Fatigability as a function of physical activity energy expenditure in older adults

Maciej S. Buchowski · Sandra F. Simmons · Lauren E. Whitaker ·
James Powers · Linda Beuscher · Leena Choi · T. Alp Ikizler · Kong Chen ·
John F. Shnelle

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Abstract Increased fatigue is a predictor of morbidity and mortality in older adults. Fatigability defines a change in performance or self-reported fatigue in response to physical activity (PA). However, the relationship of fatigability to PA-related energy expenditure (PAEE) is unknown. Changes in performance, fatigue, and energy expenditure were measured

simultaneously in 17 adults (11 females, 74–94 years old) performing eight standardized PA tasks with various energy expenditure requirements in a whole-room indirect calorimeter. Change in performance was objectively measured using a PA movement monitor and change in fatigue was self-reported on a seven-point scale for each task. Performance and perceived fatiga-

M. S. Buchowski (✉)
Energy Balance Laboratory, Division of Gastroenterology,
Hepatology and Nutrition, Department of Medicine,
Vanderbilt University,
1161 21st Avenue South,
Nashville, TN 37232, USA
e-mail: maciej.buchowski@vanderbilt.edu

T. A. Ikizler
Division of Nephrology, Department of Medicine,
Vanderbilt University,
Nashville, TN, USA

S. F. Simmons · L. Beuscher · J. F. Shnelle
Center for Quality of Aging, Department of Medicine,
Division of General Internal Medicine and Public Health,
Vanderbilt University,
Nashville, TN, USA

J. Powers
Department of Medicine, Division of General Internal
Medicine and Public Health, Vanderbilt University,
Nashville, TN, USA

L. Beuscher
School of Nursing, Vanderbilt University,
Nashville, TN, USA

L. Choi
Department of Biostatistics, Vanderbilt University,
Nashville, TN, USA

S. F. Simmons · J. Powers · J. F. Shnelle
Veterans Administration, Tennessee Valley Health Care
System, Geriatric Research Education and Clinical Center
(GRECC),
Nashville, TN, USA

K. Chen
Human Energy and Body Weight Regulation Section,
Diabetes, Endocrinology, and Obesity Branch, Division
of Intramural Research/NIDDK, National Institutes
of Health,
Bethesda, MD, USA

L. E. Whitaker
Clinical Research Center, Department of Medicine,
Vanderbilt University,
1161 21st Avenue South,
Nashville, TN 37232, USA

M. S. Buchowski · L. E. Whitaker
Vanderbilt University,
Nashville, TN, USA

bility severity scores were calculated as a ratio of change in performance and fatigue, respectively, and PAEE. We found that change in both objective performance and self-reported fatigue were associated with energy expenditure (Spearman $\rho = -0.72$ and -0.68 , respectively, $p < 0.001$) on a task requiring relatively high level of energy expenditure. The performance and perceived fatigability severity scores were significantly correlated ($\rho = 0.77$, $p < 0.001$) on this task. In summary, results of this proof of concept pilot study show that both perceived and performance fatigability severity scores are related to PAEE-induced fatigue on a task requiring relatively high level of energy expenditure. We conclude that fatigability severity is a valid measure of PAEE-induced fatigue in older adults.

Keywords Aging · Fatigue · Tiredness · Resting energy expenditure · Physical activity

Introduction

Fatigue or persistent and unexplained tiredness predicts mortality (Hardy and Studenski 2008), increases risk of disability onset (Vestergaard et al. 2009; Avlund et al. 2002), and is a significant cause of restricted physical activity (PA) in older adults (Avlund 2010; Avlund et al. 1998, 2004; Moreh et al. 2009, 2010). Fatigue is a complex construct to measure because it is subjective and there is an overlap between the patient's notion of tiredness and the clinically relevant symptom of fatigue (Zwarts et al. 2008). Fatigue is not the same as muscle weakness, and it is not a nonspecific outcome of depression, chronic illness, or aging (Chaudhuri and Behan 2004; Jason et al. 2010).

