Gender alters impact of hypobaric hypoxia on adductor pollicis muscle performance

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1Thermal and Mountain Medicine Division, United States Army Research Institute of Environmental Medicine, Natick, Massachusetts 01760; 2Veterans Affairs Medical Center and Stanford University, Palo Alto, California 94304; 3University of Colorado Health Sciences Center, Denver, Colorado 80262; and 4Sargent College of Health and Rehabilitation Sciences, Boston University, Boston, Massachusetts 02215

Received 28 November 2000; accepted in final form 12 February 2001

Fulco, Charles S., Paul B. Rock, Stephen R. Muza, Eric Lammi, Barry Braun, Allen Cymerman, Lorna G. Moore, and Steven F. Lewis. Gender alters impact of hypobaric hypoxia on adductor pollicis muscle performance. J Appl Physiol 91: 100–108, 2001.—Recently, we reported that, at similar voluntary force development during static submaximal intermittent contractile activation of the adductor pollicis muscle, fatigue developed more slowly in women than in men under conditions of normobaric normoxia (NN) (Acta Physiol Scand 167: 233–239, 1999). We postulated that the slower fatigue of women was due, in part, to a greater capacity for muscle oxidative phosphorylation. The present study examined whether a gender difference in adductor pollicis muscle performance also exists during acute exposure to hypobaric hypoxia (HH; 4,300-m altitude). Healthy young men (n = 12) and women (n = 21) performed repeated static contractions at 50% of maximal voluntary contraction (MVC) force of rested muscle for 5 s followed by 5 s of rest until exhaustion. MVC force was measured before and at the end of each minute of exercise and at exhaustion. Exhaustion was defined as an MVC force decline to 50% of that of rested muscle. For each gender, MVC force of rested muscle in HH was not significantly different from that in NN. MVC force tended to decline at a faster rate in HH than in NN for men but not for women. In both environments, MVC force declined faster (P < 0.01) for men than for women. For men, endurance time to exhaustion was shorter (P < 0.01) in HH than in NN [6.08 ± 0.7 vs. 8.00 ± 0.7 (SE) min]. However, for women, endurance time to exhaustion was similar (not significant) in HH (12.86 ± 1.2 min) and NN (13.95 ± 1.0 min). In both environments, endurance time to exhaustion was longer for women than for men (P < 0.01). Gender differences in the impact of HH on adductor pollicis muscle endurance persisted in a smaller number of men and women matched (n = 4 pairs) for MVC force of rested muscle and thus on submaximal absolute force and, by inference, ATP demand in both environments. In contrast to gender differences in the impact of HH on small-muscle (adductor pollicis) exercise performance, peak O2 uptake during large-muscle exercise was lower in HH than in NN by a similar (P > 0.05) percentage for men and women (-27.6 ± 2 and -25.1 ± 2%, respectively). Our findings are consistent with the postulate of a higher adductor pollicis muscle oxidative capacity in women than in men and imply that isolated performance of muscle with a higher oxidative capacity may be less impaired when the muscle is exposed to HH.

IN MEN AND WOMEN, ENDURANCE performance during large-muscle exercise (e.g., bicycle ergometer or treadmill) is markedly impaired by acute exposure to hypobaric and normobaric hypoxia (13). This impairment has been closely linked to a similar magnitude of reduction in maximal aerobic power for each gender (e.g., -25 to -30% at 4,300-m altitude) because of arterial hypoxemia (13). In men, under comparable hypoxic conditions, exercise utilizing smaller muscles [e.g., knee extensors (12) and adductor pollicis (11)] tends to be associated with prominent, although smaller degrees of, impairment of arterial oxygen saturation, peak oxygen uptake (V\(_{\text{O}2\text{ peak}}\)), and endurance performance. In contrast, less is known regarding the effects of hypoxia on small-muscle exercise performance in women.

