 1). Men with more severe perceived physical fatigability across the severity strata at Year 14 were older, had higher BMI, more self-reported physician-diagnosed health conditions (except hypertension and stroke), more falls in the past 12 months, higher prevalence of depression, and poor sleep quality at Year 14 (all *P*<.05, Table 1).

Additionally, at Year 7 men in the most severe perceived physical fatigability severity stratum (PFS Physical score ≥25, *n* = 208) averaged 30% fewer daily steps and about 40% less time spent in LIPA and MVPA, and 23% more time spent in sedentary behavior than

Table 1. Characteristics of Participants Stratified by PFS Perceived Physical Fatigability Severity Strata: MrOS

		PFS Physical Severity Strata						
	Overall (*N* = 1 113)	Least Severe 0–4 (*n* = 137)	5–9 (*n* = 193)	10–14 (*n* = 186)	15–19 (*n* = 201)	20–24 (*n* = 188)	Most Severe ≥25 (*n* = 208)	*p* Trend
Follow-up, years	7.2 ± 0.6	7.2 ± 0.6	7.2 ± 0.6	7.2 ± 0.7	7.2 ± 0.7	7.3 ± 0.6	7.3 ± 0.7	.137
Age at Year 14, years	84.1 ± 3.9	82.8 ± 3.5	83.1 ± 3.5	83.7 ± 3.4	84.1 ± 3.6	84.4 ± 3.9	85.8 ± 4.6	<.001
Race, White	1 024 (92.0)	125 (91.2)	176 (91.2)	172 (92.5)	183 (91.0)	172 (91.5)	196 (94.2)	.841
BMI, kg/m^2	26.9 ± 3.7	26.2 ± 3.6	26.1 ± 3.2	26.8 ± 3.3	26.7 ± 3.5	27.2 ± 3.9	27.9 ± 4.1	<.001
Education, high school degree or higher	1 087 (97.7)	135 (98.5)	191 (99.0)	178 (95.7)	198 (98.5)	186 (98.9)	199 (95.7)	.060
Health conditions								
Diabetes mellitus*	181 (16.3)	12 (8.8)	21 (10.9)	33 (17.7)	31 (15.4)	34 (18.1)	50 (24.0)	.001
Hypertension*	568 (51.0)	66 (48.2)	88 (45.6)	91 (48.9)	100 (49.8)	98 (52.1)	125 (60.1)	.072
Heart failure*	90 (8.1)	9 (6.6)	9 (4.7)	9 (4.8)	14 (7.0)	23 (12.2)	26 (12.5)	.006
Heart attack*	143 (12.8)	15 (10.9)	15 (7.8)	21 (11.3)	22 (10.9)	26 (13.8)	44 (21.2)	.002
Stroke*	55 (4.9)	8 (5.8)	5 (2.6)	9 (4.8)	10 (5.0)	7 (3.7)	16 (7.7)	.264
TIA*	113 (10.2)	15 (10.9)	12 (6.2)	16 (8.6)	23 (11.4)	15 (8.0)	32 (15.4)	.043
COPD*	112 (10.1)	6 (4.4)	11 (5.7)	14 (7.5)	19 (9.5)	28 (14.9)	34 (16.3)	<.001
Osteoporosis*	292 (26.2)	21 (15.3)	43 (22.3)	43 (23.1)	51 (25.4)	59 (31.4)	75 (36.1)	<.001
Fall history†	415 (37.3)	41 (29.9)	50 (25.9)	62 (33.3)	78 (38.8)	68 (36.2)	116 (55.8)	<.001
Depression‡	56 (5.0)	1 (0.7)	2 (1.0)	5 (2.7)	7 (3.5)	16 (8.5)	25 (12.0)	<.001
Poor sleep quality§	434 (39.0)	29 (21.2)	66 (34.2)	66 (35.5)	85 (42.3)	85 (45.2)	103 (49.5)	<.001
PFS Physical score, range 0–50	15.8 ± 9.3	1.9 ± 1.4	7.2 ± 1.4	12.1 ± 1.4	17.1 ± 1.5	21.7 ± 1.5	29.9 ± 3.8	<.001
PFS Mental score, range 0-50	7.3 ± 7.9	0.7 ± 1.5	2.4 ± 3.0	4.5 ± 4.0	7.9 ± 5.2	9.9 ± 7.2	15.8 ± 10.1	<.001
PA at Year 7 measured by SWA								
Daily step count, steps/d	6 844.7 ± 3 002.6	7 633.6 ± 3 320.8	7 917.1 ± 3 088.4	7 377.9 ± 2 775.6	6 808.8 ± 2 755.3	6 376.7 ± 2 808.1	5 311.0 ± 2 587.0	<.001
Total time spent in LIPA,ǁ min/d	78.5 ± 32.9	85.3 ± 35.2	87.9 ± 31.1	79.4 ± 30.9	79.2 ± 34.7	76.6 ± 32.5	65.4 ± 28.9	<.001
Total time spent in MVPA,¶ min/d	99.4 ± 62.4	108.2 ± 64.1	116.1 ± 68.9	103.9 ± 56.7	99.0 ± 61.9	93.3 ± 63.5	80.0 ± 53.5	<.001
Total time spent in sedentary behavior,#, min/d	822.1 ± 106.1	810.4 ± 110.0	802.4 ± 109.0	823.9 ± 107.9	825.6 ± 101.4	830.4 ± 109.2	835.5 ± 98.3	.001
PA at Year 14 measured by SWA								
Daily step count, steps/d	4 509.2 ± 2 935.2	5 929.7 ± 3 385.7	6 055.2 ± 3 290.5	4 989.3 ± 2 662.6	4 441.0 ± 2 437.7	3 719.1 ± 2 136.6	2 489.9 ± 2 016.3	<.001
Total time spent in LIPA,ǁ min/d	54.8 ± 30.4	64.3 ± 35.0	64.0 ± 32.1	57.6 ± 27.8	55.8 ± 29.5	50.6 ± 26.8	40.4 ± 25.3	<.001
Total time spent in MVPA,¶ min/d	66.9 ± 56.5	88.8 ± 70.9	86.9 ± 67.0	73.9 ± 52.0	63.0 ± 46.0	56.4 ± 50.1	40.9 ± 37.6	<.001
Total time spent in sedentary behavior,# min/d	861.4 ± 112.3	853.7 ± 125.2	841.5 ± 109.1	857.0 ± 112.6	867.3 ± 115.3	872.7 ± 115.0	873.2 ± 97.7	.003
Changes in PA between Year 7 and Year 14 measured by SWA								
Daily step count, steps/d	−2 335.5 ± 2 545.9	−1 703.9 ± 3 119.4	−1 861.9 ± 2 825.1	−2 388.7 ± 2 492.9	−2 367.8 ± 2 250.6	−2 657.6 ± 2 320.1	−2 821.1 ± 2 214.5	<.001
Total time spent in LIPA,ǁ min/d	−23.7 ± 31.0	−21.0 ± 29.7	−23.9 ± 34.0	−21.9 ± 28.5	−23.4 ± 31.0	−26.0 ± 32.2	−25.0 ± 29.9	.171
Total time spent in MVPA,¶ min/d	−32.5 ± 57.6	−19.4 ± 71.4	−29.2 ± 65.5	−30.0 ± 56.4	−36.0 ± 56.3	−36.8 ± 52.2	−39.0 ± 44.2	.001
Total time spent in sedentary behavior,# min/d	39.4 ± 107.0	43.3 ± 106.3	39.1 ± 107.2	33.1 ± 110.1	41.7 ± 101.4	42.3 ± 107.7	37.7 ± 110.0	.938

