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Absence of Work Efficiency Differences During Cycle Ergometry Exercise in Bolivian Aymara

TOM D. BRUTSAERT,[1,2] JERE D. HAAS,[2] and HILDE SPIELVOGEL[3]

ABSTRACT

Brutsaert, Tom D., Jere D. Haas, Hilde Spielvogel. Absence of work efficiency differences during cycle ergometry exercise in Bolivian Aymara. *High Alt. Med. Biol.* 5:41–59, 2004.—This study tested the hypothesis that Andean natives are adapted to high altitude (HA) via high work efficiency during exercise in hypoxia. A total of 186 young males and females were tested in Bolivia, comprising eight different subject groups. Groups were identified based on gender, ancestry (Aymara vs. European), altitude of birth (highlands vs. lowlands), and the altitude where tested (420, 3600, 3850 m). This design allows partitioning of ancestral (i.e., genetic) and developmental effects. To minimize measurement error, subjects were given two submaximal exercise tests on a cycle ergometer (on separate days). Each test consisted of four 5-min work bouts (levels), each separated by a 5-min rest period. For all groups, the oxygen consumption (V_{O_2})–work rate relationship was not different from the sea-level reference. Gross and net efficiencies (GE and NE) were not different between groups at any work level, with the exception of European men born in the lowlands and acclimatized and tested at 3600 m. These men showed slightly lower V_{O_2} at high work output, but this may be due to a nonsteady-state V_{O_2} kinetic, rather than to an altered steady-state V_{O_2}–work rate relationship per se. There were no significant group differences in delta efficiency (DE). In sum, these results provide no support for the hypothesis of energetic advantage during submaximal work in Andean HA natives. A review and analysis of the literature suggest that the same is true for HA natives in the Himalayas.

Key Words: Andes; hypoxia; altitude; energetic efficiency; adaptation; Himalayas

INTRODUCTION

In his pioneering studies of Peruvian Quechua, Alberto Hurtado was the first to suggest that natives of high altitude (HA) enjoy an energetic advantage via high work efficiency during exercise in hypoxia (Hurtado, 1932, 1964). In fact, Hurtado considered high work efficiency as "one of the most important characteristics of the native residents and possibly the best index of their acclimatization" (Hurtado, 1964). His studies document moderately higher net efficiency [external work output/(metabolic work input − resting metabolic energy expenditure)] in highland residents of Morococha, Peru (4540 m), versus Lima, Peru (sea level), during treadmill running. However, the subsequent literature is conflicted on this funda-

[1]Department of Anthropology, The University at Albany, SUNY, Albany, NY.
[2]Division of Nutritional Sciences, Cornell University, Ithaca, NY.
[3]Instituto Boliviano de Biología de Altura, La Paz, Bolivia.

mental issue. In support of Hurtado's hypothesis, some studies report higher work efficiency in Andean natives versus lowland controls when both groups are tested at altitude (Reynafarje and Velasquez, 1966; Haas et al., 1983; Hochachka et al., 1991). In contrast, other studies show no efficiency differences (Mazess, 1969a, 1969b; Favier et al., 1995), or lower efficiency (Kollias et al., 1968) between Andean highland and lowland controls. Studies conducted in other parts of the world are similarly conflicted. In the Himalayas, a number of studies report no efficiency differences (Lahiri and Milledge, 1966; Lahiri et al., 1967; Kayser et al., 1994), while at least two studies report significantly higher efficiency in Tibetans versus lowland controls (Ge et al., 1994; Niu et al., 1995). In North America, early studies in Colorado reported no differences in work efficiency related to acclimatization state or growth and development at altitude (Dill et al., 1931; Balke, 1964; Grover et al., 1967).

Of the studies above, the work of Hochachka et al. (1991) is often cited. These authors report 1.5 to 2-fold higher work efficiencies in Peruvian Quechua compared to lowland controls when both groups were tested in hypoxia and normoxia at sea level on a cycle ergometer. The study was noteworthy because it provided a plausible evolutionary–metabolic framework from which to consider hypotheses of energetic advantage in highland natives. According to Hochachka et al., many hypoxia-tolerant species display a general adaptive (evolutionary) strategy that minimizes the cost (or maximizes the efficiency) of cellular and metabolic work functions in an oxygen-limiting environment. In principle, this can be achieved by (1) maximizing the moles of ATP obtained per mole of fuel substrate metabolized, (2) maximizing the moles of ATP obtained per mole of O_2 consumed, and (3) maximizing work achieved per mole of ATP utilized. In hypothesis 1, aerobic pathways should be favored over anaerobic pathways. In hypothesis 2, carbohydrate oxidation should be favored over fat oxidation as lipids are more highly reduced and thus require more O_2 per mole of ATP obtained. In hypothesis 3, work efficiency, defined as the ratio of external power output (work) to metabolic power input (i.e., energy expenditure, EE), should be maximized.

