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Pulmonary $\dot{V}O_2$ on-kinetics and walking net $\dot{V}O_2$ associate with fatigue and mood disturbance in postmenopausal women

Stephen J. Carter[a,b,*], **Tyler H. Blechschmid**[a], **Emily B. Long**[a], **Tenzin Yangchen**[a], **Marissa N. Baranauskas**[c], **Chad C. Wiggins**[d], **John S. Raglin**[a], **Andrew R. Coggan**[e,f]

[a]Department of Kinesiology, School of Public Health – Bloomington, Indiana University, Bloomington, IN 47405, USA

[b]Indiana University Melvin and Bren Simon Comprehensive Cancer Center, Indianapolis, IN 46202, USA

[c]Department of Human Physiology & Nutrition, College of Nursing and Health Sciences, University of Colorado Colorado Springs, Colorado Spring, CO, USA

[d]Department of Kinesiology, College of Education, Michigan State University, East Lansing, MI 48815, USA

[e]Department of Kinesiology, School of Health and Human Sciences, Indiana University Indianapolis, Indianapolis, IN 46202, USA

[f]Indiana Center for Musculoskeletal Health, Indiana University School of Medicine, Indianapolis, IN 46202, USA

Abstract

Postmenopausal women often experience fatigue and mood disturbance both of which interfere with quality-of-life. Since greater physical function aids psychosocial well-being, we hypothesized the acute cardiopulmonary responses during walking may reveal important factors linked to fatigue and mood disturbance. In this cross-sectional study, women of similar body mass index (BMI) aged 55–75 y were dichotomized to mid-life (55–65 y; 83.4 ± 8.4 kg; n = 14) or older (≥65 y; 81.8 ± 10.4 kg; n = 11) groups. A 6-minute walk test was used to estimate peak aerobic capacity ($\dot{V}O_{2peak}$). A treadmill task coupled with indirect calorimetry measured mean response time (MRT) – representing the duration to reach 63 % of steady-state net oxygen uptake ($\dot{V}O_2$). Average

[*]Corresponding author at: Department of Kinesiology, Indiana University, Bloomington, IN 47405-7109, USA. stjcarte@iu.edu (S.J. Carter).

Declaration of competing interest
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement
Stephen J. Carter: Writing – review & editing, Writing – original draft, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Tyler H. Blechschmid:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Emily B. Long:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Tenzin Yangchen:** Writing – review & editing, Project administration, Investigation, Data curation. **Marissa N. Baranauskas:** Writing – review & editing, Project administration, Methodology, Investigation, Data curation. **Chad C. Wiggins:** Writing – review & editing, Validation, Software, Methodology, Formal analysis. **John S. Raglin:** Writing – review & editing, Validation, Methodology. **Andrew R. Coggan:** Writing – review & editing, Supervision, Resources, Investigation.

daily fatigue and fatigue interference were measured with the Fatigue Symptom Inventory. General mood disturbance was measured with the Profile of Mood States (POMS) questionnaire. Age-group differences were not detected in fatigue ratings, MRT, or walking net $\dot{V}O_2$. However, older women had lower aerobic capacity ($p = 0.002$, $ES = 1.39$) and greater disturbance in the POMS Depression-Dejection subscale ($p = 0.042$, $ES = 0.41$). Among all participants, and independent of $\dot{V}O_{2peak}$, MRT correlated with average daily fatigue ($r = 0.500$, $p = 0.015$), fatigue interference ($r = 0.421$, $p = 0.046$), and POMS total mood disturbance ($r_s = 0.437$, $p = 0.037$). Regression modeling revealed MRT and walking net $\dot{V}O_2$ jointly explained 55 % ($R = 0.744$, $p < 0.001$) of the variance in average daily fatigue. In conclusion, MRT and walking net $\dot{V}O_2$ may serve as important points of intervention to alleviate fatigue and mood disturbance in postmenopausal women.