Notes: All reported in mean ± *SD* or *N* (%). BMI = body mass index; COPD = chronic obstructive pulmonary disease; LIPA = light intensity physical activity; METs = metabolic equivalents; MrOS = Osteoporotic Fractures in Men Study; MVPA = moderate-to-vigorous physical activity; PA = physical activity; PFS = Pittsburgh Fatigability Scale; *SD* = standard deviation; SWA = SenseWear Armband; TIA = transient ischemic attack. Changes in PA were calculated as differences between PA at Year 14 and PA at Year 7.

*All health conditions were self-reported physician diagnosis.

†Have fallen in the past 12 months.

‡Assessed with Geriatric Depression Scale (range 0–15, score >6 indicates depression).

§Assessed with Pittsburgh Sleep Quality Index (range 0–21, score >5 indicates poor sleep quality).

ǁLight intensity physical activity: >1.5 to <3.0 METs.

¶Moderate-to-vigorous physical activity: ≥3.0 METs.

#Sedentary behavior: ≤1.5 METs, excluding sleep time.

men in the least severe stratum (PFS Physical score = 0–4, n = 137; p < .001; Table 1). Furthermore, men with more severe perceived physical fatigability had a larger decline in daily step count, time spent in MVPA (all $p \le .01$, Table 1). For population characteristics by PFS Mental severity strata, only age, self-reported physician-diagnosed diabetes, heart attack, fall history, depression, poor sleep quality, daily step count, and time spent in MVPA were different (Supplementary Table 1).

Changes in Objectively Measured PA

Overall, men decreased their daily step count and time spent in LIPA and MVPA, but increased their time spent in sedentary behavior between Year 7 and Year 14 (Supplementary Figure 1). Specifically, men decreased, on average, their step count by 2 335 ± 2 545 (34%) steps/d, 24 ± 31 (25%) min/d in LIPA, 33 ± 58 (19%) min/d in MVPA but increased 40 ± 107 (6%) min/d in sedentary behavior (Table 1). Of note, for all metrics of PA, men with a large decline in PA (% change <−50%) had the highest PA levels at Year 7, but the lowest PA levels at Year 14; men with a large increase in PA (% change >+30%) had the lowest PA level at Year 7, but the highest PA level at Year 14 (Supplementary Figure 1).

Association Between Changes in PA and Perceived Physical Fatigability

Percent change in step count showed stepwise associations with greater perceived physical fatigability in the fully adjusted Model 3 (Table 2). One *SD* higher change in step count (≈increase 2 545 steps/d over 7 years) was associated with 2.4 points lower PFS Physical scores (p < .001; Table 2). In categorical models, compared to men with a large decline (% change <−50%), men who maintained their step count (±10% change) had 4.5 points lower PFS Physical scores (p < .001; Table 2). Men who moderately increased their step count (% change >+10% and ≤+30%) had 3.4 lower PFS Physical scores; while men who largely increased their step count (% change >+30%) had 7.9 points lower PFS Physical scores (all p ≤ .01; Table 2).

