UC Berkeley
UC Berkeley Previously Published Works

## Title
Leg cycling efficiency is unaltered in healthy aging regardless of sex or training status

## Permalink
https://escholarship.org/uc/item/8td7b2d0

## Journal
Journal of Applied Physiology, 137(4)

## ISSN
8750-7587

## Authors
Duong, Justin J
Leija, Robert G
Osmond, Adam D
et al.

## Publication Date
2024-10-01

## DOI
10.1152/japplphysiol.00393.2024

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

JOURNAL OF APPLIED PHYSIOLOGY

*J Appl Physiol* 137: 857–863, 2024.
*First published August 1, 2024; doi:10.1152/japplphysiol.00393.2024*

RESEARCH ARTICLE

# Leg cycling efficiency is unaltered in healthy aging regardless of sex or training status

**Justin J. Duong, Robert G. Leija, Adam D. Osmond, Jose A. Arevalo, and George A. Brooks**

*Exercise Physiology Laboratory, Department of Integrative Biology, University of California, Berkeley, Berkeley, California, United States*

## Abstract

Muscular efficiency during exercise has been used to interrogate aspects of human muscle energetics, including mitochondrial coupling and biomechanical efficiencies. Typically, assessments of muscular efficiency have involved graded exercises. Results of previous studies have been interpreted to indicate a decline in exercise efficiency with aging owing to decreased mitochondrial function. However, discrepancies in variables such as exercise stage duration, cycling cadence, and treadmill walking mechanics may have affected interpretations of results. Furthermore, recent data from our lab examining the ATP to oxygen ratio (P:O) in mitochondrial preparations isolated from NIA mouse skeletal muscle showed no change with aging. Thus, we hypothesized that delta efficiency (Δ€) during steady-rate cycling exercise would not be altered in older healthy subjects compared with young counterparts regardless of biological sex or training status. Young (21–35 yr) and older (60–80 yr) men ($n = 21$) and women ($n = 20$) underwent continual, progressive leg cycle ergometer tests pedaling at 60 RPM for three stages (35, 60, 85 W) lasting 4 min. Δ€was calculated as: (Δ work accomplished/Δ energy expended). Overall, cycling efficiencies were not significantly different in older compared with young subjects. Similarly, trained subjects did not exhibit significantly different exercise efficiencies compared to untrained. Moreover, there were no differences between men and women. Hence, our results obtained on healthy young and older subjects are interpreted to mean that previous reports of decreased efficiency in older individuals were attributable to metabolic or biomechanical comorbidities, not aging per se.

**NEW & NOTEWORTHY** Muscular power is reduced, but the efficiency of movement is unaltered in healthy aging.

*aging; excitation-contraction coupling; human metabolism; muscle mechanical efficiency; oxidative phosphorylation efficiency*

## INTRODUCTION

Muscular efficiency[1] during exercise, the ratio of mechanical work to energy expenditure, has garnered significant interest for its relevance to understanding integration of the components of bioenergetics, metabolism, and biomechanics. Although there are several ways to compute muscular efficiency [work, gross, net, and delta efficiency (Δ€)], Δ€, defined as the change in energy expenditure associated with a change in power output, is widely recognized as the most valid measure of muscular efficiency (1, 2). Among the reasons for determining muscular efficiency is evaluating the influence of aging on the components of muscular efficiency during exercise that have important implications for determining the energetic, cardiopulmonary, and nutritive demands of activities of daily living. It has long been known that basal metabolic rate (BMR) (3) and maximal oxygen consumption capacity ($\dot{V}O_2max$) decline in aging (4). The age-related decline in aerobic fitness means that any exercise task is accomplished at a greater percentage of $\dot{V}O_2max$ and respiratory gas exchange ratio ($R = \dot{V}CO_2/\dot{V}O_2$), thereby shifting energy substrate partitioning toward carbohydrate oxidation (5). Several studies have shown decrements in locomotor efficiency (6) and increased energetic cost (7, 8) during treadmill walking in older adults. As well, decreased mitochondrial coupling efficiency has been proposed to play a major role in reduced muscular efficiency with aging (9–12). Results for cycling efficiency with aging are less definitive as some studies report lower (10–13), higher (14), or equal efficiencies (15, 16).

To date, there have been few studies to interrogate the possibility of biological sex-specific differences on muscular efficiency. Of those, most have reported similar efficiencies in men and women across different exercise modalities (12, 13, 17–19). Some report higher efficiencies in men than women during arm cranking (20), while others report higher leg cycling efficiencies in female than male competitive cyclists (21). As most studies were conducted in young healthy subjects, age-associated sex-specific differences merit further investigation.

Studies of the influence of training status on leg muscular cycling efficiency have also yielded similarly mixed results. Evidence suggests that the type of training (22),

[1]Muscular efficiency: overall efficiency of energy transduction during muscle exercise. Muscular efficiency is a collective term involving the efficiencies of mitochondrial oxidative phosphorylation, excitation-contraction coupling, actomyosin interactions, and capture of kinetic energy during locomotion.

Correspondence: G. A. Brooks (gbrooks@berkeley.edu).
Submitted 28 May 2024 / Revised 30 July 2024 / Accepted 31 July 2024


8750-7587/24 Copyright © 2024 the American Physiological Society.


Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.

amount of cycling experience (23–25), or fitness level (25, 26) do not influence cycling Δ€. In older athletes, however, there are conflicting reports that have shown increased Δ€ in endurance-trained athletes compared with their sedentary counterparts (10). Similarly, others have reported improvements in efficiency as a result of training (9, 11, 12). Long-term endurance training has been proposed to maintain exercise efficiency with aging (27). In contrast, others have noted significantly decreased efficiency despite training (28). Despite these studies, the interface between age and training status has not been thoroughly explored.