Keywords

Aging; Mean response time; Physical activity; Profile of mood states; Menopause; Women's health

1. Introduction

The age-related decline in physical function hastens a maladaptive cycle highlighted by restricted physical activity and systemic deconditioning (Carter et al., 2020). The broader implications of such changes can elicit a knock-on effect that predisposes fall risk, disability, and social isolation. However, the consequent effects of advancing age on physical function differ by biological sex. Women have greater rates of age-related disability compared to age-matched men (Hardy et al., 2008; Hosseinpoor et al., 2012). Data from the Study of Women's Health Across the Nation (SWAN) indicates the prevalence of physical function limitations increases from 19 % in women 40–55 years of age to 50 % in women 56–66 years of age (El Khoudary et al., 2019). This designates the mid-life phase as a *"critical window"* not only for declining physical function but also a strategic opportunity for intervention.

While walking speed is an indicator of global physical function, a recent prospective study confirmed walking speed in postmenopausal women was a stronger predictor of cardiovascular disease and all-cause mortality than handgrip strength or timed chair stands (Luo et al., 2023). Interestingly, a systematic review and meta-analysis suggested slowed walking speed *precedes* the emergence of depressive symptoms in older adults (Chan et al., 2020). Further reports show that depressive symptoms are significantly increased among those experiencing fatigue – highlighting the burden of co-occurrence (Corfield et al., 2016). Given the age-related trend demonstrating women are more likely to experience fatigue and mood disturbance compared to men (Meng et al., 2010), it is of interest to examine the link between indices of physical function and psychosocial well-being in postmenopausal women.

The concurrent, age-related decline in peak aerobic capacity (i.e., $\dot{V}O_{2peak}$) (Stathokostas et al., 2004) and rise in walking net oxygen uptake ($\dot{V}O_2$) (Carter et al., 2024a) narrows the physiologic reserve – making even routine activities of daily living (ADLs) a challenging affair. While ADLs are often performed at submaximal intensity, they frequently resemble a cyclic stop-and-go pattern. This, in turn, places a substantial emphasis on the oxygen transport system to swiftly meet the energetic demands of working tissues – evidenced by pulmonary $\dot{V}O_2$ on-kinetics. It is reasonable that delayed on-kinetics and/or an elevated walking net $\dot{V}O_2$ could be related to fatigue and mood disturbance, yet this notion has not been evaluated in postmenopausal women.

Based on the rationale that greater physical function aids psychosocial well-being, we reasoned the acute cardiopulmonary responses during submaximal walking may reveal important factors linked to fatigue and mood disturbance in postmenopausal women. Based on the growing shift to incorporate exercise training as a form of personalized medicine (Buford et al., 2013), identifying suitable targets are first needed to inform evidence-based interventions. The following investigation represents an initial step to determine potential points of intervention. Hypotheses were as follows: 1) age would positively relate to self-reported measures of fatigue, 2) indicators of mood disturbance would positively associate with self-reported measures of fatigue, and 3) $\dot{V}O_2$ on-kinetics and walking net $\dot{V}O_2$ would positively relate to self-reported measures of fatigue and mood disturbance independent of $\dot{V}O_{2peak}$.

2. Methods

2.1. Design

Secondary analyses were performed on baseline data from a randomized pilot study exploring the effects of pre-workout dietary nitrate on indices of physical function in postmenopausal women (Baranauskas et al., 2021; Carter et al., 2024b). Participants (*n* = 25) were included if they had data on primary variables of interest including the Fatigue Symptom Inventory, Profile of Mood States, 6-miniute walk test, and $\dot{V}O_2$ during a treadmill task. Participants provided written informed consent after a detailed explanation of the experimental procedures and associated risks / benefits. All procedures were approved by the local Institutional Review Board at Indiana University Bloomington and performed in agreement with guidelines set forth by the Declaration of Helsinki. The primary investigation was registered on Clinicaltrials.gov (NCT04370756).