Similarly, when exploring different intensity levels of PA, one *SD* higher change in total time spent in LIPA and MVPA (≈increase 31 min/d for LIPA and 58 min/d for MVPA over 7 years) were associated with 1.4 and 1.9 points lower PFS Physical scores, respectively (p < .01). Yet, the amount of change in sedentary behavior was not associated with perceived physical fatigability. Moreover, in categorical models, percent change in MVPA showed a clear stepwise association with perceived physical fatigability after adjusting for total time spent in all PA and other covariates (p-trend < .001), whereas change in LIPA showed a less pronounced stepwise association with perceived physical fatigability (p-trend = .009). Specifically, compared to men with a large decline in total time spent in MVPA (% change <−50%), PFS Physical scores were 1.9, 3.2, 4.3, and 4.4 points lower for men with moderate decline (% change ≥−50% and <−10%), maintained (% change ±10%), moderate increased (% change >+10% and ≤+30%) or large increase (% change >+30%) their total time spent in MVPA, respectively (all p ≤ .01; Table 2). No associations were observed between percent change in time spent in sedentary behavior and perceived physical fatigability.

Association Between Changes in PA and Perceived Mental Fatigability

Overall, the associations between changes in PA and perceived mental fatigability were similar, but smaller in magnitude than the associations with perceived physical fatigability. One *SD* higher change in step count (≈increase 2 545 steps/d over 7 years) was associated with 1.1 points lower PFS Mental scores (p < .001; Table 3). Similarly, 1 *SD* higher change of total time spent in LIPA and MVPA (≈increase 31 min/d for LIPA and 58 min/d for MVPA over 7 years) were associated with 0.9 and 1.0 points lower PFS Mental scores, respectively (p < .01; Table 3). Furthermore, percent changes in step count, total time spent in LIPA and MVPA, showed stepwise associations with perceived mental fatigability (p-trend ≤ .01; Table 3). For instance, compared to men with the large decline in time spent in MVPA, men who moderately declined, maintained, moderately increased, or largely increased their time spent in MVPA had 1.2, 1.8, 2.9, or 3.4 points lower PFS Physical scores (all p < .05), respectively (Table 3).

Discussion

Our prospective longitudinal study of older men demonstrates that changes in objectively measured PA over an average of 7 years of follow-up showed stepwise associations with perceived physical and mental fatigability, independent of initial PA levels. Specifically, maintaining or increasing daily step count, time spent in LIPA and particularly time spent in MVPA was associated with significantly lower PFS Physical scores. Notably, the magnitude of associations of changes in PA and perceived fatigability were about two thirds smaller for PFS Mental scores compared to PFS Physical scores. Collectively, these findings suggest that men who maintained or increased their free-living PA in later life may experience lower perceived fatigability, especially physical fatigability. However, given the observational nature of our study and 1-time point assessment of fatigability, we cannot rule out that men may have adjusted their daily PA levels in order to concurrently tolerate their fatigue levels (ie, self-pace or adjust their activity) (23). Future studies that measure PA and fatigability simultaneously at multiple time points will lead to a better understanding of the bidirectional relations and allow for drawing causal conclusions.

Men in our study overall reduced their daily step count and total time spent in PA over an average of 7.2 years. Particularly, they largely reduced their time spent in LIPA (25%) and MVPA (19%), but increased their time spent in sedentary behavior (6%). These changes in PA are consistent with previous research. For example, in a population of older adults about 77 years old in the Monongahela-Youghiogheny Health Aging Team, self-reported average minutes per day of MVPA decreased by about half (≈33 min/d) over 8 years (42). In the English Longitudinal Study of Aging (ELSA), participants mean 61 years old showed an overall trend for increasing levels of inactivity and a reduction in vigorous activity over 10-years of follow-up (43). However, because participants in ELSA were younger than men in MrOS, they also found that participants increased their LIPA as a replacement for reduction in vigorous activity; whereas, in our study, we found that men tended to reduce their activities consistently for LIPA and MVPA. We suspect that the reduction in PA observed in our study is likely owing to decreased levels of functional fitness, such as reductions in muscle strength, flexibility, agility, and endurance (44,45), which compressed the total amount of energy potentially used by an individual within a day and limited the overall total time spent in PA, especially in MVPA (23).

One important finding in our study is that maintaining or increasing daily step count and total time spent in activity, particularly MVPA, resulted in lower perceived fatigability. The directionality of these

Table 2. Associations Between Changes in Physical Activity Metrics and Perceived Physical Fatigability Using the Pittsburgh Fatigability Scale: MrOS (*N* = 1 113)