It has been suggested that a new concept termed fatigability, rather than fatigue, may be more associated with PA-related energy expenditure (PAEE) and clinically relevant to the changes in daily PA (Alexander et al. 2010). Fatigability has two components: *perceived fatigability* defined as a change in the feeling of fatigue and *performance fatigability* defined as a decrement in physical performance (e.g., speed of walking). Both components must consider the amount of energy expenditure or work performed (Eldadah 2010). For example, if a person reports increased fatigue after a 6-min walk while the second

person does not after the same walk with the same speed, the first person has a higher perceived fatigability than the second person does. If the first person's walking speed decreases by 50% in min 6 compared to min 1, while the second person has only a 20% decrease during the same time period, the first person has a higher performance fatigability than the second person.

There are no established criteria for assessing fatigability, and there have been only a few studies measuring changes in fatigue or performance also while measuring PAEE in any population, including older adults (Murphy 2009; Murphy et al. 2008). Results of these studies suggest that the objective changes in PA performance and concurrent subjective changes in fatigue are related, and EE may be a key physiological indicator connecting both measures. In a laboratory, PA-related energy expenditure could be measured with accuracy and precision using gold standard whole-room indirect calorimetry. It can be rationalized that the fatigability measure, defined as change in fatigue over time in relation to PAEE, would normalize the interindividual variability. Using a standardized physical challenge, such as a timed walk or sit-to-stand tests, could reduce the intra-individual variability over time. Thus, the goal of this study was to measure changes in performance and fatigue across a series of standardized physical tasks that required different levels of energy expenditure and explore the relationships among these measures.

Methods

Participants

Seventeen older adults were recruited from local senior residential facilities. Inclusion criteria required participants to be greater than 65 years of age, able to sign an informed consent, and general good health based on self-reported medical history (Table 1). Exclusion criteria were inability to perform PA tasks without human assistance (assistive devices, such as a cane or walker were acceptable), heavy smoking, implanted electronic medical device (e.g., pacemaker), and chronic medical condition or psychiatric illness. The informed consent process was approved by the university-affiliated institutional review board.

Table 1 Characteristics of study participants

Measure	All (<i>n</i> =17)	Males (<i>n</i> =6)	Females (<i>n</i> =11)
Age (years)	79.4±7.8 (69–94)	81.5±6.2 (67–91)	78.2±8.6 (69–94)
Height (cm)	162.5±8.7 (145–175)	171.2±5.4* (162–175)	157.8±6.0 (145–164)
Weight (kg)	71.1±14.8 (44–103)	85.7±10.7* (73–103)	63.1±9.6 (44–78)
Body mass index (kg/m ²)	26.8±4.3 (18–33)	29.3±3.4* (24–33)	25.4±4.3 (18–31)
Preperformance fatigue	2.35±1.69 (1–6)	3.67±2.34 (1–6)	1.63±0.50 (1–2)

Values are reported as means±standard deviation (ranges)

*different from females ($p<0.001$)

Study design and procedures

During a screening visit conducted by research personnel, details of the study were discussed, all questions answered, and participants were asked to avoid any unusual PA and stress on the day before the study. Transportation to the Clinical Research Center (CRC) was provided in the morning of the study after breakfast. Vital signs were measured by the CRC nurses, and each participant spent approximately 3.5 h in the whole-room indirect calorimeter while the rates of energy expenditure and PA (body movement) were recorded minute by minute. The room calorimeter is an airtight room with windows and airtight pass and is equipped with a toilet, sink, desk, chair, telephone, multimedia, and exercise equipment. A computerized system with a touch monitor and an audible signal prompts participants to start and finish each standardized physical activity. An intercom system allows research staff to communicate with the person inside the room. The room assures high-precision measurements in a controlled environment and seminaturalistic conditions (i.e., not wearing a breathing mask) and allows for adjusting the intensity of any PA task to the individual's capability. Technical details of the indirect calorimeter measurement approach have been reported elsewhere (Sun et al. 1994; Donahoo et al. 2004). Participants followed a structured protocol consisting of eight PA tasks characteristic of daily living for older adults. Each PA task lasted 6 min, and the tasks were separated by 10-min rest periods. The duration of each PA task allowed the EE measurement to reach proximal steady state and was feasible for participants to complete. Tasks 1 and 2 were sorting small objects with hands while sitting and handwriting. These sedentary activities require low levels of