2.2. Participants

Participants were self-reported postmenopausal (> 1 year since last menses) not taking hormone replacement therapy who exercised <3 times per week. Inclusion criteria were: 1) biological women between 18 and 75 years of age (verified by government issued driver identification); 2) clearance from physician for study participation; 3) body mass index (BMI) between 25.0 and 39.9 kg/m^2; and 4) ability to ambulate without assistance. Exclusion criteria were: 1) current smoker; 2) diagnosed with major cardiometabolic disease; 3) taking medications known to affect heart rate or blood vessel function; 4) cognitive characteristics that would interfere with study participation; 5) living beyond 80 km from Bloomington, IN and 6) anticipated elective surgery or travel plans during the study period.

2.3. Anthropometrics

Following an overnight fast, participants removed their shoes and donned hospital scrubs. Height and body mass were then measured to the nearest 0.1cm using a stadiometer and 0.1kg on a digital scale, respectively. BMI was determined by dividing body mass (in kilograms) by standing height in meters squared. Estimates of lean mass and fat mass were obtained from a total body scan using dual-energy X-ray absorptiometry (iDXA; GE Healthcare, Madison, WI).

2.4. Standardized treadmill task

Cardiopulmonary responses were collected during a 6-min, fixed-speed (0.89 m/s at 0 % grade) treadmill task via indirect calorimetry (Vmax Encore, Vyaire Medical, Mettawa, IL). This workload was selected as it aligns with prior work demonstrating 0.90 m/s may serve as an optimal cut-point to distinguish women at higher risk for all-cause mortality (Luo et al., 2023). Following standard gas and flow calibration, participants were outfitted with an oronasal mask (7450 Series, Hans Rudolph, Shawnee, KS) and heart rate (HR) monitor (Model H9/10, Polar, Stamford, CT). Participants remained standing for a 3 min period for rested measures of $\dot{V}O_2$ and HR. Mean response time (MRT), frequently referred to as tau (τ), corresponded with the duration in time needed to reach 63 % steady-state walking net $\dot{V}O_2$. Consistent with methods described by Wiggins et al. (Wiggins et al., 2019), breath-by-breath $\dot{V}O_2$ data were first prepared for non-linear regression by setting the time at which movement was initiated to *"0."* The final 20 s of standing rest and the initial 20 s after commencing movement were excluded to reduce the interaction of cardiodynamic phase I $\dot{V}O_2$ response on subsequent modeling of MRT. Data were fit to the following non-linear regression equation: $\Delta y(t) = A0 + A1(1 - e^{(-(t - \mathrm{TD1})/\mathrm{MRT1}})$ where y is $\dot{V}O_2$, MRT and TD represent the time constant and time delay of each exponential function, respectively. Data were filtered 5 times with each pass removing outlying breaths defined as a $\dot{V}O_2$ value ≥3 standard deviations from the best-fit regression model. MRT values reported herein were generated from the final best-fit regression model. Since resting $\dot{V}O_2$, skeletal muscle mass, and mitochondrial function decline with advancing age (Roberts and Rosenberg, 2006; Short et al., 2005), we subtracted standing $\dot{V}O_2$ from gross walking $\dot{V}O_2$ to isolate walking net $\dot{V}O_2$. Note we have previously used this method (Carter et al., 2024a; Carter et al., 2022; Singh et al., 2019), as it isolates the "economy" for the task. Fig. 1 illustrates the operational distinction between MRT and walking net $\dot{V}O_2$.

2.5. Estimated $\dot{V}O_{2peak}$

Participants performed a standardized 6-minute walk test in accordance with guidelines by the American Thoracic Society (ATS statement, 2002). Briefly, participants were outfitted with a HR monitor and remained seated for 10–15 min prior to the test. Participants were then instructed to *"walk as far as possible for six minutes."* Distance traveled was recorded in meters and used estimate $\dot{V}O_{2peak}$ from the published regression equation developed by Sagat and colleagues (Šagát et al., 2023). Data were expressed in $\mathrm{mL} \bullet \mathrm{kg}^{-1} \bullet \mathrm{min}^{-1}$.