	Model 1*		Model 2†		Model 3‡		
Changes in PA Metrics	β (95% CI)	*p* Value	β (95% CI)	*p* Value	β (95% CI)	*p* Value	*p* Trend
Change in step count (steps/d)							
Per *SD* increase (≈2 525 steps/d)	−1.1 (−1.6, −0.6)	<.001	−0.9 (−1.4, −0.4)	.001	−2.4 (−3.0, −1.8)	<.001	
Large decline	Ref		Ref		Ref		<.001
Moderate decline	−3.5 (−4.7, −2.3)	<.001	−2.7 (−3.9, −1.5)	<.001	−2.8 (−3.9, −1.6)	<.001	
Maintained	−4.9 (−6.8, −3.0)	<.001	−3.9 (−5.7, −2.0)	<.001	−4.5 (−6.3, −2.7)	<.001	
Moderate increase	−4.0 (−6.4, −1.6)	<.001	−2.7 (−5.0, −0.3)	.03	−3.4 (−5.7, −1.1)	.004	
Large increase	−7.7 (−10.4, −5.0)	<.001	−6.4 (−9.0, −3.8)	<.001	−7.9 (−10.5, −5.3)	<.001	
Change in time spent in LIPA§ (min/d)							
Per *SD* increase (≈31 min/d)	−0.4 (−0.9, 0.1)	.13	−0.4 (−0.9, 0.2)	.19	−1.4 (−3.0, −0.7)	<.001	
Large decline	Ref		Ref		Ref		.009
Moderate decline	−2.4 (−3.7, −1.1)	<.001	−1.5 (−2.7, −0.2)	.02	−1.6 (−2.8, −0.3)	.01	
Maintained	−2.6 (−4.3, −0.9)	<.001	−1.9 (−3.5, −0.2)	.03	−2.2 (−3.8, −0.5)	.01	
Moderate increase	−3.3 (−5.5, −1.1)	<.001	−2.5 (−4.6, −0.3)	.03	−2.8 (−5.0, −0.6)	.01	
Large increase	−1.7 (−3.9, 0.5)	.13	−0.9 (−3.1, 1.2)	.39	−1.9 (−4.0, 0.3)	.10	
Change in time spent in MVPA‖ (min/d)							
Per *SD* increase (≈58 min/d)	−0.7 (−1.3, −0.2)	.01	−0.6 (−1.2, −0.1)	.01	−1.9 (−2.5, −1.2)	<.001	
Large decline	Ref		Ref		Ref		<.001
Moderate decline	−2.5 (−3.8, −1.3)	<.001	−1.8 (−3.0, −0.6)	.004	−1.9 (−3.1, −0.7)	.002	
Maintained	−3.3 (−5.1, −1.5)	<.001	−2.6 (−4.3, −0.9)	.003	−3.2 (−5.0, −1.5)	<.001	
Moderate increase	−4.4 (−6.6, −2.1)	<.001	−3.5 (−5.7, −1.3)	.002	−4.3 (−6.5, −2.1)	<.001	
Large increase	−3.9 (−5.6, −2.3)	<.001	−3.2 (−4.8, −1.6)	<.001	−4.4 (−6.0, −2.7)	<.001	
Change in time spent in sedentary behavior¶ (min/d)							
Per *SD* increase (≈107 min/d)	−0.1 (−0.6, 0.5)	.77	−0.1 (−0.6, 0.4)	.63	−0.1 (−0.7, 0.5)	.66	
Decline	Ref		Ref		Ref		.12
Maintained	0.1 (−1.6, 1.9)	.87	−0.2 (−1.9, 1.6)	.86	−0.04 (−1.7, 1.7)	.97	
Moderate increase	0.6 (−1.4, 2.5)	.57	0.1 (−1.7, 1.9)	.94	0.9 (−1.0, 2.8)	.34	
Large increase	−0.8 (−3.5, 1.9)	.55	−0.8 (−3.4, 1.8)	.54	1.5 (−1.3, 4.3)	.30	

Notes: BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; LIPA = light intensity physical activity; METs = metabolic equivalents; MrOS = Osteoporotic Fractures in Men Study; MVPA = moderate-to-vigorous physical activity; PA = physical activity; PFS = Pittsburgh Fatigability Scale; *SD* = standard deviation. Changes in PA were calculated as differences between PA at Year 14 and PA at Year 7. % change in PA were calculated as the differences between PA at Year 14 and PA at Year 7 divided by PA at Year 7. For each of the PA metrics: large decline (% change < −50%), moderate decline (% change ≥ −50% and < −10%), maintained (% change ≥ −10% and ≤ +10%), moderate increase (% change > +10% and ≤ +30%), and large increase (% change > +30%). Since the distribution of change in sedentary behavior had a narrower range, we categorized men into four groups: declined (% change < −10%), maintained (% change ≥ −10% and ≤ +10%), moderate increase (% change > +10% and ≤ +30%), and large increase (% change > +30%). A 4-point difference in PFS Physical scores and a 3-point different in PFS Mental scores were previously associated with 0.05 m/s usual gait speed change per year (13).

*Model 1 adjusted for age at Year 14 and study site.

†Model 2 adjusted for Model 1 + education, BMI (kg/m^2), change in number of self-reported medical conditions between Year 7 and Year 14 (including diabetes, hypertension, congestive heart failure, heart attack, coronary or myocardial infarction, stroke, peripheral vascular disease, COPD, and fall history), depression, poor sleep quality, and seasonality change.

‡Model 3 adjusted for Model 2 + step count at Year 7 for change in step count model. For changes in time spent in LIPA, MVPA, and sedentary behavior, models adjusted for Model 2 + total time spent in all PA (METs >1.5) at Year 7.

§Light intensity physical activity: >1.5 to <3.0 METs.

‖Moderate-to-vigorous physical activity: ≥3.0 METs.

¶Sedentary behavior: ≤1.5 METs excluding sleep time.

Table 3. Associations Between Changes in Physical Activity Metrics and Perceived Mental Fatigability Using the Pittsburgh Fatigability Scale: MrOS (*N* = 1 113)