We recently observed a slower development of fatigue, a longer endurance time to exhaustion, and a faster early recovery of an isolated small-muscle, the adductor pollicis, in women than in men associated with high-intensity, intermittent static contractions performed under normoxic conditions (14). Because the adductor pollicis muscle of men and women contains a uniformly high percentage of slow-twitch high-oxidative-capacity fibers (21, 33), our observations led us to postulate (14) that the superior muscle performance of women under exercise conditions involving complete motor unit recruitment (24, 29) was linked partly to a greater capacity for oxidative phosphorylation in the fast-twitch fibers of women’s adductor pollicis muscle. For a given ATP requirement during exercise, an iso-

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lated muscle that has a greater potential for oxidative phosphorylation, as reported for the vastus lateralis muscle of women compared with men (30, 37), is likely to be less reliant on anaerobic pathways and reactions that cause local metabolic conditions associated with impaired muscle contractile performance.

In the present study, we tested the hypothesis that voluntary performance during high-intensity, intermittent static contractions of the adductor pollicis muscle is less impaired during acute exposure to hypobaric hypoxia in women than in men. Our hypothesis was tested by comparing adductor pollicis muscle performance in men and women under conditions of normobaric normoxia and hypobaric hypoxia. The rationale for this hypothesis was based on findings that, taken together, imply that muscle with a higher oxidative capacity may more effectively regulate muscle oxidative phosphorylation under hypoxic conditions (2, 5, 7, 19).

In addition to the adductor pollicis muscle experiments, the present subjects also performed conventional large-muscle dynamic exercise to \( \dot{V}O_2 \) peak under the same environmental conditions. Comparison of small-muscle intermittent static exercise and large-muscle dynamic exercise under normobaric and hypobaric conditions allowed us to more closely link the adductor pollicis muscle performance findings with physiological conditions specific to this muscle group and its mode of exercise.

**METHODS**

**Subjects**

Twenty-one healthy women with normal menstrual cycles and no history of oral contraceptive use or pregnancy in the preceding year and 12 healthy men gave written informed consent before participating in the study. For the women, no statistically significant differences in adductor pollicis muscle performance were observed between their follicular and luteal menstrual cycle phases in normoxia or in hypobaric hypoxia (unpublished observations). Age, height, and weight (mean ± SE) were 22 ± 1 yr, 166 ± 1 cm, and 65 ± 2 kg for the women and 29 ± 1 yr, 180 ± 2 cm, and 80 ± 3 kg for the men. All male and female subjects were right-hand dominant.

In response to a questionnaire regarding participation in physical activity and sport, the 12 men reported exercising 23 ± 1 days/mo (range 16–28 days, median 24 days) in activities such as running, bicycling, football, soccer, kayaking, and volleyball. Similarly, the 21 women reported participating 19 ± 2 days/mo (range 4–28 days, median 24 days) in activities such as running, bicycling, walking, swimming, and badminton.

**Study Locations**

Women performed normobaric normoxia muscle testing at the Geriatric Research Education and Clinical Center of the Palo Alto Veterans Affairs Medical Center (Palo Alto, CA; altitude 30 m). Men performed normobaric normoxia testing at the US Army Research Institute of Environmental Medicine (Natick, MA; altitude 50 m). Women and men were tested under conditions of hypobaric hypoxia in a laboratory on the summit of Pikes Peak, CO (4,300-m altitude, 464 Torr). For both genders, testing in normoxia always preceded testing in hypoxia, with ≥2 wk between testing at each location. Subjects were transported via airplane and automobile to Pikes Peak from California or Massachusetts in <6 h. For all subjects, adductor pollicis muscle experiments were conducted within the first 24 h and \( \dot{V}O_2 \) peak tests within the 1st wk of altitude exposure. At both locations, for the adductor pollicis muscle experiments, the identical muscle apparatus, testing and calibration procedures, force transducer, and force feedback display were used by the same investigators. Ambient temperature was maintained in a comfortable range (20–23°C) at each location.

**General Experimental Design and Procedures**

**Adductor pollicis muscle testing.** To ensure familiarization with all equipment, personnel, and procedures and to learn to execute intermittent static contractions exclusively with the adductor pollicis muscle, subjects underwent at least one adductor pollicis muscle familiarization session before the definitive experiments. Familiarization sessions consisted of practicing repeated submaximal static contractions interspersed with periodic maximal contractions.