2.6. Psychometric assessments

Having been used in multiple older adult populations including individuals with and without severe physical and psychiatric disorders (Hann et al., 1998), the 13-item Fatigue Symptom Inventory was used to evaluate fatigue severity and impact on daily functioning. Specific dimensions were average daily fatigue (item 3) and fatigue interference (mean of 6 items). Responses were scored with a Likert-scale ranging from 0 to 10 with a higher score representing greater fatigue.

The Profile of Mood State (POMS) questionnaire was used to assess specific and general mood (McNair et al., 1971). The POMS is a 65-item, Likert-format (i.e., 0 = *"not at all"* and 4 = *"extremely"*) questionnaire that measures specific mood factors including: 1) tension-anxiety, 2) depression-dejection, 3) anger-hostility, 4) fatigue-inertia, 5) confusion-bewilderment, and 6) vigor-activity. Total mood disturbance was calculated from the difference in the sum of negative mood variables and the positive variable of vigor-activity. Participants completed the POMS on the basis of the standard instructional format (i.e., *"last week including today"*). For comparative purposes, results from Nyenhuis and colleagues (Nyenhuis et al., 1999) that assessed the POMS in 170 older adults (57 % women, age = 68 ± 9 years) were used to standardize scores to a population norm (Z-score = observed value—population mean/population SD). Z-scores were then converted to T-scores with a mean of 50 and SD of 10 [$\mathrm{T-score} = 50 + (10 \times \mathrm{Z-score})$].

2.7. Statistical analyses

Data homogeneity and normality were assessed with Levene's and Shapiro-Wilk test(s), respectively. Normally distributed data are shown as means and standard deviations, whereas non-normally distributed data are shown as medians and interquartile ranges. Between-group comparisons were performed with unpaired t-test and Mann-Whitney U test where appropriate. Effect size (ES) was determined by Hedges' g or $\frac{Z}{\sqrt{N}}$ for normally and non-normally distributed data, respectively. Relationships of interest were evaluated using Pearson's r or Spearman rho (r_s): low (0.10–0.39), moderate (0.40–0.69), strong (0.70–0.89) (Schober et al., 2018). Multiple linear regression was used to explain the variance in average daily fatigue and fatigue interference. Collinearity diagnostics for all variables were within acceptable limits and variable inflation factors for all models were <1.05. Data were analyzed with SPSS (v29.0, Armonk, NY). Figures were constructed using GraphPad Software (v10.0, La Jolla, CA). Statistical significance was set a priori and defined as a two-sided alpha of ≤0.05.

3. Results

Descriptive characteristics are shown in Table 1. Apart from age, participants were well-matched and did not differ by key indicators of health including body composition, blood pressure, socioeconomic status (e.g., education, income), and history of anxiety / depression. Based on BMI, 10 of 25 (40 %) participants were *"overweight"* (25.0–29.9 kg/m^2) whereas 15 of 25 (60 %) were *"obese"* (>30.0 kg/m^2).

Though $\dot{V}O_{2peak}$ was significantly lower ($p = 0.002$, $ES = 1.39$) in older women (Table 2), $\dot{V}O_{2peak}$ values were 23.5 % greater than the minimum value ($15.0\ \text{mL} \bullet \text{kg}^{-1} \bullet \text{min}^{-1}$) needed for functional independence (Shephard, 2009). Mean response time and walking net $\dot{V}O_2$ were not different between groups. Similarly, differences were not detected for fatigue ratings or POMS total mood disturbance. Evaluation of the POMS subscales, however, showed that older women had greater disturbance in Depression-Dejection [mid-life, 45(4) vs. older 50(7); $p = 0.042$, $ES = 0.41$].