Hence, the purpose of this study was to interrogate the effects of aging on Δ€ during submaximal, steady-rate cycling in healthy young and older adults. In addition, we aimed to determine if sex and endurance training influenced exercise efficiency. Based on results of our studies on mitochondrial preparations isolated from young and old, male and female NIA mice (29), it was hypothesized that Δ€: *1*) would be unaltered in older compared with young persons and *2*) would be unaffected by sex or *3*) training status.

## MATERIALS AND METHODS

### Subjects

Younger (21–35 yr) and older (60–80 yr) healthy men ($n$ = 21) and women ($n$ = 20) ($n_{total}$ = 41) were recruited from the University of California, Berkeley campus and the surrounding community via fliers, word of mouth, e-mail, and social media. Subjects were included in the study if they had a body mass index of ≥18.5 and <30 kg/m$^2$, were nonsmokers, were diet and weight stable, had a vital capacity 1-s forced expiratory volume of >70% via spirometry, and were injury and disease free, as determined by physical examination by a physician. Body fat percentage was assessed via skinfold measurements. Training status was determined from self-reported exercise habits on individual intake exercise history questionnaires and confirmed from $\dot{V}O_2$peak results. Untrained participants reported <2 days a week of physical activity. Trained participants reported >5 days of physical activity per week for a minimum of 30 min per day. This study was approved by the University of California Berkeley Committee for the Protection of Human Subjects and conformed to the standards set by the Declaration of Helsinki (CPHS 2018-08-11312). Eligible volunteers gave written informed consent after discussing the purposes, procedures, and associated risks.

### Exercise Testing Protocol

Following initial screenings, all subjects underwent a graded exercise test (GXT) conducted on an electronically braked leg cycle ergometer (Lode Gronigen, Netherlands). Expired respiratory gasses were continuously monitored throughout the test via an open-circuit automated indirect calorimeter (Parvo Medics TrueOne 2400 Metabolic System, Salt Lake City, UT) that was calibrated using room air and a certified calibration gas (16% $O_2$, 4% $CO_2$). Testing began with 5 min of resting data collection with the subject seated quietly on the ergometer. They were then instructed to begin cycling for a 2-min warm-up period at 25 W at a set cadence of 60 rpm. This cadence was dictated by a metronome and reinforced visually using a tachometer displayed on a screen. Following the 2-min warm-up, subjects completed three 4-min stages of 35, 60, and 85 W while maintaining a target cadence of 60 RPM. These three stages were used to determine efficiency. Subjects subsequently pedaled at a self-selected cadence for the remainder of the test as power output was increased by 30 W/min until ventilatory threshold [respiratory exchange ratio (RER, or R = $\dot{V}CO_2/\dot{V}O_2$) 0.97–1.0] for older subjects or volitional exhaustion for younger subjects was reached (2). $\dot{V}O_2$peak was estimated from measures of ventilatory threshold for the older population using American College of Sports Medicine (ACSM) Guidelines (30).

### Energy Costs of Rest and Exercise

As previously, the energy cost of rest and exercise were calculated from measurements of $\dot{V}O_2$ and RER (1, 31).

### Efficiency

Gross, net, and Δefficiency (Δ€) were calculated as previously described by Gaesser and Brooks (1). Δ€ was calculated as the ratio of the change in external work and the associated change in energy expenditure between stages as follows:

$$\Delta€(\%) = (\Delta\,\text{Work Accomplished}/\Delta\,\text{Energy Expenditure}) \times 100$$

In addition, Δ€ was calculated from the inverse of the slope of $\dot{V}O_2$ on external power output during the 35, 60, and 85 W stages.

Moreover, gross and net efficiencies were calculated as traditionally (1):

**Table 1.** *Subject demographic information*

| | Young | | | | Older | | | |
|---|---|---|---|---|---|---|---|---|
| | Trained | | Untrained | | Trained | | Untrained | |
| | Men | Women | Men | Women | Men | Women | Men | Women |
| $n$ | 6 | 6 | 4 | 7 | 7 | 5 | 5 | 5 |
| Age, yr | 30 ± 4 | 28 ± 6 | 29 ± 1 | 22 ± 1 | 69 ± 3 | 69 ± 6 | 73 ± 2 | 70 ± 3 |
| Height, cm | 178.1 ± 6.2 | 168.4 ± 8.3 | 167.6 ± 2.9 | 157.2 ± 5.3 | 174.8 ± 6.8 | 161.8 ± 7.6 | 174.4 ± 7.2 | 165.6 ± 8.1 |
| Weight, kg | 78.0 ± 7.5 | 61.1 ± 3.4 | 80.1 ± 9.6 | 54.9 ± 5.8 | 79.2 ± 9.3 | 59.0 ± 8.0 | 85.1 ± 15.5 | 66.5 ± 6.4 |
| Body fat, % | 10.5 ± 3.8 | 20.0 ± 4.6 | 19.3 ± 3.6 | 23.0 ± 4.4 | 17.4 ± 1.1 | 23.0 ± 6.3 | 19.3 ± 3.6 | 27.3 ± 1.3 |
| $\dot{V}O_2$peak, L/min | 4.0 ± 0.3 | 3.0 ± 0.5* | 2.6 ± 0.4$ | 1.5 ± 0.2*$ | 2.7 ± 0.3# | 1.8 ± 0.6*# | 1.8 ± 0.6#$ | 1.4 ± 0.2#$ |
| Rel $\dot{V}O_2$peak, mL/kg/min | 52.6 ± 3.7 | 47.8 ± 6.1* | 34.2 ± 1.9$ | 29.1 ± 5.7*$ | 33.3 ± 4.2# | 26.3 ± 4.2*# | 20.5 ± 0.3#$ | 20.7 ± 1.6#$ |

All values are means ± SD. *Significantly different from men. #Significantly different from young. $Significantly different from trained.


Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.

**Table 2.** *Cycling Δ€ in young and older volunteers by exercise stage*

| | Young | | Older | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| | *35–60 W* | | | |
| Δ€, % | | | | |
| Trained | 28.8 ± 0.8 | 29.1 ± 0.8 | 28.7 ± 2.0 | 28.8 ± 0.5 |
| Untrained | 29.7 ± 2.0 | 29.0 ± 1.0 | 29.4 ± 1.4 | 29.0 ± 2.9 |
| | *60–85 W* | | | |
| Δ€, % | | | | |
| Trained | 26.4 ± 3.3 | 26.2 ± 2.3 | 26.5 ± 2.7 | 26.5 ± 1.9 |
| Untrained | 26.4 ± 2.1 | 26.4 ± 2.0 | 26.3 ± 2.8 | 25.4 ± 1.0 |

All values are means ± SD.

$$\text{Gross Efficiency}(\%) = [\text{W(kcal)}/\text{EE(kcal)}] \times 100$$

$$\text{Net Efficiency}(\%) = [\text{W(kcal)}/[\text{EE(kcal)} - \text{ER(kcal)}] \times 100$$

where EE = energy of exercise in kcal, ER = energy of rest in kcal, and W = external work done in kcal.

### Statistical Analyses

Relationships between age, sex, and training status were evaluated using three-way repeated-measures ANOVA (age × sex × training status). When significant *F* ratios were identified, Student-Newman Keuls post hoc analyses were performed. A *P* value of $<0.05$ was considered statistically significant. Analyses were performed using GraphPad Prism 10.2.2 software. Group sample sizes were predicted based on power analyses using results of our previous studies. All data are presented as means ± SD.

## RESULTS

### Subject Characteristics

As anticipated, we observed significant age- and sex-related differences in height, weight, $\dot{V}O_2$peak, and age (Table 1). Briefly, older individuals weighed significantly more than those in the young group ($P < 0.05$). And, as expected, $\dot{V}O_2$peak was significantly lower in older individuals than in younger counterparts ($P < 0.05$). Also, $\dot{V}O_2$peak was greater in trained than in untrained individuals ($P < 0.05$). Moreover, men had higher $\dot{V}O_2$peak values than women when matched for training status ($P < 0.05$), but interestingly $\dot{V}O_2$peak was not different due to sex in the older untrained groups.

### Computed Efficiencies

#### *Δ Efficiency.*

Results of this investigation are presented in Table 2 and Fig. 1, a plot of metabolic power (W) as a function of external power output on the leg cycle ergometer (W). All relevant results are contained in this W/W figure in which slopes of the rise in metabolic rate depend on the external power output. Apparent differences in the y-intercept were associated with body size. Otherwise, for untrained, young, women (UTYW) ($r^2 = 0.86$), the W/W relationship for all other groups $r^2 \geq 0.95$. Hence, there were no differences in Δ€ due to age, sex, or training state.

#### *Gross and net efficiencies.*

Women exhibited increased gross efficiency ($P < 0.01$) at all three stages (Table 3). There were no differences in gross efficiency due to age or training. Furthermore, there were no differences in net efficiencies due to age, sex, or training status.

## DISCUSSION

Our aim was to interrogate the influence of age, sex, and training status on Δ€ during leg cycling. We hypothesized that leg cycling Δefficiency (Δ€) would be unaltered during subventilatory threshold steady-rate exercise regardless of age, sex, or training status. Our results support the conclusion that cycling exercise efficiency is not impaired in older adults. Furthermore, in agreement with some existing literature, we found no difference with training history or biological sex (12, 26).

Our preference for using Δ€ as opposed to other modes of computation comes from considerations of first principles as previously articulated (1, 2, 32). Moreover, while data are rare, we are aware of two reports in which working leg muscle and whole body $\dot{V}O_2$ were simultaneously measured over a range of exercise power outputs (33, 34). Slopes of whole body and leg rates of $O_2$ consumption rose in parallel yielding efficiency values as reported here.