EE. Tasks 3 through 6 were considered light intensity activities and included reaching a shelf with a light (0.25-kg) object, sweeping the floor, moving a 0.5 kg weight while standing and bending, and moving 1.5 kg weight while walking using both hands. Light activities were expected to require higher levels of energy expenditure than the sedentary activities. Walking across the room (3 m) with turns and repeatedly moving from a sitting to standing position with arm support (sit to stand) tasks were considered moderate activities (Fig. 1). Before the testing in the chamber, participants self-rated their fatigue level as the baseline fatigue measure (Table 2, left column).

Anthropometric measures

Body weight was measured by the CRC nurses to the nearest 0.1 kg with a digital scale (Detecto-Medic, Detecto Scales, Inc., Northbrook, IL) while the participants wore light clothing and no shoes. Height was measured using a wall-mounted stadiometer (Perspective Enterprises, Portage, MI).

Energy expenditure measures

Measurements of energy expenditure during resting and performing PA tasks were calculated from the rates of oxygen (O₂) consumption and carbon dioxide (CO₂) production using measured concentrations of oxygen and carbon dioxide of the air inside the room calorimeter and multiplying by the flow rate of purged air using Weir's equation (Weir 1949). The accuracy and precision of our metabolic chamber for measuring energy expenditure as determined by the alcohol combustion test was 99.2±0.5% [mean±

Fig. 1 The normalized overlaid plot for a representative participant (79-year-old male, weight=73.2 kg, height=174 cm) during a stay in the whole-room indirect calorimeter. *Solid line* represents energy expenditure (EE) measured by room calorimetry and *dashed line* PA counts obtained from Actigraph GT3M activity monitors worn at hip and wrist. Physical activity (PA) tasks were performed for 6 minutes and separated by 10-

minute rest. The task were: *T1* - moving objects with hands while sitting, *T2* - handwriting, *T3* -reaching shelf with a light (0.25 kg object), *T4* - sweeping floor, *T5* - moving 0.5 kg weight while standing, *T6* - moving 1.5 kg weight horizontally (2 meters), *T7* - walking across the room (3 m) with turns, *T8* - sit-to-stand from a chair with arm support

standard deviation (SD)] over 12 h and $98.6 \pm 2.1\%$ over 30 min.

Baseline energy expenditure (in kilocalories/minute)

Baseline energy expenditure was measured during 30-min sitting in a reclining position with minimal movement. Mean energy expenditure for 15 min (from 11th to 25th minute) was used as baseline energy expenditure measure (Levine et al. 2000).

Physical activity-related energy expenditure

Energy expenditure during performing each PA task was calculated as a ratio of total and resting energy expenditure (in kilocalories/minute) and expressed as metabolic equivalents (METs, Rothney et al. 2010).

The METs reflect energy spent for an activity and is independent of individual characteristics such as body weight (Ainsworth et al. 2000). Total PAEE (METs) for each task includes energy spent during active task performance (6 min) and during rest after the task (10 min).

Fatigability measures

Change in perceived fatigue

After finishing each task, a participant was asked to rate changes in their fatigue level on a seven-point scale (Table 2, right column). The scale ranged from “extremely more energetic” to “extremely more

Table 2 Fatigue and change in fatigue scales

Fatigue scale items	Score	Change in fatigue scale items
Extremely tired	7	Extremely more tired
Somewhat tired	6	Somewhat more tired
A little tired	5	A little more tired
Neither tired or energetic	4	Neither more tired or energetic
A little energetic	3	A little more energetic
Somewhat energetic	2	Somewhat more energetic
Extremely energetic	1	Extremely more energetic

tired.” A score of 4 was assigned if there was no change in perceived fatigue level. If the participant reported having less energy, they were asked if they were “a little, somewhat, or extremely more tired”. If the participant reported having more energy, they were asked if they were “a little, somewhat or extremely more energetic.” This branching question format requires discrimination only among three categories at a time but produces a seven-point scale score. This scale was pilot tested in 42 elderly subjects and generated stable self-reports of fatigue changes on two different walking and standing assessments similar to those used in this study.