	Model 1*		Model 2†		Model 3‡		
Changes in PA Metrics	β (95% CI)	*p* Value	β (95% CI)	*p* Value	β (95% CI)	*p* Value	*p* Trend
Change in step count (steps/d)							
Per *SD* increase (≈2 525 steps/d)	−0.6 (−1.1, −0.1)	.01	−0.4 (−0.9, 0.0)	.07	−1.1 (−1.7, −0.6)	<.001	
Large decline	Ref		Ref		Ref		<.001
Moderate decline	−2.1 (−3.2, −1.1)	<.001	−1.6 (−2.6, −0.5)	.003	−1.6 (−2.6, −0.6)	.002	
Maintained	−3.4 (−5.1, −1.7)	<.001	−2.8 (−4.4, −0.5)	.001	−3.1 (−4.8, −1.4)	<.001	
Moderate increase	−2.1 (−4.3, 0.0)	.05	−1.4 (−3.5, 0.8)	.22	−1.7 (−3.9, 0.4)	.11	
Large increase	−4.6 (−7.0, −2.2)	<.001	−3.6 (−6.0, −1.2)	.003	−4.4 (−6.8, −2.0)	<.001	
Change in time spent in LIPA§ (min/d)							
Per *SD* increase (≈31 min/d)	−0.4 (−0.9, 0.1)	.09	−0.3 (−0.8, 0.1)	.17	−0.9 (−1.5, −0.3)	.002	
Large decline	Ref		Ref		Ref		.009
Moderate decline	−2.4 (−3.5, −1.3)	<.001	−1.8 (−2.9, −0.6)	.002	−1.8 (−2.9, −0.7)	.001	
Maintained	−2.1 (−3.6, −0.7)	<.001	−1.6 (−3.1, −0.1)	.03	−1.8 (−3.2, −0.3)	.02	
Moderate increase	−2.2 (−4.1, −0.2)	.03	−1.7 (−3.7, 0.2)	.08	−1.9 (−3.9, −0.0)	.05	
Large increase	−2.4 (−4.3, −0.5)	.02	−1.8 (−3.7, −0.1)	.06	−2.4 (−4.3, −0.4)	.02	
Change in time spent in MVPA‖ (min/d)							
Per *SD* increase (≈58 min/d)	−0.5 (−0.9, 0.0)	.05	−0.4 (−0.9, 0.1)	.09	−1.0 (−1.6, −0.5)	<.001	
Large decline	Ref		Ref		Ref		<.001
Moderate decline	−1.6 (−2.7, −0.5)	<.001	−1.1 (−2.2, −0.3)	.05	−1.2 (−2.3, −0.1)	.03	
Maintained	−1.9 (−3.5, −0.4)	.02	−1.4 (−2.9, 0.1)	.08	−1.8 (−3.3, −0.2)	.03	
Moderate increase	−3.0 (−4.9, −1.0)	<.001	−2.5 (−4.4, −0.5)	.01	−2.9 (−4.9, −1.0)	.003	
Large increase	−3.2 (−4.6, −1.7)	<.001	−2.7 (−4.2, −1.3)	<.001	−3.4 (−4.9, −1.9)	<.001	
Change in time spent in sedentary behavior¶ (min/d)							
Per *SD* increase (≈107 min/d)	0.1 (−0.4, 0.5)	.74	0.1 (−0.4, 0.5)	.78	−0.1 (−0.6, 0.4)	.77	
Decline	Ref		Ref		Ref		.18
Maintained	0.4 (−1.2, 2.0)	.63	0.4 (−1.2, 1.9)	.63	0.4 (−1.1, 2.0)	.58	
Moderate increase	0.7 (−1.0, 2.4)	.44	0.4 (−1.2, 2.1)	.60	0.9 (−0.8, 2.6)	.629	
Large increase	−0.0 (−2.4, 2.3)	.98	0.1 (−2.2, 2.4)	.92	1.4 (−1.1, 3.9)	.27	

Notes: BMI = body mass index; CI = confidence interval; COPD = chronic obstructive pulmonary disease; LIPA = light intensity physical activity; METs = metabolic equivalents; MrOS = Osteoporotic Fractures in Men; MVPA = moderate-to-vigorous physical activity; PA = physical activity; PFS = Pittsburgh Fatigability Scale; *SD* = standard deviation. Changes in PA were calculated as differences between PA at Year 14 and PA at Year 7. % change in PA were calculated as the differences between PA at Year 14 and PA at Year 7 divided by PA at Year 7. For each of the PA metrics: large decline (% change < −50%), moderate decline (% change ≥ −50% and < −10%), maintained (% change ≥ −10% and ≤ +10%), moderate increase (% change > +10% and ≤ +30%), and large increase (% change > +30%). Since the distribution of change in sedentary behavior had a narrower range, we categorized men into four groups: declined (% change < −10%), maintained (% change ≥ −10% and ≤ +10%), moderate increase (% change > +10% and ≤ +30%), and large increase (% change > +30%). A 4-point difference in PFS Physical scores and a 3-point different in PFS Mental scores were previously associated with 0.05 m/s usual gait speed change per year (13).

*Model 1 adjusted for age at Year 14 and study site.

†Model 2 adjusted for Model 1 + education, BMI (kg/m^2), change in number of self-reported medical conditions between Year 7 and Year 14 (including diabetes, hypertension, congestive heart failure, heart attack, coronary or myocardial infarction, stroke, peripheral vascular disease, COPD, and fall history), depression, poor sleep quality, and seasonality change.

‡Model 3 adjusted for Model 2 + step count at Year 7, for change in step count model. For changes in time spent in LIPA, MVPA, and sedentary behavior, models adjusted for Model 2 + total time spent in all PA (METs >1.5) at Year 7.

§Light intensity physical activity: >1.5 to <3.0 METs.

‖Moderate-to-vigorous physical activity: ≥3.0 METs.