Definitive muscle fatigue experiments were performed using a device that permitted static contractions isolated to the adductor pollicis muscle (11, 27). The right hand and arm of the subject were secured in supination with the fingers flexed and thumb abducted. A force transducer (model SSM-250, Interface, Scottsdale, AZ; sensitivity 1.5 mV/kg) was attached by an inextensible link to a strap looped around the interphalangeal joint of the right thumb. The force transducer was interfaced with an amplifier (model 13-421202, Gould, Cleveland, OH; 90% response time in 2 ms), chart recorder (model 2200, Gould), and oscilloscope. Subjects had visual contact with the oscilloscope tracings at all times to provide them with feedback for maintaining the correct force during submaximal contractions.

After the subject was seated and the hand and thumb were properly oriented and secured, three 5-s baseline maximal voluntary contractions (MVCs) were performed. There was a 1-min rest between each MVC. For each subject, the highest MVC force attained (MVC force of rested muscle, i.e., strength) was used to set the target force of submaximal contractions.

After an additional 1-min rest, exercise was initiated with an MVC, the subjects rested for 5 s, and then the first submaximal contraction was performed. Submaximal exercise consisted of intermittent, 5-s static muscle contractions at a target force of 50% of rested MVC force followed by 5 s of rest (i.e., duty cycle 0.5). At the end of every minute (i.e., every 6th contraction), an MVC was performed for the full 5 s instead of the 50% MVC force contraction. An investigator timing the events verbally instructed the subjects to start and stop each submaximal and maximal contraction. During each maximal or submaximal contraction, subjects were required to increase muscle force (in N) as rapidly as possible to the maximal or target level, respectively. When MVC force fell to or below target or the target force could not be maintained for 5 s, the subjects were considered exhausted and were instructed to stop the submaximal contractions. An MVC was performed immediately on reaching exhaustion. Endurance time to exhaustion was calculated as the time from the start of the MVC of rested muscle immediately preceding the first submaximal contraction to the end of the MVC performed at the point of exhaustion. Figure 1 illustrates the study protocol and specific measurements obtained. For the women, arterial oxygen saturation was con-
Adductor Pollicis Muscle Force Exerted During Submaximal Exercise

The percentage of rested MVC force used during submaximal adductor pollicis muscle exercise was similar (both \( P = NS \)) in normoxia and hypoxia for men (51.9 ± 1 and 51.0 ± 1\%), respectively) and women (52.3 ± 1 and 53.0 ± 1\%, respectively). In each environment, the percentage of rested MVC force used during submaximal adductor pollicis muscle exercise was similar \( (P = NS) \) for men and women. Absolute force developed during submaximal adductor pollicis muscle exercise was similar (both \( P = NS \)) in normoxia and hypoxia for men (74 ± 2 and 77 ± 2 N, respectively) and women (58 ± 3 and 61 ± 3 N, respectively). In contrast, absolute force developed during submaximal exercise was greater for men than for women in normoxia and hypoxia (both \( P < 0.01 \)).

Adductor Pollicis Muscle Fatigue Rate

Overall muscle fatigue rate tended to be faster in hypoxia than in normoxia for men (−13 ± 2 vs. −8 ± 3 N, respectively) and women (−10 ± 2 vs. −5 ± 1 N, respectively). The rate of force decline in MVC was similar (both \( P = NS \)) in normoxia and hypoxia for men (66 ± 6 and 67 ± 6\%, respectively) and women (58 ± 5 and 59 ± 5\%, respectively). In contrast, the rate of MVC force decline was greater for men than for women in normoxia and hypoxia (both \( P < 0.01 \)).