However, because hypotheses 1 through 3 above are difficult to test noninvasively, a number of important points should be emphasized, particularly with respect to hypothesis 3 (increased work efficiency), which is the focus of this paper. First, metabolic EE is almost always measured indirectly via the consumption of oxygen (V_{O_2}). Because V_{O_2} measures are affected by changes in both metabolic pathways and fuel substrates, hypothesis 3 cannot be evaluated independently of hypotheses 1 and 2. For example, an increased reliance on oxidative pathways (hypothesis 1) should result in an increase in the measured V_{O_2} and thus will have the effect of *decreasing* work efficiency. Second, work efficiency measures are ratio constructs that derive from the linear relationship of metabolic EE to external work. This relationship does not pass through the origin (zero), and the calculated work efficiencies that result are therefore a nonlinear function of absolute work output. This fact makes quantitative efficiency differences between groups very difficult to interpret, particularly at relatively low power outputs in the 30- to 100-W range. Similarly, at low power output, small measurement errors, particularly in external work, will result in large work efficiency errors. The latter is certainly a concern for treadmill exercise, where large measurement error in external work is expected, but it is also a concern for cycle ergometry; as many ergometers are poorly calibrated, often in error by more than 40% (Van Praagh et al., 1992). A final consideration is that the framework of Hochachka et al. is evolutionary and thus places little explicit emphasis on the possibility that efficiency measures show phenotypic plasticity.

The present study was designed to address hypothesis 3. The approach was to measure external work and V_{O_2} during a series of submaximal workloads on a cycle ergometer. To minimize measurement error, a lengthy protocol was applied twice on separate days to each of 186 young subjects from Bolivia who comprised eight distinct subject groups distinguished by sex, ethnicity (Aymara vs. European), place of birth (highlands vs. lowlands), and testing environment (3850, 3600, 420 m).

The factoral study design is important because it allows for the comparison of different ethnic groups who were born and raised in *similar* environments. Such comparisons provide a means of testing the hypothesis of evolutionary adaptation on the work efficiency phenotype. Additionally, the comparison of similar ethnic groups born and raised in *different* environments allows evaluation of phenotypic plasticity relative to work efficiency.

MATERIALS AND METHODS

Subjects and study design

Nonsmoking males and females between the ages of 17 and 35 yr were recruited. All subjects were screened by a physician to determine that they were in good health, and all subjects gave consent after being informed of the risks and benefits associated with the study. The study protocol was approved by the Cornell University Human Subjects Committee and the Human Subjects Committee of the Instituto Boliviano de Biología de Altura (IBBA), in La Paz, Bolivia.

There were three major distinctions between study groups: ethnicity (Aymara Amerindian vs. European ancestry), place of birth (highlands vs. lowlands), and testing altitude. In addition, some participants (groups) can be distinguished on migration and acclimatization status. If Aymara and European groups are native to the highlands and lowlands, respectively, then migrant individuals are those born and raised in a nonnative environment. Acclimatization status is defined relative to HA and is used to describe lowland-born individuals with more than two continuous months at HA (acclimatized) or highland-born individuals with more than two continuous months in the lowlands (deacclimatized). The groups studied are described in the following.

Groups 1 and 2. Aymara, born and raised at HA, tested at 3850 m (group 1, males, $n = 25$; group 2, females, $n = 25$). These subjects were Aymara speakers living in a rural village (3850 m) about 10 miles from the southern shore of Lake Titicaca. A village health post (hospital) was used to set up a centrally located exercise testing laboratory. Participants were subsistence farmers descended from Amerindian groups that may have had a ~10,000-year history in the high Andes (Cardich, 1994). Historic and genetic data make clear that such populations have experienced admixture with European populations since Spanish times (Chakraborty et al., 1989). The extent of admixture in this sample is unknown, but another study by our group suggests that admixture levels can be held relatively low if subjects self-identify as Amerindian and are recruited from rural regions. Using genetic markers, a global admixture rate of about 2% Spanish ancestry was calculated in 39 male, rural, highland-born Peruvians recruited for an exercise study near Cerro de Pasco, Peru (4338 m) (Brutsaert et al., 2003). No subject in that sample showed an individual European admixture proportion greater than 10%. While the histories of the Quechua and Aymara ethnic groups in the Andes may be different relative to the Spanish conquest, there is no reason to expect substantial admixture differences between these two groups.