Change in performance

Performance change was calculated as the percent decrease from the first to the last minute in the total amount of PA for each task objectively measured using an Actigraph-GT3X activity monitor (Actigraph, Pensacola, FL), which was placed on each participant’s waist on the dominant side and on their dominant wrist. Actigraph data from two sites were collected as vector magnitude counts at a 1-s epoch. The output counts reflect the overall intensity of the body movement (PA) over time interval (Matthews 2005). Counts from waist and wrist monitors were summed as a measure of total amount of PA per minute.

Performance and perceived fatigability severity

These measures represent change in fatigue and performance in relation to energy expenditure for each task. The PAEE was calculated as the area under the curve (AUC) including energy spent during performing the task and the posttask resting period. Performance fatigability severity was defined as the ratio of change in performance (percent decrease in PA activity counts per minute) and PAEE for the task. Perceived fatigability severity was defined as the ratio of change in self-reported fatigue (Table 2, right column) and PAEE for the task.

Data analyses

Linear regressions were used to examine pair-wise relationships among PAEE, changes in performance, and fatigue. Cluster bootstrap was used to adjust for within-subject correlations among the eight PA tasks

measured within the same subject. Wilcoxon rank sum test was used to test the difference in preperformance fatigue scores between males and females. Spearman's rank correlations were used to examine correlations between changes in performance and fatigue and performance and perceived fatigability severity. Data are presented as means, standard deviations (SD), or ranges. All analyses were performed using STATA 11.0 (StataCorp, College Station, TX) and the programming language R version 2.10.0.

Results

Participant characteristics

Demographic and anthropometric characteristics of study participants are shown in Table 1 for the group ($n=17$) and for males and females separately. Age was similar between male and female study participants but male participants were taller and heavier (both $p<0.001$). Preperformance fatigue (Table 2, left column) also was higher in males, but not statistically significant (3.67 and 1.63, Wilcoxon rank sum test $p=0.110$).

Energy expenditure during the tasks

The plot for a representative participant in Fig. 1 illustrates the timeline, PA, and PAEE measures in a

Fig. 2 Energy expenditure (EE) for PA tasks measured in a whole room indirect calorimeter and expressed in metabolic equivalents MET (a ratio of total and resting EE). Each point represents one person ($n=17$). The task were: *T1* - moving objects with hands while sitting, *T2* - handwriting, *T3* -reaching shelf with a light (0.25 kg object), *T4* - sweeping floor, *T5* - moving 0.5 kg weight while standing, *T6* - moving 1.5 kg weight horizontally (2 meters), *T7* - walking across the room (3 m) with turns, *T8* - sit-to-stand from a chair with arm support

room calorimeter. Figure 2 shows PAEE (METs) and ranges for each task. There was interindividual variability in PAEE that was directly related to energy required to perform each task. The highest PAEE level and highest variability were for the sit-to-stand task (task 8) and the lowest for sorting objects using hands and handwriting sedentary tasks (tasks 1 and 2). Walking for 6 min at a self-selected pace (task 7) did not require more energy than the light activity tasks (tasks 3 to 6), and the PAEE variability were similar for these tasks.

PAEE, change in fatigue, and perceived fatigability severity

There was a significant negative association ($\rho=-0.18$, $p<0.0001$) between PAEE and self-reported change in fatigue across all tasks, but in the task-by-task analysis, only sit to stand showed a significant correlation ($\rho=-0.69$, $p<0.01$). Figure 3 illustrates the relationship between changes in fatigue for sedentary, low intensity, and moderate tasks and PAEE. For example, in persons who reported maximum change in fatigue (score 7) for the sit-to-stand task (task 8), PAEE varied from 1.8 to 3.5 METs. In persons who expended ~ 4 MET for this task, perceived fatigue varied from no change (score 4) to extreme change (score 7). Change in fatigue on other tasks was in a lower score range (2–6). Subsequent perceived fatigability severity score (ratio of change

in fatigue to PAEE) is presented in Table 3. For the sit-to-stand task, perceived fatigability severity score was 0.21 ± 0.07 and ranged from 0.11 to 0.36. Corresponding values for a low activity and sedentary tasks showed in Fig. 3 were 0.21 ± 0.03 and 0.21 ± 0.04 , respectively.