¶Sedentary behavior: ≤1.5 METs excluding sleep time.

associations concur with previous cross-sectional studies (15,17), yet no previous study has shown any prospective stepwise associations in a longitudinal design. Our study, using the PFS—a validated measurement of perceived fatigability in older adults—extends knowledge and revealed that men who increased or managed to maintain their PA over the 7 years had lower PFS Physical scores regardless of their Year 7 PA levels. The stepwise relations between percent changes in PA and perceived fatigability was significant for daily step count, time spent in LIPA and particularly time spent in MVPA, indicating a potential greater magnitude of association between higher intensity activities and fatigue. It could be that higher intensity activities led to reduced fatigability, or that those with habitually lower fatigability (which we could not assess because we did not have repeat assessments of fatigability) are more likely to increase or maintain activity levels over time. Exercise interventions designed to increase higher-intensity PA levels are relatively rare in older adults due to safety concerns, but one randomized trial among older adults with rheumatoid arthritis found that MVPA significantly reduced self-reported fatigue, potentially through improvement in aerobic capacity, endurance, and physical strength of participants (46). We also acknowledge that bidirectionality may exist between PA and fatigability. However, we postulate that changes in PA may precede fatigability in this study given (a) the order of PA and PFS data collection in MrOS; (b) our previous work implying a pathway from PA to fatigability then to gait speed (21), and (c) adjustment for time spent in all PA at Year 14 instead of at Year 7 (Model 3) yielding same results (data not shown). Thus, increasing/maintaining PA contributed to lower fatigability beyond the cross-sectional associations of PA and fatigability. Future studies with concurrent and multiple measures of PA and fatigability can use structural equation models to better decipher the temporality between changes in PA and fatigability.

Another important finding is the differential magnitude of effect of the associations between changes in PA and perceived physical versus mental fatigability. The weaker associations between changes in PA and perceived mental fatigability suggest that mental fatigability may be more sensitive to cognitive, emotional, and motivational factors (4), whereas physical fatigability is more related to physical function and fitness (3). Although PA is associated with social functioning, emotionality, and mental health (47,48), it may take a greater volume of PA and/or longer duration of being physically active to confer benefits on perceived mental fatigability. Furthermore, the type of activity (eg, social vs exercise) and the environment where the activity occurs may also influence perceived mental fatigability. As perceived fatigability has been linked with life-space mobility (29), walking outside in a complex outdoor environment might have impact on perceived mental fatigability more than indoor activities, because of the higher cognitive demands. This emphasizes the need to explore different underlying mechanisms of PA on perceived physical versus mental fatigability, to provide important knowledge foundations for designing unique interventions to reduce either physical or mental fatigability.

This study has several strengths, including the large prospective cohort of men in their ninth decade of life with objective PA measured over 7 years, use of a sensitive and valid measure of one's perception (ie, vulnerability) of fatigue in relation to a range of activities, and adjustment for several potential confounders. Limitations of this study include that MrOS is a cohort of predominately healthy older white men limiting generalizability to other race/ethnic groups and to women. A greater portion of the sample died or terminated before Year 14, making our results prone to survival bias, thus likely underestimating declines in PA. Additionally, PA was measured at different seasons over 2 visits (Kappa statistics = −0.03, only 23% of participants wore the SWA during the same season at both visits), which may have resulted in changes in PA due to seasonality differences, not actual lifestyle change. Participants who wore the SWA in spring/winter at Year 7, but wore it in the summer at Year 14 had the smallest decline in step count and total time spent in LIPA and MVPA between visits. Furthermore, men who wore the SWA in summer/fall at Year 7, but wore it in the winter at Year 14 had the largest decline in step count and total time spent in LIPA and MVPA between visits. However, we addressed this issue by adjusting for seasonality in our analytic models. Lastly, our findings should not be interpreted as causal, even though we adjusted for many covariates at Year 14 and changes in medical conditions between Year 7 and Year 14 because they were more directly related to fatigability, and better represented the disease burden over the follow-up. In addition, it is important to note that maintainers may not benefit from habitually lower PA. This subgroup (~2%) who sustained PA lower than the sample median at both Year 7 and Year 14 had nonsignificantly higher mean PFS scores than the rest of maintainers, warranting further exploration given the very small sample size.

In conclusion, maintaining or increasing either step count, total time spent in LIPA, and particularly total time spent in MVPA showed a strong prospective stepwise association with both lower perceived physical and mental fatigability scores over a 7-year follow-up in older men. Our findings are informative for exercise prescription to reduce fatigability in older adults.

Supplementary Material

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

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Conflict of Interest

None declared.

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References

1. Eldadah BA. Fatigue and fatigability in older adults. *PMR*. 2010;2(5):406–413. doi:10.1016/j.pmrj.2010.03.022
2. Schrack JA, Simonsick EM, Glynn NW. Fatigability: a prognostic indicator of phenotypic aging. *J Gerontol A Biol Sci Med Sci*. 2020;75(9):e63–e66. doi:10.1093/gerona/glaa185