Data analyses. For each subject, in each environment, overall muscle fatigue rate was calculated from the slope of individual linear regression analysis of the fall in MVC force (in N) relative to exercise time (in min). Mean slopes (fatigue rates) were calculated for each gender in each environment. For each gender, paired t-tests were used to identify normoxia vs. hypoxia differences in MVC force of rested muscle, absolute force developed during submaximal exercise, muscle fatigue rate (in N/min), endurance time to exhaustion, MVC force at exhaustion, and \( \dot{V}O_2 \) peak. For each of these dependent variables, differences between genders in each environment were determined using independent t-tests for unequal variances. For these within- and between-gender comparisons, the Bonferroni adjustment procedure was used to correct for potential type 1 errors due to multiple t-tests. \( P < 0.0125 \) was therefore accepted as statistically significant after these adjustments were made. Three-way ANOVAs (environment × exercise time × gender) with repeated measures on two factors (environment and exercise time) were used to identify gender differences in MVC force during exercise (i.e., percent decline in the first 3 min of exercise). If an ANOVA identified a significant \( F \) value, Tukey’s multiple-comparison procedure was used to detect statistical significance of specific differences. For the analyses based on the ANOVAs, a difference of \( P < 0.05 \) was accepted as statistically significant. Values are means ± SE or individual values.

RESULTS

MVC Force of Rested Muscle

MVC force of rested adductor pollicis muscle was similar in normoxia and hypoxia for men \( [143 ± 5 \text{ and } 152 ± 4 \text{ N}] \), respectively, \( P = \text{not significant} \ (NS) \) and women \( [111 ± 4 \text{ and } 115 ± 5 \text{ N}] \), respectively, \( P = NS \). In normoxia and hypoxia, MVC force of rested muscle was greater for men than for women \( (P < 0.01) \).

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2 N/min, respectively, \( P < 0.05 \) but not for women (\(-5 \pm 1\) vs. \(-4 \pm 1\) N/min, respectively, \( P = \text{NS} \)). Overall fatigue rate for men was 2-fold faster in normoxia (\(-8 \pm 2\) vs. \(-4 \pm 1\) N/min, respectively, \( P < 0.01 \)) and 2.5-fold faster in hypoxia (\(-13 \pm 2\) vs. \(-5 \pm 1\) N/min, respectively, \( P < 0.01 \)) for men than for women.

**First Three Minutes of Exercise**

For each gender, the decline of MVC force from rest to the end of minute 3 of adductor pollicis muscle exercise was similar (\( P = \text{NS} \)) in normoxia and hypoxia (Fig. 2). By the end of minute 1 of exercise, MVC force had, from rest (i.e., 100% MVC), fallen nearly threefold more for men than for women in normoxia (\(-21 \pm 2\) vs. \(-6 \pm 1\%), \( P < 0.01 \)) and hypoxia (\(-23 \pm 3\) vs. \(-8 \pm 1\%), \( P < 0.01 \)). During the next 2 min of exercise in each environment, MVC force continued to decline for both genders. By the end of minute 3 of exercise in each environment, the difference between women and men in MVC force, expressed as a percentage of MVC force of rested muscle, remained similar to that at the end of minute 1.

**Progression Toward Exhaustion**

Percentages of men and women remaining (i.e., those not reaching exhaustion) after each minute for the first 12 min of exercise in normoxia and hypoxia are shown in Fig. 3. In normoxia, all men were able to exercise for \( \geq 4 \) min. However, the percentage of men remaining each minute declined steadily from minute 4 to minute 12. After minute 12 of normoxic exercise, 100% of the men had reached their point of exhaustion. In hypoxia, the percentage of men remaining at each minute between minute 4 and minute 10 was 8–50% (median 25%) lower than in normoxia.

In contrast to men in normoxia, all women in normoxia were able to exercise for \( \geq 8 \) min, and 57% of women remained by minute 12. The percentage of women remaining each minute declined progressively, but sharply higher percentages of women than men remained exercising beyond minute 4. Moreover, in direct contrast to the much faster rate of dropout during hypoxic than normoxic exercise in men, the percentage of women remaining after each minute of exercise tended to be similar in hypoxia and normoxia when the progression toward exhaustion in hypoxia was compared with that in normoxia, the percentage of women remaining at each minute between minute 4 and minute 10 was only 0–23% (median 9%) lower in hypoxia.

**Adductor Pollicis Muscle Endurance Time to Exhaustion**

For men, endurance time to exhaustion was shorter (\( P < 0.01 \)) in hypoxia (6.08 \( \pm 0.7 \) min) than in normoxia (8.00 \( \pm 0.7 \) min); for women, endurance time was similar (\( P = \text{NS} \)) in both environments (12.86 \( \pm 1.2 \) min in hypoxia vs. 13.95 \( \pm 1.0 \) min in normoxia). Endurance time to exhaustion was longer (\( P < 0.01 \)) for women than for men in normoxia and hypoxia (Fig. 4).