PAEE, change in performance, and performance fatigability

Change in performance was significantly correlated with PAEE across all tasks ($\rho=0.07$, $p=0.003$). However, similar to the change in perceived fatigue, interindividual variability was directly related to the PAEE required for the tasks. Figure 4 shows that among participants who spent 3.5 to 4.0 METs for the sit-to-stand task change in performance varied from a 20% increase to an 80% decrease in activity counts ($\rho=-0.72$, $p<0.01$). Performance fatigability severity score (ratio of change in performance to PAEE) for this task was 1.24 ± 1.23 and varied from -0.37 (increase in performance) to 3.43 MET^{-1} . In comparison, performance fatigability severity score for other light intensity tasks was 0.25 ± 0.61 and varied from 0.68 to 2.06 MET^{-1} (Table 3).

Relationship of performance and perceived fatigability measures

The two measures of fatigability severity were significantly correlated ($\rho=0.77$, $p<0.001$) only for the sit-to-stand task (task 8) requiring a relatively high level of energy expenditure (~ 3 METs, Fig. 5).

Discussion

This is the first study to measure changes in performance and self-reported fatigue simultaneously with energy expenditure in older adults performing daily living tasks requiring various levels of PAEE. The results of this pilot study showed that changes in performance and self-reported fatigue were significantly correlated with energy required for performing the PA tasks. Significant between-person variability in PAEE allowed for the calculation of performance and perceived fatigability scores for each task. The two scores were significantly correlated only on a task

Fig. 3 Relationship between physical activity-related energy expenditure (PAEE) and self-reported change in tiredness during sorting objects using hands, moving 1.5 kg weight horizontally (2 meters), and sit-to-stand PA tasks. Each point represents one task performed by one person ($n=17$)

Table 3 Physical activity-related energy expenditure (PAEE) and performance and perceived fatigability severity scores in older adults ($n=17$) after performing PA tasks in the whole-room indirect calorimeter

Task	PAEE ^a METs	Performance fatigability severity ^b	Perceived fatigability severity ^c
Sedentary activities ^d	18.77±2.86 (15.84 to 33.36)	0.03±1.56 (−4.25 to 3.49)	0.22±0.03 (0.13 to 0.32)
Light activities ^e	22.19±2.08 (17.58 to 29.05)	0.25±0.61 (−0.68 to 2.06)	0.21±0.04 (0.14 to 0.34)
Sit-to-stand test ^f	28.89±4.96 (19.25 to 36.17)	1.24±1.23 (−0.37 to 3.43)	0.21±0.07 (0.11 to 0.36)

Values are reported as means±standard deviation (ranges)

^aEnergy expenditure for performing task(s) calculated as AUC using trapezoidal function in Matlab (Mathworks, Natick, MA)

^bCalculated as a ratio of change in performance (in percent) in counts between min 1 and 6 and energy expenditure (METs) for each task

^cCalculated as a ratio of reported change in fatigue (scale 1–7) and energy expenditure (METs) for each task

^dSedentary activity tasks included sorting small objects with hands while sitting and handwriting

^eLight activity tasks included reaching shelf with a small weight (0.2 kg) using a dominant hand, sweeping floor, moving weight between tables with both hands (1.5 kg for 2 m horizontally) while standing/walking, and sorting laundry (light objects) while standing and bending, and walking across the room (3 m) with turns

^fModerate activity task was sit to stand from a chair with arm support

requiring a relatively high level of energy expenditure (~3.5 MET).