3. LaSorda KR, Gmelin T, Kuipers AL, et al. Epidemiology of perceived physical fatigability in older adults: the Long Life Family Study. *J Gerontol A Biol Sci Med Sci.* 2020;75(9):e81–e88. doi:10.1093/gerona/glz288
4. Renner SW, Bear TM, Brown PJ, et al. Validation of perceived mental fatigability using the Pittsburgh Fatigability Scale. *J Am Geriatr Soc.* 2021;69(5):1343–1348. doi:10.1111/jgs.17017
5. Glynn NW, Santanasto AJ, Simonsick EM, et al. The Pittsburgh Fatigability Scale for older adults: development and validation. *J Am Geriatr Soc.* 2015;63(1):130–135. doi:10.1111/jgs.13191
6. Cohen RW, Meinhardt AJ, Gmelin T, et al. Prevalence and severity of perceived mental fatigability in older adults: the Long Life Family Study. *J Am Geriatr Soc.* 2021;69(5):1401–1403. doi:10.1111/jgs.17075
7. Wanigatunga AA, Varadhan R, Simonsick EM, et al. Longitudinal relationship between interleukin-6 and perceived fatigability among well-functioning adults in mid-to-late life. *J Gerontol A Biol Sci Med Sci.* 2019;74(5):720–725. doi:10.1093/gerona/gly120
8. Cooper R, Popham M, Santanasto AJ, Hardy R, Glynn NW, Kuh D. Are BMI and inflammatory markers independently associated with physical fatigability in old age? *Int J Obes.* 2019;43(4):832–841. doi:10.1038/s41366-018-0087-0
9. Qiao Y, Martinez-Amezcua P, Wanigatunga AA, et al. Association between cardiovascular risk and perceived fatigability in mid-to-late life. *J Am Heart Assoc.* 2019;8(16):e013049. doi:10.1161/JAHA.119.013049
10. Wasson E, Rosso AL, Santanasto AJ, et al. Neural correlates of perceived physical and mental fatigability in older adults: a pilot study. *Exp Gerontol.* 2019;115:139–147. doi:10.1016/j.exger.2018.12.003
11. Baran TM, Zhang Z, Anderson AJ, McDermott K, Lin F. Brain structural connectomes indicate shared neural circuitry involved in subjective experience of cognitive and physical fatigue in older adults. *Brain Imaging Behav.* 2020;14(6):2488–2499. doi:10.1007/s11682-019-00201-9
12. Simonsick EM, Glynn NW, Jerome GJ, Shardell M, Schrack JA, Ferrucci L. Fatigued, but not frail: perceived fatigability as a marker of impending decline in mobility-intact older adults. *J Am Geriatr Soc.* 2016;64(6):1287–1292. doi:10.1111/jgs.14138
13. Simonsick EM, Schrack JA, Santanasto AJ, Studenski SA, Ferrucci L, Glynn NW. Pittsburgh Fatigability Scale: one-page predictor of mobility decline in mobility-intact older adults. *J Am Geriatr Soc.* 2018;66(11):2092–2096. doi:10.1111/jgs.15531
14. Gresham G, Dy SM, Zipunnikov V, et al. Fatigability and endurance performance in cancer survivors: analyses from the Baltimore Longitudinal Study of Aging. *Cancer.* 2018;124(6):1279–1287. doi:10.1002/cncr.31238
15. Schnelle JF, Buchowski MS, Ikizler TA, Durkin DW, Beuscher L, Simmons SF. Evaluation of two fatigability severity measures in elderly adults. *J Am Geriatr Soc.* 2012;60(8):1527–1533. doi:10.1111/j.1532-5415.2012.04062.x
16. Glynn NW, Gmelin T, Renner SW, et al. Perceived physical fatigability predicts all-cause mortality in older adults. *J Gerontol A Biol Sci Med Sci.* 2022;77(4):837–841. doi:10.1093/gerona/glab374
17. Wanigatunga AA, Simonsick EM, Zipunnikov V, et al. Perceived fatigability and objective physical activity in mid- to late-life. *J Gerontol A Biol Sci Med Sci.* 2018;73(5):630–635. doi:10.1093/gerona/glx181
18. Urbanek JK, Zipunnikov V, Harris T, Crainiceanu C, Harezlak J, Glynn NW. Validation of gait characteristics extracted from raw accelerometry during walking against measures of physical function, mobility, fatigability, and fitness. *J Gerontol A Biol Sci Med Sci.* 2018;73(5):676–681. doi:10.1093/gerona/glx174
19. Schrack JA, Kuo P-L, Wanigatunga AA, et al. Active-to-sedentary behavior transitions, fatigability, and physical functioning in older adults. *J Gerontol A Biol Sci Med Sci.* 2019;74(4):560–567. doi:10.1093/gerona/gly243
20. Palmberg L, Rantalainen T, Rantakokko M, et al. The associations of activity fragmentation with physical and mental fatigability among community-dwelling 75-, 80-, and 85-year-old people. *J Gerontol A Biol Sci Med Sci.* 2020;75(9):e103–e110. doi:10.1093/gerona/glaa166
21. Qiao YS, Gmelin T, Renner SW, et al. Evaluation of the bidirectional relations of perceived physical fatigability and physical activity on slower gait speed. *J Gerontol A Biol Sci Med Sci.* 2021;76(10):e237–e244. doi:10.1093/gerona/glaa281
22. Qiao Y, van Londen GJ, Brufsky JW, et al. Perceived physical fatigability improves after an exercise intervention among breast cancer survivors: a randomized clinical trial. *Breast Cancer.* 2022;29(1):30–37. doi:10.1007/s12282-021-01278-1
23. Alexander NB, Taffet GE, Horne FM, et al. Bedside-to-bench conference: research agenda for idiopathic fatigue and aging. *J Am Geriatr Soc.* 2010;58(5):967–975. doi:10.1111/j.1532-5415.2010.02811.x
24. Schrack JA, Wanigatunga AA, Zipunnikov V, Kuo P-L, Simonsick EM, Ferrucci L. Longitudinal association between energy regulation and fatigability in mid-to-late life. *J Gerontol A Biol Sci Med Sci.* 2020;75(9):e74–e80. doi:10.1093/gerona/glaa011
25. Knoop V, Cloots B, Costenoble A, et al. Fatigue and the prediction of negative health outcomes: a systematic review with meta-analysis. *Ageing Res Rev.* 2021;67:101261. doi:10.1016/j.arr.2021.101261
26. Kratz AL, Murphy SL, Braley TJ, et al. Development of a person-centered conceptual model of perceived fatigability. *Qual Life Res.* 2019;28(5):1337–1347. doi:10.1007/s11136-018-2093-z
27. Voss MW, Carr LJ, Clark R, Weng T. Revenge of the "sit" II: does lifestyle impact neuronal and cognitive health through distinct mechanisms associated with sedentary behavior and physical activity? *Ment Health Phys Act.* 2014;7(1):9–24. doi:10.1016/j.mhpa.2014.01.001
28. Erickson KI, Hillman CH, Kramer AF. Physical activity, brain, and cognition. *Curr Opin Behav Sci.* 2015;4:27–32. doi:10.1016/j.cobeha.2015.01.005
29. Moored KD, Rosso AL, Gmelin T, et al. Life-space mobility in older men: the role of perceived physical and mental fatigability. *J Gerontol A Biol Sci Med Sci.* 2021. doi:10.1093/gerona/glab286
30. 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(5):557–568. doi:10.1016/j.cct.2005.05.005
31. 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(5):569–585. doi:10.1016/j.cct.2005.05.006
32. Ensrud KE, Blackwell TL, Cauley JA, et al. Objective measures of activity level and mortality in older men. *J Am Geriatr Soc.* 2014;62(11):2079–2087. doi:10.1111/jgs.13101
33. Jakicic JM, Marcus M, Gallagher KI, et al. Evaluation of the SenseWear Pro Armband to assess energy expenditure during exercise. *Med Sci Sports Exerc.* 2004;36(5):897–904. doi:10.1249/01.mss.0000126805.32659.43
34. Cawthon PM, Blackwell TL, Cauley JA, et al. Objective assessment of activity, energy expenditure, and functional limitations in older men: the Osteoporotic Fractures in Men Study. *J Gerontol A Biol Sci Med Sci.* 2013;68(12):1518–1524. doi:10.1093/gerona/glt054
35. Mackey DC, Manini TM, Schoeller DA, et al. Validation of an armband to measure daily energy expenditure in older adults. *J Gerontol A Biol Sci Med Sci.* 2011;66(10):1108–1113. doi:10.1093/gerona/glr101
36. Ainsworth BE, Haskell WL, Leon AS, et al. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc.* 1993;25(1):71–80. doi:10.1249/00005768-199301000-00011
37. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc.* 2000;32(Suppl 9):S498–S504. doi:10.1097/00005768-200009001-00009
38. Ainsworth BE, Haskell WL, Herrmann SD, et al. 2011 Compendium of physical activities: a second update of codes and MET values. *Med Sci Sports Exerc.* 2011;43(8):1575–1581. doi:10.1249/MSS.0b013e31821ece12
39. Almeida OP, Almeida SA. Short versions of the Geriatric Depression Scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. *Int J Geriatr Psychiatry.* 1999;14(10):858–865. doi:10.1002/(sici)1099-1166(199910)14:10<858::aid-gps35>3.0.co;2-8
40. Buysse DJ, Reynolds CF, Monk TH, Hoch CC, Yeager AL, Kupfer DJ. Quantification of subjective sleep quality in healthy elderly men and women using the Pittsburgh Sleep Quality Index (PSQI). *Sleep.* 1991;14(4):331–338. doi:10.1093/sleep/14.4.331