**MVC Force at Exhaustion**

At exhaustion, MVC force had fallen to a similar (\( P = \text{NS} \)) percentage of MVC force of rested muscle in normoxia and hypoxia for men (55 \( \pm 1 \) and 53 \( \pm 2\% \), respectively) and women (53 \( \pm 1 \) and 55 \( \pm 1\% \), respectively). In addition, MVC force fell to a similar (\( P = \text{NS} \)) percentage of MVC force of rested muscle at the point of exhaustion for men and women in normoxia and hypoxia.

**Arterial Oxygen Saturation During Adductor Pollicis Muscle Exercise**

In normoxia, women’s arterial oxygen saturation was 97 \( \pm 1\% \) at rest and remained about the same (i.e., \( \pm 1\% \)) over the duration of adductor pollicis muscle exercise and recovery. In hypobaric hypoxia, women’s arterial oxygen saturation was 85 \( \pm 1\% \) during seated rest and rose to 88 \( \pm 1\% \) at exhaustion from adductor pollicis muscle exercise (\( P < 0.05 \)). During rest and exercise, women’s arterial oxygen...
saturation was lower in hypobaric hypoxia than in normoxia ($P < 0.01$).

$\text{VO}_2$ \text{peak}

For each gender, $\text{VO}_2$ \text{peak} was lower ($P < 0.01$) in hypobaric hypoxia than in normoxia. $\text{VO}_2$ \text{peak} declined by a similar percentage ($P = \text{NS}$) from normoxic to hypobaric hypoxic conditions for men (from $56.5 \pm 1$ to $40.7 \pm 1$ ml·kg$^{-1}$·min$^{-1}$, i.e., $-27.6 \pm 2\%$) and women (from $40.4 \pm 1$ to $30.1$ ml·kg$^{-1}$·min$^{-1}$, i.e., $-25.1 \pm 2\%$).

Gender Pairs Matched for MVC Force

To examine whether the gender difference in the impact of hypobaria on adductor pollicis muscle performance was related to a lower muscle energy demand for women, we matched, after completion of muscle testing, an equal number ($n = 4$) of women and men as closely as possible for MVC force of rested muscle in normoxic and hypoxic conditions. Matching was accomplished by ranking and comparing the results for each gender in normoxia and hypoxia and then progressively discarding data for some women and men until mean MVC force did not differ ($P = \text{NS}$) within and between genders for both environments. As a result of matching on MVC force of rested muscle, the submaximal contraction forces produced in normoxic and hypoxic conditions by the men were $74 \pm 3$ and $76 \pm 1$ N, respectively, and those produced by the women were $73 \pm 4$ and $76 \pm 8$ N, respectively. Our matching procedure
therefore enabled men and women to be compared at similar (P = NS) absolute submaximal contraction forces and, by inference, similar muscle ATP demand, in normoxia and hypoxia.

At a similar absolute submaximal contraction force, these men were unable to maintain MVC force as well as women (P < 0.01) at the end of minute 1 of exercise in normoxia (84 ± 3 vs. 95 ± 2% MVC force of rested muscle, respectively) and hypoxia (77 ± 4 vs. 92 ± 4% MVC force of rested muscle, respectively; Fig. 5A). During the next 2 min of exercise in each environment, MVC force continued to decline for both genders. By the end of minute 3 of exercise, MVC force relative to that of rested muscle fell in normoxia to 74 ± 1% for men and 82 ± 3% for women and in hypoxia to 64 ± 8% for men and 82 ± 3% for women [genders tended to differ (P < 0.05) in both environments]. The women also tended to have longer muscle endurance times than men (P < 0.05) in normoxia (11.00 ± 2 vs. 8.00 ± 1 min) and hypoxia (12.50 ± 3 vs. 5.50 ± 1 min; Fig. 5B). In addition, for men, endurance times to exhaustion tended to be shorter (P < 0.05) in hypoxia (5.50 ± 1 min) than in normoxia (8.00 ± 1 min), but for women endurance times were similar (P = NS) in both environments (12.50 ± 3 and 11.00 ± 2 min in hypoxia and normoxia, respectively).