These preliminary findings have clear clinical implications. First, measuring fatigability allows for categorizing individuals objectively as having higher or lower fatigability severity levels based on the change in fatigue and performance on a standardized test(s) in relation to PAEE. Second, the high correlation of objective performance fatigability with the more subjective perceived fatigability measure for higher intensity tasks provides a valid method for monitoring changes in fatigability over time, during progressive disease, or in response to intervention. This approach is superior to traditional monitoring of periodic changes in perceived fatigue, which rely exclusively on subjective self-report ratings. Finally, if the change in both perceived and performance fatigability severity are related to free-living PA, an intervention could be designed to decrease or limit fatigability, especially in individuals who have higher fatigability scores at lower energy expenditure level.

This dynamic approach to measuring fatigability could be more proximally related to how older adults manage their PA and a more clinically relevant outcome measure than global fatigue, especially if the intent is to increase PA capacity and prevent functional decline. Clinically relevant hypotheses should be rigorously tested in future work, and this same approach also might be applicable to patients with chronic illnesses such as cancer, HIV–AIDS,

kidney disease, and neurological disorders, many of whom frequently report fatigue (Abhijit and Peter 2004; Lou 2009; Mitchell 2010; Vucic et al. 2010; Schifitto et al. 2011)

Fatigability scores are task specific; therefore, it is difficult to compare the values across the tasks, especially those requiring a lower PAEE level (e.g., sedentary activities). The variability in these tasks was not energy expenditure related and was most likely associated with cognitive fatigue, which was not the

Fig. 4 Relationship between physical activity-related energy expenditure (PAEE) and change in performance [Performance change (%) = 100 * (pre-measurement – post-measurement)/post-measurement physical activity (PA)] during sorting objects using hands, moving 1.5 kg weight horizontally (2 meters), and sit-to-stand PA tasks. Each point represents one task performed by one person ($n=17$)

Fig. 5 Relationship between performance and perceived fatigability sit-to-stand PA task. Perceived fatigability was calculated as a ratio of reported change in tiredness (scale 1-7) and energy expenditure (METs). Performance fatigability was calculated as a ratio of change in performance (%) and energy expenditure (METs). Each point represents one person ($n=17$)

focus of this study. Studies to explore this phenomenon are warranted.

This pilot study had some limitations. Due to the relatively small number of participants, we did not have the statistical power to detect the effects of confounding factors such as personal characteristics (e.g., sex, age, body size, and composition) and comorbidities. Based on the literature, such person-specific variables and other clinical factors might have contributed to the variability in self-reported fatigue not related to energy expenditure, especially for tasks with low energy requirements. These factors should be explicated in future trials (Moreh et al. 2010). Another limitation was the relatively low (eight) number of tasks performed and narrow range of energy expenditure (from ~1.2 to ~4.0 METs). The tasks, however, represented activities typical for less physically active older adults' daily living. Finally, participants were allowed to self-pace during these tasks contributing to observed between-individual variability in PAEE. We offset for the variability in the amount of work performed by measuring precisely minute-to-minute energy expenditure. Nevertheless, future studies, especially those conducted outside the laboratory, should standardize all PA testing parameters.

This study has several strengths. To our knowledge, this is the first study to quantify changes in

performance simultaneously with fatigue in the context of energy expenditure in older adults performing structured PA tasks. This study was conducted using a reference standard whole-room indirect calorimetry to measure oxygen uptake and energy expenditure and advanced accelerometry to measure PA changes during task performance. This approach is superior to other methods of energy expenditure measurement including portable calorimetry, which requires wearing a mask, limits the ability to make certain movements, and alters the energy cost of movement significantly. The measurement approach used in this study may be a starting point for more sophisticated methods to identify clinical and biomechanical factors that affect fatigability. We suggest that fatigability severity scores could be used as a valid measure of PA-induced fatigue over time, and they might be sensitive to intervention.

In summary, the results of this proof of concept study show that both perceived and performance fatigability severity scores are related to PAEE-induced fatigue on a task requiring relatively high level of energy expenditure (~3.5 METs). We conclude that fatigability severity is a valid measure of PAEE-induced fatigue in older adults.

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