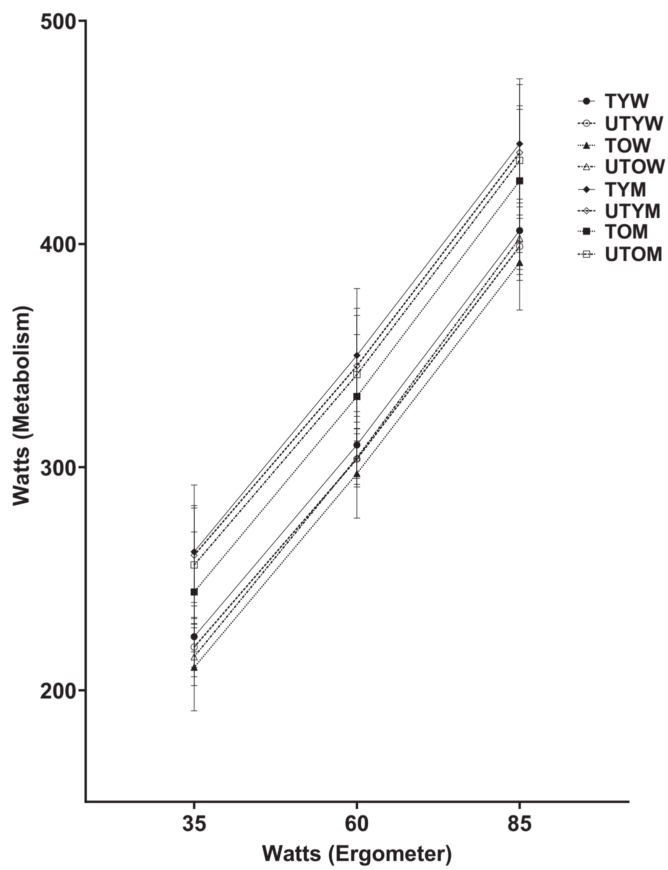


**Figure 1.** Metabolic power (Watts) derived from assessments of $\dot{V}O_2$ and RER ($=\dot{V}CO_2/\dot{V}O_2$) as functions of exercise power during steady-rate exercise in eight study cohorts of younger (Y; 21–35 yr) and older (O; 60–80 yr) healthy men (M; $n = 21$) and women (W; $n = 20$) volunteers ($n_{total} = 41$); see text for details. Relationships between age, sex, and training status were evaluated using three-way repeated-measures ANOVA (age × sex × training status). A *P* value of $<0.05$ was considered statistically significant. T, trained; UT, untrained.


Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.

**Table 3.** *Gross and net cycling efficiencies on young and older volunteers by exercise stage*

| | Young | | Older | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| | *35 W* | | | |
| Gross, % | | | | |
| Trained | 13.8 ± 1.4 | 15.3 ± . 06* | 14.2 ± 1.5 | 16.7 ± 1.5* |
| Untrained | 13.5 ± 1.0 | 16.0 ± 1.0* | 13.9 ± 1.4 | 15.8 ± 0.8* |
| Net, % | | | | |
| Trained | 23.8 ± 2.4 | 23.4 ± 1.2 | 23.8 ± 1.5 | 25.6 ± 2.7 |
| Untrained | 24.2 ± 0.9 | 24.3 ± 1.3 | 23.9 ± 2.2 | 24.8 ± 0.9 |
| | *60 W* | | | |
| Gross, % | | | | |
| Trained | 17.5 ± 1.4 | 19.1 ± 0.7* | 18.0 ± 1.5* | 20.3 ± 1.3* |
| Untrained | 17.4 ± 1.1 | 19.3 ± 1.6* | 17.7 ± 1.5* | 19.1 ± 0.7* |
| Net, % | | | | |
| Trained | 25.5 ± 1.7 | 25.5 ± 0.8 | 25.7 ± 1.6 | 26.8 ± 1.7 |
| Untrained | 26.1 ± 0.8 | 26.2 ± 0.5 | 25.7 ± 1.3 | 26.3 ± 1.4 |
| | *85 W* | | | |
| Gross, % | | | | |
| Trained | 19.2 ± 1.2 | 20.7 ± 1.0* | 20.0 ± 1.7 | 21.7 ± 1.2* |
| Untrained | 19.2 ± 1.0 | 21.3 ± 0.7* | 19.5 ± 1.6 | 20.9 ± 0.8* |
| Net, % | | | | |
| Trained | 25.5 ± 1.3 | 25.6 ± 1.0 | 26.2 ± 1.8 | 26.7 ± 1.5 |
| Untrained | 25.9 ± 1.4 | 26.2 ± 0.4 | 26.0 ± 1.5 | 26.0 ± 1.2 |

All values are means ± SD. *Significantly different from men.

Our indifference to the utility of gross and net efficiency calculations has been previously presented (1, 2, 32). Simply, the baseline artifacts of gross and net calculations give predictable, but invalid results. Net efficiencies are greater than gross because of subtraction of resting energy expenditure from the dominator (0.0 and ER, respectively). As well, gross and net efficiencies rise as power output increases because the constant baseline, ER correction becomes relatively less. To reiterate (1, 32), the apparent rise in muscular efficiency at high power outputs is an artifact, and contrary to Δ€ that is either constant or decreasing slightly as power output increases.

Of the four typical descriptions of exercise efficiency, gross and Δ€ are the most commonly reported (2, 10, 35, 36). We and others have previously asserted that Δ€ represents the most reliable measure of muscular efficiency as contributions from metabolic processes not contributing to mechanical work are eliminated (1, 6, 17, 37). Although there is abundant evidence that Δ€ and energetic cost of exercise are altered in older adults during treadmill walking (6–8, 12), the influence of age on cycling Δ€ is not apparent (10, 13, 16). However, age-related changes in joint biomechanics and muscle compliance could affect human gait. Therefore, the biomechanics of walking and running could affect measures of efficiency and economy in aging. Thus, for studies of the energetics in the aged and infirm, leg cycling, as opposed to treadmill walking is the choice to assess muscular efficiency.

In contrast to the results reported here, Conley et al. (13) reported decreased cycling Δ€ in elderly subjects and attributed it to a decline in mitochondrial-coupling efficiency. However, like us using steady-rate cycling protocols, Murias et al. (16) reported no age-related decrements in leg cycling efficiency.