**DISCUSSION**

Our major finding confirmed the hypothesis that voluntary performance during intermittent static contractions of the adductor pollicis muscle is less impaired during acute exposure to hypobaric hypoxia in women than in men. Moreover, under hypoxic conditions, women did not display the increase in overall fatigue rate and decrease in endurance time to exhaustion found in men. To our knowledge, this finding represents the first direct demonstration of a gender difference in the impact of hypoxia on human muscle performance. In contrast to our adductor pollicis muscle observations, for large-muscle exercise in hypoxia, each gender demonstrated a similar degree of decline of \( \dot{V}O_2 \) peak from normoxic values. In this discussion, we identify the most likely reasons for the distinct gender difference in the effect of hypoxia on performance during adductor pollicis muscle exercise, explain the physiological significance of this observation, and distinguish our adduc-

![Fig. 4. Adductor pollicis muscle endurance time to exhaustion for men and women in normoxia and hypoxia. For each environment, women had a significantly longer endurances time than men (P < 0.01). Endurance time was reduced for men (P < 0.01) but not for women (P = NS) in hypoxia compared with normoxia.](image)

**Fig. 5.** A: adductor pollicis muscle MVC force, expressed as percent MVC force of rested muscle, after minute 1 of submaximal adductor pollicis muscle contractions in each of the 4 pairs of men and women matched for MVC force of rested muscle in normoxia and hypoxia. Each woman maintained a higher percentage of MVC force than each man under normoxic and hypoxic conditions. B: adductor pollicis muscle endurance time to exhaustion in each of the 4 pairs of men and women matched for MVC force of rested muscle in normoxia and hypoxia. For each environment, women had a longer endurance time than each man. Alphanumeric characters represent the 4 male-female pairs matched on MVC force of rested adductor pollicis muscle: N, normoxia; H, hypoxia; 1–4, numbers of the matched pairs. Male-female pairs are compared with a line of identity (diagonal line).
tor pollicis muscle findings from those of more conventional large-muscle effort.

Our specific exercise protocol and the unique characteristics of the adductor pollicis muscle likely contributed to the present findings. The protocol involved static contractions performed at 50% of MVC force in a 5-s activity-5-s recovery duty cycle. This type of exercise is fueled largely by muscle high-energy phosphate breakdown during contractions and resynthesis of high-energy phosphates by oxidative phosphorylation during recovery (6, 41). In men and women, the adductor pollicis muscle contains a uniformly high percentage (~80%) of slow-twitch, high-oxidative-capacity fibers (21, 33). In addition, during adductor pollicis muscle contractions at 50% of MVC force, virtually all motor units are recruited (24, 29), and the rapid and repeated generation of this force in the present protocol likely augmented the need for fast-twitch fiber recruitment (10, 18). Our finding of a markedly slower development of adductor pollicis muscle fatigue for women than for men after only 1 min of exercise under normoxic conditions is supported by earlier observations (14) and is postulated to be linked with a greater capacity for oxidative phosphorylation in the fast-twitch fibers of the adductor pollicis muscle of women. A greater fast-twitch fiber oxidative capacity would promote more rapid resynthesis of muscle high-energy phosphate between contractions and result in more complete removal of products of high-energy phosphate breakdown such as P_i and ADP, accumulations of which have been associated with impaired muscle performance (3, 35).