41. Goldman SE, Ancoli-Israel S, Boudreau R, et al. Sleep problems and associated daytime fatigue in community-dwelling older individuals. *J Gerontol A Biol Sci Med Sci*. 2008;63(10):1069–1075. doi:10.1093/gerona/63.10.1069
42. Metti AL, Best JR, Shaaban CE, Ganguli M, Rosano C. Longitudinal changes in physical function and physical activity in older adults. *Age Ageing*. 2018;47(4):558–564. doi:10.1093/ageing/afy025
43. Smith L, Gardner B, Fisher A, Hamer M. Patterns and correlates of physical activity behaviour over 10 years in older adults: prospective analyses from the English Longitudinal Study of Ageing. *BMJ Open*. 2015;5(4):e007423. doi:10.1136/bmjopen-2014-007423
44. Jackson AS, Sui X, Hébert JR, Church TS, Blair SN. Role of lifestyle and aging on the longitudinal change in cardiorespiratory fitness. *Arch Intern Med*. 2009;169(19):1781–1787. doi:10.1001/archinternmed.2009.312
45. Cousins JM, Petit MA, Paudel ML, et al. Muscle power and physical activity are associated with bone strength in older men: the Osteoporotic Fractures in Men Study. *Bone*. 2010;47(2):205–211. doi:10.1016/j.bone.2010.05.003
46. Kucharski D, Lange E, Ross AB, et al. Moderate-to-high intensity exercise with person-centered guidance influences fatigue in older adults with rheumatoid arthritis. *Rheumatol Int*. 2019;39(9):1585–1594. doi:10.1007/s00296-019-04384-8
47. Paluska SA, Schwenk TL. Physical activity and mental health. *Sports Med*. 2000;29(3):167–180. doi:10.2165/00007256-200029030-00003
48. Parker SJ, Strath SJ, Swartz AM. Physical activity measurement in older adults: relationships with mental health. *J Aging Phys Act*. 2008;16(4):369–380. doi:10.1123/japa.16.4.369