In comparing results from established laboratories, it appears that diverse investigators agree on the use of steady-rate exercise tasks to elicit metabolic responses. At a practical level, studies of exercise protocols involve continuous or continual ramp protocols to elicit changes in $\dot{V}O_2$ and RER. However, depending on the persons tested, exercise ramp increments could be too large or the time of measurement too short for subjects to achieve steady rates of $O_2$ consumption with RER < 1.0. Hence, the presence of non-steady rate $O_2$ responses to exercise may account for variations in $\dot{V}O_2$ kinetics reported on aging individuals. In the present report, we used small work increments and allowed 4 min for $\dot{V}O_2$ to respond. Given that persons with overt metabolic or cardiovascular diseases were excluded from our study, and that participants were exercised at the same absolute workloads and cadence, the lack of difference with age indicates that mitochondrial coupling was not compromised during submax steady-rate exercise in our subjects. However, in other study populations, evidence of decreased efficiency during steady-rate cycling may be used to screen for cardiopulmonary or mitochondrial dysfunction in particular individuals (10, 13). Indeed, when data from highly competent research laboratories show compromised muscular efficiencies in older participants, then a rather simple exercise ergometer test might be useful in unmasking the presence of mitochondrial gene defects, or other metabolic or biomechanical deficits.

Our data showed no difference in net efficiency across age, sex, or training status. This is in contrast to several studies showing decreased efficiency with aging (38–40). Our results are, however, consistent with those of Gaesser et al. (6), who found no difference between older adults compared with their younger counterparts. The lower efficiency in older subjects reported in previous literature (38–40) is likely an artifact derived from lower absolute power outputs or the presence of biomechanical or metabolic comorbidities in older study participants rather than increased exercise efficiency in younger adults (6).

### Sex Differences

We found no differences in delta or net efficiency between men and women. However, we did see a sex-specific difference in gross efficiency with women showing increased gross efficiency compared with their male counterparts, persisting across age and training status. Most likely, the appearance of a gross efficiency advantage was due to the effects of body mass on the baseline $\dot{V}O_2$. For the most part, our results are consistent with several studies indicating a lack of sex-specific differences in efficiency during leg cycling (13, 17, 19). Comparison of elderly adults and their middle-aged counterparts found no differences in Δ€, contractile coupling efficiency, or mitochondrial coupling efficiency between sexes (13). This remains true across several exercise modalities including treadmill walking, arm cycling, and cross-country skiing (12, 18, 19). In contrast, Hopker et al. (21) reported increased gross cycling efficiency in young women cyclists compared with men. Although this aligns with our current results, comparisons at the same absolute work rates between men and women may not be indicative of changes of efficiency with sex. As the women in the present study were significantly smaller in stature and exhibited lower $\dot{V}O_2$peak values than the men, the contribution of nonwork energy expenditure was likely reduced as a function of higher relative workloads. Using relative intensities between men and women, Yasuda et al. (19)


Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.

found no changes in gross efficiency during arm or leg cycling in untrained young men and women.

Interestingly, we did find a difference when normalizing Δ€ to lean body mass. This is in contrast to a study by Berry et al. (41), who saw no effect of body mass on cycling efficiency. Amati et al. (42) found that weight loss had no influence on gross exercise efficiency. Although Hopker et al. (39) reported that normalization of leg lean mass was sufficient to ameliorate differences in cycling gross efficiencies between men and women, we found that lean mass normalization caused a decrease in cycling Δ€, particularly for older women. As we only assessed total lean body mass, this could account for the difference in our results.

### Training Status

In agreement with much of the existing literature, we show no influence of training status on cycling Δ€ (6, 23–26). Mogensen et al. (26) found endurance-trained young males showed no improvement in cycling Δ€ compared with their untrained counterparts. Examination of isolated mitochondria taken from muscle biopsies in these subjects revealed no differences in mitochondrial oxidative phosphorylation coupling efficiency, as defined by P/O ratio, with training. Furthermore, the authors found no correlation between mitochondrial coupling efficiency and cycling efficiency (26). In contrast, several studies in older adults have noted increased exercise efficiency with training and training status (9–12). For example, Conley et al. (9) reported that after 6 mo of endurance training, older adults were reported to have improved mitochondrial energy coupling resulting in increased cycling Δ€. In addition, Broskey et al. (10) found significantly higher Δ€ in older athletes than in their sedentary counterparts, a difference that they attributed to improved mitochondrial function and content. However, they found mitochondrial coupling efficiency was not different between the athlete and sedentary groups and had no relationship with any measure of exercise efficiency (10).

Louis et al. (11) found that older cyclists exhibited lower Δ€ than younger cyclists. This difference was eliminated after the implementation of a 3-wk strength training program. Then again, it appears that a minimum of exercise experience is necessary to reliably use ergometry to assess muscular efficiency. Again, the largest variance in our data was observed when testing young, untrained female study participants (Fig. 1).

### Comparison of Empirical Results with American College of Sports Medicine Guidelines Predictions

The ACSM guidelines (30) are the standard for clinical exercise testing (CET) and prescription. In fact, we used ACSM predictions to assess the reliability of our $\dot{V}O_2$max determinations on some older study participants. Overall, for all study cohorts, we found excellent agreement between our measurements of $\dot{V}O_2$ during graded exercise and ACSM predictions ($r^2 = 0.95$). Use of ACSM prediction equations in CET and prescription is supported.