Our finding of a similar adductor pollicis muscle performance for women in hypoxia and normoxia is consistent with the hypothesis of a relatively high oxidative capacity in the fast-twitch fibers of the adductor pollicis muscle of women. When compared in hypoxia vs. normoxia, each gender performed adductor pollicis muscle contractions at a similar absolute force and thus a similar absolute muscle ATP requirement. Muscle with increased mitochondrial content can produce a given amount of ATP via oxidative phosphorylation with reduced concentrations of key metabolic regulators, e.g., ADP (5) or substrate (19). A prominent theory for control of oxidative phosphorylation in active muscle holds that regulation may be exerted via interaction between the muscle phosphorylation potential ([ATP]/[ADP][P_i]), where [ATP], [ADP], and [P_i] are concentrations of ATP, ADP, and P_i, respectively), the mitochondrial redox state ([NADH]/[NAD^+]'), where [NADH] and [NAD^+] are concentrations of NADH and NAD^+), and effectors of cytochrome oxidase such as oxygen (7). In this control scheme, the relative impact of [ATP]/[ADP][P_i], [NADH]/[NAD^+]'), and oxygen depends on specific metabolic conditions prevailing in active muscle. Under hypoxic conditions, changes in [ATP]/[ADP][P_i] and [NADH]/[NAD^+] can, within limits, compensate for decreased PO_2, leaving ATP flux constant (2). The present finding of a lack of effect of hypoxia on women's adductor pollicis muscle performance supports the hypothesis that muscle with a greater intrinsic oxidative capacity has a greater ability to sustain a given rate of ATP production via oxidative phosphorylation with smaller compensatory changes in [ATP]/[ADP][P_i] and [NADH]/[NAD^+]. This property would reduce activation of anaerobic pathways and reactions that lead to metabolic conditions associated with accelerated muscle fatigue under hypoxic conditions.

In normoxia and hypoxia, mean MVC force of rested adductor pollicis muscle for the group of 12 men was ~30% higher than that for the group of 21 women. Correspondingly, during submaximal contractions performed at 50% of individual MVC force, absolute force developed, and, by inference, muscle ATP demand averaged ~26–28% higher for men than for women in normoxia and hypoxia. To examine whether the gender difference in the impact of hypoxia on adductor pollicis muscle performance was related to a lower muscle energy demand for women, we matched as many men and women as possible (n = 4 pairs) with respect to MVC force of rested muscle and, therefore, on absolute force development during each submaximal contraction in normoxia and hypoxia. Our observations of muscle performance for women that was superior to that for men in normoxia and hypoxia under conditions of matched force and, likely, similar muscle ATP demand support the hypothesis that, compared with men, the adductor pollicis muscle of women can, during exposure to hypoxia, more effectively regulate oxidative phosphorylation and, thereby, lessen muscle metabolic conditions associated with fatigue.

In addition to local factors in active muscle, neural processes that may contribute to fatigue development (15) could differ between women and men (36). Neural factors that could affect the present findings of slower fatigue development in women than in men in normoxia and hypoxia may relate to a potential female-male difference in central motor drive, neuromuscular propagation, and/or a fall in neural excitation of muscle of reflex origin. There is, however, little or no published evidence supporting a major role for the first two factors under the present experimental conditions. Almost 50 years ago, Merton (27) reported that, for adductor pollicis muscle, voluntary activation could account for virtually all force production in fresh and fatigued muscle. Using more sensitive techniques, Herbert and Gandevia (20) recently observed that voluntary activation could explain ~90% of voluntary force production in adductor pollicis muscle with no difference between genders. For adductor pollicis (11) and other muscle groups (1, 12, 17, 42), there is little or no evidence for impairment of central motor drive due to hypoxic conditions similar to those of the present study. In addition, virtually no published data link moderate or severe hypoxia (17) or gender with impaired neuromuscular propagation.

Activation of metabolically sensitive group III and IV afferent nerve endings in fatigued muscles has been implicated in a reflex decline in motoneuron discharge to active muscle (16) via reduction of motor drive in the central nervous system (15) or spinal cord (31). A reflex
increase in sympathetic nerve activity to inactive muscle is a prominent manifestation of group III and IV metaboreflex activity (40). Accumulation of metabolites such as H\(^+\), P\(_i\), and H\(_2\)PO\(_4\) in active muscle has been linked with impaired force generation (3, 28, 35), excitation of group III and IV muscle afferents (16), and reflex increases in sympathetic nerve activity (26, 39, 40). Moreover, there is published evidence that 1) accumulation of these metabolites and reflex increases in sympathetic nerve activity are reduced by interventions to increase muscle oxidative capacity (5, 22, 38) and 2) during adductor pollicis muscle exercise, reflex increases in muscle sympathetic nerve activity are smaller in women than in men (8). The above findings therefore support the hypothesis that a better voluntary performance of the adductor pollicis muscle for women than for men under normoxic and hypobaric conditions is linked with a greater oxidative capacity of this muscle, which results in more slowly developing direct, intramuscular fatigue and a related decline in reflex impairment of muscle excitation.