Correlations were not detected between age and average daily fatigue or age and POMS subscales. Age and fatigue interference were significantly related ($r = 0.417$; $p = 0.038$), however, significance was lost after adjusting for $\dot{V}O_{2peak}$. Average daily fatigue and fatigue interference aligned well with the multidimensional POMS as evidenced by the significant positive associations with several subscales including Tension-Anxiety ($r_s = 0.543, 0.598$), Anger-Hostility ($r_s = 0.504, 0.524$), and Fatigue-Inertia ($r_s = 0.559, 0.787$).

To account for the potential influence of $\dot{V}O_{2peak}$, correlational analyses in Table 3 were adjusted with $\dot{V}O_{2peak}$. Mean response time positively related to average daily fatigue ($r = 0.500$; $p = 0.015$), fatigue interference ($r = 0.421$; $p = 0.046$), and POMS total mood disturbance composite ($r_s = 0.437$; $p = 0.037$). Note that Fig. 2A–D depict unadjusted relationships of interest. Multiple linear regression revealed MRT (partial $r = 0.502$; $p = 0.015$) and walking net $\dot{V}O_2$ (partial $r = 0.647$; $p < 0.001$) jointly accounted for 55 % of the variance in average daily fatigue (Model 1; Table 4). In Model 2, MRT (partial $r = 0.525$; $p = 0.010$) significantly correlated with fatigue interference independent of age (partial $r = 0.410$; $p = 0.052$) with the total model (R^2) accounting for 40 % of the variance.

4. Discussion

In the present work, we reasoned the acute cardiopulmonary responses during walking may reveal important factors linked to fatigue and mood disturbance in postmenopausal women. Accordingly, we report the following: 1) age positively associated with fatigue interference – ostensibly due to the influence of $\dot{V}O_{2peak}$; 2) Tension-Anxiety, Anger-Hostility, and Fatigue-Inertia each positively associated with average daily fatigue and fatigue interference; 3) MRT and walking net $\dot{V}O_2$ were independent correlates that jointly explained 55 % of variance in average daily fatigue. Such information may be useful to inform targeted interventions to reduce the burdens of fatigue and mood disturbance in postmenopausal women.

Though multifaceted, the age-related increase in walking net $\dot{V}O_2$ is believed to be attributed to the characteristic distal-to-proximal shift in torque and power among older adults (DeVita and Hortobagyi, 2000). Such changes require more positive work from hip extensors (i.e., hip strategy), as opposed to plantar flexors (i.e., ankle strategy), resulting in a higher walking net $\dot{V}O_2$ and utilization of the physiologic reserve (Hunter et al., 2021). To our knowledge, the present work is first to demonstrate a positive link between walking net $\dot{V}O_2$ and the POMS Confusion-Bewilderment subscale – independent of $\dot{V}O_{2peak}$. Data from the

Baltimore Longitudinal Study of Aging have shown a positive association between higher energetic cost of walking and Alzheimer's Disease pathology (e.g., amyloid-beta status) (Dougherty et al., 2021). Additional evidence has indicated a higher ratio of energetic cost of walking to estimated $\dot{V}O_{2peak}$ (i.e., "cost-to-capacity ratio") was associated with subsequent ventricular enlargement, an index of central brain atrophy (Qiao et al., 2022). While the exact physiological underpinnings are unclear, these data highlight the intriguing link between brain health and energetic cost of walking. Though higher levels of aerobic fitness (i.e., $\dot{V}O_{2peak}$) have been long connected with brain health in older adults (Colcombe et al., 2003; Voss et al., 2013), it remains unclear if exercise-related interventions seeking to optimize walking net $\dot{V}O_2$ may attenuate /prevent neurocognitive decline.