### Limitations

Subjects were not height- or weight-matched between age, sex, or training status. We did not investigate in vitro measures of efficiency or human mitochondrial function; instead, we relied on studies of mitochondrial preparations isolated from mouse muscle. We also had relatively small sample sizes for all groups with most participants having a university affiliation. An unexpected observation in the older cohort was that the reported amount of physical activity was a poor predictor of $\dot{V}O_2$peak; an interpretation of that result being $\dot{V}O_2$peak is a parameter of cardiovascular capacity, and not necessarily physical activity level in older participants. In subsequent metabolic studies on young individuals, young women were studied during their midfollicular menstrual phase (43). However, menstrual cycle phase was not controlled for in screening of young female volunteers.

And finally, a limitation in studies of muscular efficiency is that the exercise tasks used are of low intensities, below ventilatory and lactate thresholds. This practice is to ensure the energy expenditure is captured in measuring $\dot{V}O_2$. However, during higher power outputs that elicit lactatemia, lactate is disposed of via oxidation (44, 45); the result being little effect on the $\dot{V}O_2$/power output relationship (46).

### Conclusions

We demonstrate that muscular cycling efficiency, as determined by Δ€ during steady-rate, subventilatory threshold exercise was not altered by age in healthy humans. Furthermore, neither sex nor training status affected muscular efficiency. These data are interpreted to mean that the coupling of mitochondrial oxidative phosphorylation is unaltered in aging. This conclusion is supported by our work on isolated mitochondria (unpublished observations). Our results obtained on healthy young and older participants interpreted that previous reports of decreased muscular efficiencies in older individuals were attributable to underlying metabolic or biomechanical comorbidities, not aging per se.

### Perspectives and Significance

We show the preservation of delta muscular efficiency (Δ€) in older men and women. We are cognizant of reports of diminished muscular efficiency in older individuals. We accept validity of those results but attribute them to the presence of comorbidities affecting either the biomechanics of locomotion or decreased coupling of oxidative phosphorylation in muscle mitochondrial reticula.

## DATA AVAILABILITY

Data will be made available upon reasonable request.

## ACKNOWLEDGMENTS

The investigators thank the study participants for their time, efforts, and experimental discomforts. We thank Rosemary Agostini for advice and support, and the essential roles of our exceptional undergrad research apprentices, Livi Artanegara, Heidi Avalos, Jennah Brown, Joshua Johnson, Kayla Lee, Queenie Li, Nika Talebizadeh, Albert Truong, Sainjargal Uuganbayar, Victoria Wat, Emily Yang, and Catherine Zhu, are acknowledged. Special thanks to Susan E. Hoffman, Director University of California, Berkeley Osher Lifelong Learning Institute for advice.


Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.

## GRANTS

This work is supported by NIH grant R01 AG059715 to G.A.B. and an award from the University of California, Berkeley Center for Research and Aging (CREA).

## DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

## AUTHOR CONTRIBUTIONS

G.A.B. conceived and designed research; J.J.D., R.G.L., A.D.O., J.A.A., and G.A.B. performed experiments; J.J.D., R.G.L., A.D.O., J.A.A., and G.A.B. analyzed data; J.J.D., R.G.L., J.A.A., and G.A.B. interpreted results of experiments; J.J.D. and R.G.L. prepared figures; J.J.D. and G.A.B. drafted manuscript; J.J.D., R.G.L., A.D.O., J.A.A., and G.A.B. edited and revised manuscript; J.J.D., R.G.L., A.D.O., J.A.A., and G.A.B. approved final version of manuscript.