Earlier findings (13) support our observation of similar percent declines from normoxic values in peak cycle ergometer or treadmill oxygen uptake in women and men. Thus the present finding of a gender difference in the effect of hypobaria on adductor pollicis muscle but not larger muscle performance in the same subjects would appear inconsistent. This potential discrepancy can be resolved by considering salient features of 1) systemic and local muscle oxygen transport in hypobaria and 2) the comparative energetics of large-muscle dynamic exercise vs. intermittent static contractions of the adductor pollicis muscle. These factors likely combine to create distinctly different local muscle metabolic states for the two exercise modes in similar hypobaric environments. In peak large-muscle dynamic exercise at 464 Torr, a high cardiac output and commensurately short pulmonary capillary red cell transit time (4) typically result in a 4–8% drop from resting values in arterial oxygen saturation (23) that aggravates the existing hypoxemia. In contrast, the small increase over resting values in arterial oxygen saturation we observed for hypobaric adductor pollicis muscle exercise in women is similar to previous small-muscle exercise findings under comparable hypobaric hypoxia conditions in men (12) and appears linked, in part, with only a minor increase in cardiac output typical for exercise engaging a small-muscle mass (25). For peak cycle or treadmill exercise, the local effect of the greater systemic hypoxemia (i.e., smaller muscle capillary-mitochondrial PO\(_2\) gradient) would be exacerbated by high muscle blood flow (34) and relatively brief muscle capillary red cell transit time associated with a combination of very high energy demand (9) and short recovery periods for oxidative resynthesis of ATP (9, 32) during rapidly repeated high-intensity dynamic contractions. By comparison, the lower ATP demand (9) and the duty cycle (i.e., 5 s of work–5 s of rest) of the static contractions performed in the adductor pollicis muscle exercise protocol may have provided optimal conditions for expression of an intrinsic gender difference in the effect of hypoxia on muscle fatigability.

In summary, adductor pollicis muscle performance during high-intensity, intermittent static contractions is less impaired in women than in men during acute exposure to hypobaric hypoxia. This finding contrasts with that of similar declines in VO\(_2\) peak during large-muscle dynamic exercise for both genders under hypoxic conditions. Unique properties of the adductor pollicis muscle that include, for both genders, a high percentage of slow-twitch high oxidative fibers and complete motor unit recruitment at the target force used and findings of a much smaller force loss for women than men after only 1 min of exercise in normoxia and hypoxia suggest that the superior muscle performance of women relates to a greater capacity for oxidative phosphorylation in their fast-twitch fibers. A greater fast-twitch fiber oxidative capacity would promote more rapid resynthesis of muscle high-energy phosphates between intense muscle contractions and faster removal of products of high-energy phosphate breakdown that have been linked with impaired muscle performance.

We are extremely grateful to Ken W. Kambis, John T. Reeves, Beth Beidleman, Stacy Zamudio, and George A. Brooks, whose hard work and dedication allowed this project to proceed smoothly, and to all of our outstanding volunteers. Most of all, we are grateful to the late Gail Butterfield, who will always be remembered for her limitless dedication, enthusiasm, and good nature.

The work presented here was partly supported by Defense Women's Health Research Program Grant DI950050, awarded to the US Army Research Institute of Environmental Medicine, titled “Effect of Menstrual Cycle Phase on Muscle Fatigue and Physical Performance During Altitude Acclimatization,” and Defense Women's Health Research Program Grant DAM7-94-BA0, awarded to the University of Colorado Health Sciences Center, titled “Women at Altitude: Effects of Menstrual Cycle Phase on High-Altitude Acclimatization.” The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official position of the Army position, policy, or decision unless so designated by other documentation.

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to US Army Regulation 70-25 and US Army Medical Research Materials Command Regulation 70-25 on the use of volunteers in research.

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