Our prior work in postmenopausal women suggests 31 % of the variance in walking net $\dot{V}O_2$ is related to knee extensor rate of torque development (normalized to maximal isometric voluntary contraction) (Carter et al., 2024a). While resistance and/or velocity-based exercise may offer suitable strategies to promote broader physical function (Bezerra et al., 2019), postmenopausal women are also beset by a high rate of decay in pulmonary function (Triebner et al., 2017). Indeed, the combined effects of age-/menopause-related changes to the pulmonary system exacerbates the energetic cost of breathing (Janssens, 2005) – which contribute to a higher walking net $\dot{V}O_2$ with advancing age. Notably, this is not something predictably improved by general exercise training (Roman et al., 2016). In the present work, MRT, independent of $\dot{V}O_{2peak}$, correlated with average daily fatigue, fatigue interference, and POMS total mood disturbance composite. Since declining pulmonary function slows $\dot{V}O_2$ on-kinetics and likely disrupts recovery, it is reasonable that such changes would adversely contribute to feelings of fatigue and general mood disturbance. Recently inspiratory muscle training (IMT) has gained interest due to the purported health benefits in postmenopausal women including improved pulmonary function (Feriani et al., 2017), respiratory pump (Rodrigues et al., 2023) and cardiovagal modulation (Rodrigues et al., 2018). While these benefits would promote physical function, it remains unclear whether IMT could speed MRT or reduce walking net $\dot{V}O_2$ in postmenopausal women.

Limitations in the present work should be considered. First, we recognize the inability to establish direction or causality in the observed relationships. Second, evaluation of MRT and walking net $\dot{V}O_2$ were performed during a fixed-workload treadmill task. Though the workload was selected as it aligns with the workload (0.89 m/s) deemed to be an optimal cut-point to distinguish postmenopausal women at elevated risk for mortality (Luo et al., 2023), future work may consider overground walking at self-selected speeds. Third, most study participants were educated, White women without overt cardiometabolic or neurodegenerative disease. Lastly, we acknowledge modest potential for confounding among outcomes of interest owing to the risk of day-to-day variation and self-report bias. Therefore, extrapolation of these data to other populations should be performed with caution. Future research should consider a larger sample size to corroborate or refute the findings herein.

5. Conclusion

To reduce the risk of declining physical function and attendant consequences on psychosocial well-being, evidence-based interventions are needed for postmenopausal women. Based on the present work, strategies targeting MRT and walking net $\dot{V}O_2$ are compelling targets to alleviate the burdens fatigue and mood disturbance in postmenopausal women.

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Data availability

Data will be made available on request.

Abbreviations:

bpm	beats per minute
BMI	body mass index
HR	heart rate
MRS	mean response time
mm Hg	millimeters of mercury
mL/kg/min	milliliters per kilogram body mass per minute, millimeters of mercury
min	minute
m/s	meters per second
POMS	Profile of Mood States
TMD	total mood disturbance
$\dot{V}O_2$**,**	oxygen uptake
y	years

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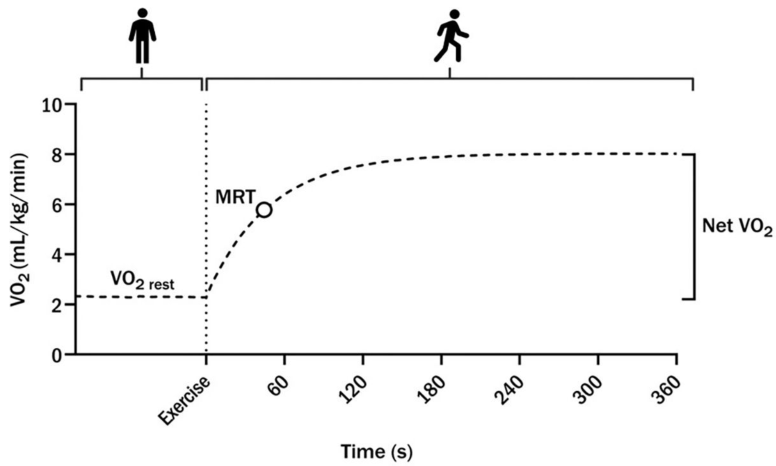

Fig. 1.