## REFERENCES


1. **Gaesser GA**, **Brooks GA.** Muscular efficiency during steady-rate exercise: effects of speed and work rate. *J Appl Physiol* 38: 1132–1139, 1975. doi:10.1152/jappl.1975.38.6.1132.
2. **Poole DC**, **Rossiter HB**, **Brooks GA**, **Gladden LB.** The anaerobic threshold: 50+ years of controversy. *J Physiol* 599: 737–767, 2021. doi:10.1113/JP279963.
3. **Benedict FG**, **Cathcart EP.** *Muscular Work: a Metabolic Study with Special Reference to the Efficiency of the Human Body as a Machine*. Washington: Carnegie Institution of Washington, 1913.
4. **Rogers MA**, **Hagberg JM**, **Martin WH 3rd**, **Ehsani AA**, **Holloszy JO.** Decline in VO2max with aging in master athletes and sedentary men. *J Appl Physiol (1985)* 68: 2195–2199, 1990. doi:10.1152/jappl.1990.68.5.2195.
5. **Brooks GA**, **Mercier J.** Balance of carbohydrate and lipid utilization during exercise: the “crossover” concept. *J Appl Physiol (1985)* 76: 2253–2261, 1994. doi:10.1152/jappl.1994.76.6.2253.
6. **Gaesser GA**, **Tucker WJ**, **Sawyer BJ**, **Bhammar DM**, **Angadi SS.** Cycling efficiency and energy cost of walking in young and older adults. *J Appl Physiol (1985)* 124: 414–420, 2018. doi:10.1152/japplphysiol.00789.2017.
7. **Ortega JD**, **Farley CT.** Effects of aging on mechanical efficiency and muscle activation during level and uphill walking. *J Electromyogr Kinesiol* 25: 193–198, 2015. doi:10.1016/j.jelekin.2014.09.003.
8. **Mian OS**, **Thom JM**, **Ardigo LP**, **Narici MV**, **Minetti AE.** Metabolic cost, mechanical work, and efficiency during walking in young and older men. *Acta Physiol (Oxf)* 186: 127–139, 2006. doi:10.1111/j.1748-1716.2006.01522.x.
9. **Conley KE**, **Jubrias SA**, **Cress ME**, **Esselman PC.** Elevated energy coupling and aerobic capacity improves exercise performance in endurance-trained elderly subjects. *Exp Physiol* 98: 899–907, 2013. doi:10.1113/expphysiol.2012.069633.
10. **Broskey NT**, **Boss A**, **Fares EJ**, **Greggio C**, **Gremion G**, **Schluter L**, **Hans D**, **Kreis R**, **Boesch C**, **Amati F.** Exercise efficiency relates with mitochondrial content and function in older adults. *Physiol Rep* 3: e12418, 2015. doi:10.14814/phy2.12418.
11. **Louis J**, **Hausswirth C**, **Easthope C**, **Brisswalter J.** Strength training improves cycling efficiency in master endurance athletes. *Eur J Appl Physiol* 112: 631–640, 2012. doi:10.1007/s00421-011-2013-1.
12. **Woo JS**, **Derleth C**, **Stratton JR**, **Levy WC.** The influence of age, gender, and training on exercise efficiency. *J Am Coll Cardiol* 47: 1049–1057, 2006. doi:10.1016/j.jacc.2005.09.066.
13. **Conley KE**, **Jubrias SA**, **Cress ME**, **Esselman P.** Exercise efficiency is reduced by mitochondrial uncoupling in the elderly. *Exp Physiol* 98: 768–777, 2013. doi:10.1113/expphysiol.2012.067314.
14. **Venturelli M**, **Schena F**, **Scarsini R**, **Muti E**, **Richardson RS.** Limitations to exercise in female centenarians: evidence that muscular efficiency tempers the impact of failing lungs. *Age (Dordr)* 35: 861–870, 2013. doi:10.1007/s11357-011-9379-1.
15. **Babcock MA**, **Paterson DH**, **Cunningham DA.** Influence of ageing on aerobic parameters determined from a ramp test. *Eur J Appl Physiol Occup Physiol* 65: 138–143, 1992. doi:10.1007/BF00705071.
16. **Murias JM**, **Kowalchuk JM**, **Paterson DH.** Speeding of VO2 kinetics with endurance training in old and young men is associated with improved matching of local O2 delivery to muscle O2 utilization. *J Appl Physiol (1985)* 108: 913–922, 2010. doi:10.1152/japplphysiol.01355.2009.
17. **Fares EJ**, **Isacco L**, **Monnard CR**, **Miles-Chan JL**, **Montani JP**, **Schutz Y**, **Dulloo AG.** Reliability of low-power cycling efficiency in energy expenditure phenotyping of inactive men and women. *Physiol Rep* 5: e13233, 2017. doi:10.14814/phy2.13233.
18. **Hegge AM**, **Bucher E**, **Ettema G**, **Faude O**, **Holmberg HC**, **Sandbakk O.** Gender differences in power production, energetic capacity and efficiency of elite cross-country skiers during whole-body, upper-body, and arm poling. *Eur J Appl Physiol* 116: 291–300, 2016. doi:10.1007/s00421-015-3281-y.
19. **Yasuda N**, **Gaskill SE**, **Ruby BC.** No gender-specific differences in mechanical efficiency during arm or leg exercise relative to ventilatory threshold. *Scand J Med Sci Sports* 18: 205–212, 2008. doi:10.1111/j.1600-0838.2007.00637.x.
20. **Beaven CM**, **Willis SJ**, **Cook CJ**, **Holmberg HC.** Physiological comparison of concentric and eccentric arm cycling in males and females. *PLoS One* 9: e112079, 2014. doi:10.1371/journal.pone.0112079.
21. **Hopker J**, **Jobson S**, **Carter H**, **Passfield L.** Cycling efficiency in trained male and female competitive cyclists. *J Sports Sci Med* 9: 332–337, 2010.
22. **Stuart MK**, **Howley ET**, **Gladden LB**, **Cox RH.** Efficiency of trained subjects differing in maximal oxygen uptake and type of training. *J Appl Physiol Respir Environ Exerc Physiol* 50: 444–449, 1981. doi:10.1152/jappl.1981.50.2.444.
23. **Nickleberry BL Jr**, **Brooks GA.** No effect of cycling experience on leg cycle ergometer efficiency. *Med Sci Sports Exerc* 28: 1396–1401, 1996. doi:10.1097/00005768-199611000-00008.
24. **Böning D**, **Gönen Y**, **Maassen N.** Relationship between work load, pedal frequency, and physical fitness. *Int J Sports Med* 5: 92–97, 1984. doi:10.1055/s-2008-1025887.
25. **Marsh GD**, **Paterson DH**, **Govindasamy D**, **Cunningham DA.** Anaerobic power of the arms and legs of young and older men. *Exp Physiol* 84: 589–597, 1999. doi:10.1111/j.1469-445X.1999.01848.x.
26. **Mogensen M**, **Bagger M**, **Pedersen PK**, **Fernstrom M**, **Sahlin K.** Cycling efficiency in humans is related to low UCP3 content and to type I fibres but not to mitochondrial efficiency. *J Physiol* 571: 669–681, 2006. doi:10.1113/jphysiol.2005.101691.
27. **Tanaka H**, **Seals DR.** Endurance exercise performance in Masters athletes: age-associated changes and underlying physiological mechanisms. *J Physiol* 586: 55–63, 2008. doi:10.1113/jphysiol.2007.141879.
28. **Mallory LA**, **Scheuermann BW**, **Hoelting BD**, **Weiss ML**, **McAllister RM**, **Barstow TJ.** Influence of peak VO2 and muscle fiber type on the efficiency of moderate exercise. *Med Sci Sports Exerc* 34: 1279–1287, 2002. doi:10.1097/00005768-200208000-00008.
29. **Leija RG**, **Tovar AP**, **Curl CC**, **Osmond AD**, **Arevalo JA**, **Duong JJ**, **Brooks GA.** Dysregulated mitochondrial respiration occurs with aging. *FASEB J* 36: 3510, 2022. doi:10.1096/fasebj.2022.36.S1.R3510.
30. **Liguori G**; **American College of Sports Medicine (ACSM).** *ACSM's Guidelines for Exercise Testing and Prescription* (11the ed.). Philadelphia, PA: Wolters Kluwer, 2022.
31. **Lusk G.** ANIMAL CALORIMETRY: Twenty-Fourth Paper. Analysis of the oxidation of mixtures of carbohydrate and fat. A correction. *J Biol Chem* 59: 41–42, 1924. doi:10.1016/S0021-9258(18)85293-0.
32. **Brooks GA**, **Gaesser GA**, **Poole DC.** Efficiency of cycling exercise: misunderstandings of physiology. *J Physiol* 602: 3233–3235, 2024. doi:10.1113/JP286770.
33. **Poole DC**, **Gaesser GA**, **Hogan MC**, **Knight DR**, **Wagner PD.** Pulmonary and leg VO2 during submaximal exercise: implications for muscular efficiency. *J Appl Physiol (1985)* 72: 805–810, 1992. doi:10.1152/jappl.1992.72.2.805.
34. **Friedlander AL**, **Jacobs KA**, **Fattor JA**, **Horning MA**, **Hagobian TA**, **Bauer TA**, **Wolfel EE**, **Brooks GA.** Contributions of working muscle to whole body lipid metabolism are altered by exercise intensity and training. *Am J Physiol Endocrinol Physiol* 292: E107–E116, 2007. doi:10.1152/ajpendo.00148.2006.



Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.

35. **Dube JJ**, **Broskey NT**, **Despines AA**, **Stefanovic-Racic M**, **Toledo FG**, **Goodpaster BH**, **Amati F.** Muscle characteristics and substrate energetics in lifelong endurance athletes. *Med Sci Sports Exerc* 48: 472–480, 2016. doi:10.1249/MSS.0000000000000789.
36. **Ettema G**, **Loras HW.** Efficiency in cycling: a review. *Eur J Appl Physiol* 106: 1–14, 2009. doi:10.1007/s00421-009-1008-7.
37. **Coyle EF**, **Sidossis LS**, **Horowitz JF**, **Beltz JD.** Cycling efficiency is related to the percentage of type I muscle fibers. *Med Sci Sports Exerc* 24: 782–788, 1992.
38. **Bell MP**, **Ferguson RA.** Interaction between muscle temperature and contraction velocity affects mechanical efficiency during moderate-intensity cycling exercise in young and older women. *J Appl Physiol (1985)* 107: 763–769, 2009. doi:10.1152/japplphysiol.91654.2008.
39. **Hopker JG**, **Coleman DA**, **Gregson HC**, **Jobson SA**, **Von der Haar T**, **Wiles J**, **Passfield L.** The influence of training status, age, and muscle fiber type on cycling efficiency and endurance performance. *J Appl Physiol (1985)* 115: 723–729, 2013. doi:10.1152/japplphysiol.00361.2013.
40. **Brisswalter J**, **Wu SS**, **Sultana F**, **Bernard T**, **Abbiss CR.** Age difference in efficiency of locomotion and maximal power output in well-trained triathletes. *Eur J Appl Physiol* 114: 2579–2586, 2014. doi:10.1007/s00421-014-2977-8.
41. **Berry MJ**, **Storsteen JA**, **Woodard CM.** Effects of body mass on exercise efficiency and VO2 during steady-state cycling. *Med Sci Sports Exerc* 25: 1031–1037, 1993.
42. **Amati F**, **Dubé JJ**, **Shay C**, **Goodpaster BH.** Separate and combined effects of exercise training and weight loss on exercise efficiency and substrate oxidation. *J Appl Physiol (1985)* 105: 825–831, 2008. doi:10.1152/japplphysiol.90384.2008.
43. **Leija RG**, **Curl CC**, **Arevalo JA**, **Osmond AD**, **Duong JJ**, **Huie MJ**, **Masharani U**, **Brooks GA.** Enteric and systemic postprandial lactate shuttle phases and dietary carbohydrate carbon flow in humans. *Nat Metab* 6: 670–677, 2024. doi:10.1038/s42255-024-00993-1.
44. **Bergman BC**, **Wolfel EE**, **Butterfield GE**, **Lopaschuk GD**, **Casazza GA**, **Horning MA**, **Brooks GA.** Active muscle and whole body lactate kinetics after endurance training in men. *J Appl Physiol (1985)* 87: 1684–1696, 1999. doi:10.1152/jappl.1999.87.5.1684.
45. **Donovan CM**, **Brooks GA.** Endurance training affects lactate clearance, not lactate production. *Am J Physiol Endocrinol Physiol* 244: E83–E92, 1983. doi:10.1152/ajpendo.1983.244.1.E83.
46. **Brooks GA**, **Donovan CM**, **White TP.** Estimation of anaerobic energy production and efficiency in rats during exercise. *J Appl Physiol Respir Environ Exerc Physiol* 56: 520–525, 1984. doi:10.1152/jappl.1984.56.2.520.



Downloaded from journals.physiology.org/journal/jappl by George Brooks (2600:1010:A021:BFA9:78F3:A4FD:0595:AF4C) on October 24, 2024.