Operational distinction between mean response time (MRT) and walking net oxygen uptake ($\dot{V}O_2$) during a fixed-workload (0.89 m/s at 0 % grade) treadmill task.

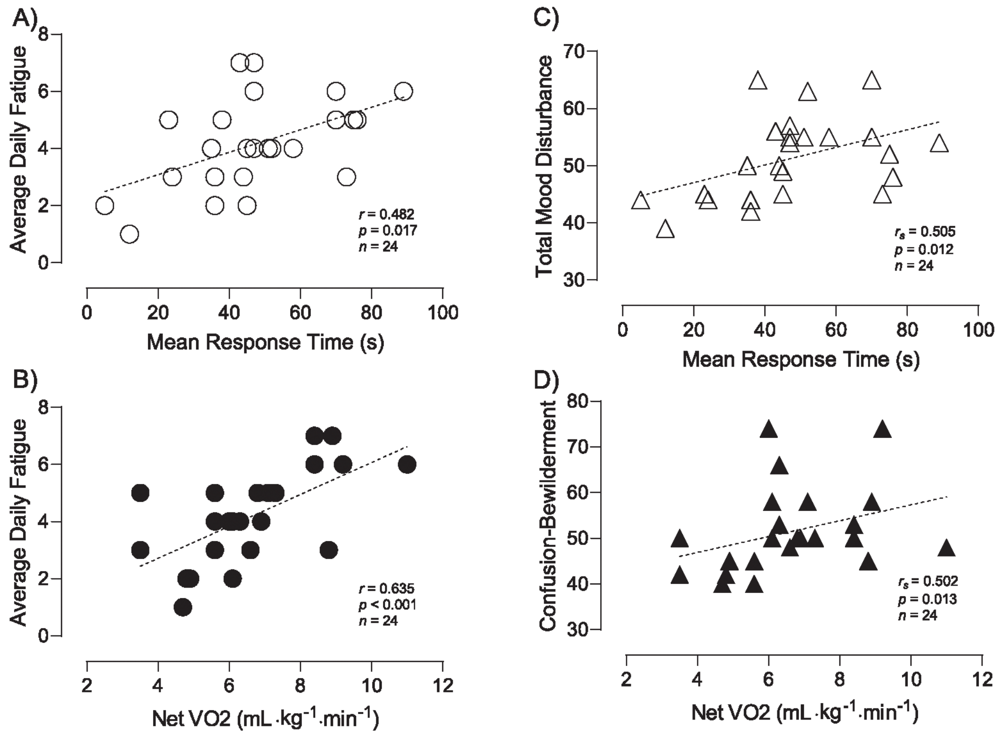

Fig. 2.

A-D: Unadjusted scatterplots of variables of interest. Note the mean response time coincided with the duration to reach 63 % of steady-state walking net $\dot{V}O_2$ during a fixed-workload (0.89 m/s) treadmill task. Statistical significance was $p < 0.05$.

Table 1

Descriptives ($n = 25$).

Variables	**Mid-life** $n = 14$	**Older** $n = 11$	***p*-value**
Age (y)	61 ± 3	69 ± 4 *	< 0.001
Height (m)	1.62 ± 0.06	1.64 ± 0.06	0.410
Mass (kg)	83.4 ± 8.4	81.8 ± 10.4	0.681
Lean Mass (kg)	42.9 ± 4.7	43.9 ± 5.2	0.642
Fat Mass (kg)	39.4 ± 6.9	35.6 ± 5.9	0.156
BMI (kg/m^2)	31.7 ± 3.8	30.3 ± 3.4	0.314
Heart rate (bpm)	67 ± 8	64 ± 9	0.366
Systolic BP (mm Hg)	130 ± 13	130 ± 10	0.970
Diastolic BP (mm Hg)	77 ± 10	73 ± 7	0.340
Mental Health History (yes) [n (%)]			
Anxiety / Depression	6 (43)	4 (36)	0.747
Depression Medications (yes) [*n* (%)]	7 (50)	3 (11)	0.259
Employed (yes) [*n* (%)]	12 (86)	7 (64)	0.209
Marital Status [*n* (%)]			
Married or living with sig. other Education	8 (57)	5 (45)	1.000
Bachelor’s Degree (yes) [*n* (%)]	13 (93)	10 (91)	0.442
Annual Income [*n* (%)] ≥ $50 k	11 (79)	7 (64)	1.000

Values are shown as means ± standard deviation unless noted otherwise. BMI, body mass index; BP, blood pressure.

* Statistical significance at *p*-value < 0.05.

Table 2

Age-group comparisons.

Variables	Mid-life $n = 14$	Older $n = 11$	*p* -value	ES
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)	24.0 ± 3.5	19.2 ± 3.4	0.002	1.39
MRT (s)[a]	46 ± 24	48 ± 18	0.869	0.07
Walking net VO2 ($mL \cdot kg^{-1} \cdot min^{-1}$)[a]	6.7 ± 1.6	6.4 ± 2.0	0.712	0.15
Average Daily Fatigue[b]	4.1 ± 1.5	4.1 ± 1.8	0.978	0.01
Fatigue Interference[b]	14.5 ± 6.7	20.2 ± 10.7	0.119	0.63
POMS TMD[b]	51(10)	55(12)	0.337	0.19
POMS Tension-Anxiety[b]	48(8)	50(12)	0.600	0.11
POMS Depression-Dejection[b]	45(4)	50(7)[†]	0.042	0.41
POMS Anger-Hostility[b]	49(10)	51(12)	0.508	0.13
POMS Fatigue-Inertia[b]	51(14)	52(16)	0.978	0.02
POMS Confusion-Bewilderment[b]	50(13)	50(8)	0.934	0.19
POMS Vigor-Activity[b]	47(12)	46(11)	0.869	0.03

Values are shown as means ± standard deviations or median (interquartile range). POMS, Profile of Mood States; TMD, total mood disturbance. ES, effect size.

[a] $n = 13$ for mid-life group.

[b] higher number indicative of greater disturbance.

[†] Statistically significant between-group difference at *p* -value ≤0.05.

Table 3

Correlation matrix ($n = 24$).

Variables	[a]Mean response time	[a]Walking net VO_2
Average Daily Fatigue	0.500 *	0.632 **
Fatigue Interference	0.421 *	0.057
POMS TMD	0.437 *	0.344
POMS Tension-Anxiety	0.448 *	0.203
POMS Depression-Dejection	0.176	0.106
POMS Anger-Hostility	0.435 *	0.088
POMS Fatigue-Inertia	0.330	0.393
POMS Confusion-Bewilderment	0.296	0.504 *
POMS Vigor-Activity	−0.234	−0.361

disturbance; VO_2, oxygen uptake.

[a]Adjusted for VO_{2peak}. Average daily fatigue and fatigue interference were assessed with the Fatigue Symptom Inventory wherein a higher value indicates greater disturbance; POMS, Profile of Mood States questionnaire; TMD, total mood.

** p-value < 0.01.

* p-value < 0.05.

Table 4

Linear regression models ($n = 24$).

	Model R	R^2	Partial r	p -value
Model 1				
Average Daily Fatigue	0.74	0.55		
MRT (s)			0.502*	0.015
Walking net VO_2 ($mL \cdot kg^{-1} \cdot min^{-1}$)			0.647*	< 0.001
Model 2				
Fatigue Interference	0.63	0.40		
Age (y)			0.410	0.052
MRT (s)			0.525*	0.010

Mean response time (MRT) representing the duration needed to reach 63 % steady-state net oxygen uptake (VO_2) during a fixed-workload (0.89 $m \cdot s^{-1}$ at 0 % grade) treadmill task. Higher fatigue ratings denote greater disturbance.

*Statistical significance p -value < 0.05.