Group 3. European migrants, born and raised at HA, tested at 3600 m (males, $n = 22$). These subjects came from established migrant communities in La Paz, Bolivia (3600 m), and were tested in the Bioenergetics Laboratory of the IBBA. While some participants were the children or grandchildren of recent European migrants, the majority could trace at least one ancestral line back to Spanish migrants who arrived in Bolivia more than three generations ago. Family history interviews were used to establish no admixture with Amerindian populations, although it is likely that at least some admixture is present in the sample. As a nongenetic indicator of population admixture, four surnames, reflecting grand-parental generations, were obtained from each subject (Chakraborty et al., 1989; Greksa, 1992). No subject in this group had a surname of either Aymara or Quechua origin.

Groups 4 and 5. Acclimatized Europeans, born and raised at LA, tested at 3600 m (group 4, males, $n = 27$; group 5, females, $n = 12$). These subjects were expatriate European and North American professionals, born and raised at low altitude and living and working in the city of La Paz. These subjects were also tested at the IBBA. Participants were studied after at least 2 months of acclimatization to high altitude, sufficient for full ventilatory, renal, and hematological acclimatization (Huang et al., 1984).

Group 6. Deacclimatized Aymara, born and raised at HA, tested at 420 m (males, n = 25). These subjects came from established migrant communities in Santa Cruz, Bolivia (420 m). Participants were originally residents of the Bolivian highlands, similar to group 1, but had migrated to the lowlands as adults, after 18 yr of age. Most migrated for professional reasons or in search of work. Study inclusion criteria specified a deacclimatization period to the lowlands of at least 2 months before entry into the study. These subjects, and all other subject groups tested in the lowlands, were tested at the Centro de Enfermedades Tropicales (CENETROP) in Santa Cruz, Bolivia.

Group 7. Europeans, born and raised at LA, tested at 420 m (males, n = 25). These subjects were upper-class Brazilians of European ancestry who were attending medical school in Santa Cruz, Bolivia (420 m). Although ethnically different from the Europeans studied at high altitude, this subject group represented a lowland control group that was similar in body size and composition, as well as socioeconomic status, to the acclimatized Europeans tested at altitude (group 3).

Group 8. Aymara migrants, born and raised in the lowlands, tested at 420 m (males, n = 25). These subjects came from established migrant communities in Santa Cruz. Participants were the children or grandchildren of highlanders who migrated to the Bolivian lowlands. All were born and raised in the city of Santa Cruz and had never been to high altitude.

ANTHROPOMETRY

Standard anthropometry was performed on each subject by the same investigator. Measurements included height, weight, and skinfolds at subscapular, suprailiac, biceps, and triceps sites. Body density was calculated according to age and sex-specific equations published by Durnin and Womersley (1974). Kashiwazaki et al. (Kashiwazaki et al., 1998) have tested the validity of a number of reference equations against doubly labeled water measures of body composition in Bolivian Aymara and conclude that these reference equations are the best available for use in Andean native populations. Percent body fat was calculated from the Siri equation. Hemoglobin concentration [Hb] was measured by a photometric method using a Hemocue blood hemoglobin analyzer from capillary blood obtained by finger prick (Hemocue, Angelholm, Sweden). The Hemocue was calibrated according to specifications given by the manufacturer.

Exercise testing

All subjects in all locations were tested using the same equipment. Aymara subjects at altitude were tested in a rural village setting (mean barometric pressure 471 mmHg, mean laboratory temperature 17°C). European subjects at HA were tested at the IBBA (mean barometric pressure 499 mmHg, mean laboratory temperature 19°C). Lowland subjects were tested at the CENETROP (mean barometric pressure 725 mmHg, mean temperature 27°C).

Subjects were tested on the mechanically braked cycle ergometer described by Van Praagh et al. (1992). External work on this ergometer is incremented by the addition of weights to a balance arm attached to a belt that brings resistance against a flywheel. Unlike many other mechanically braked ergometers, and most electronically braked ergometers, this ergometer has the advantage of being easily calibrated, and the balance-arm mechanism ensures highly reproducible workloads. Most subjects were familiar with cycling exercise as this is a common mode of transport in Bolivia. However, some of the Aymara women (group 2) had little experience with this exercise modality. In such cases, the women were well familiarized with the stationary ergometer prior to testing and were given sufficient practice to achieve a smooth pedal cadence during testing.

Each subject was given two identical submaximal exercise tests on separate days. Each test began with a 5-min resting period with the subject seated on the cycle ergometer. Exercise bouts were 5 min in duration and were separated by 5-min rest periods. For males, four work bouts were performed on a given day at 1.00, 1.50, 2.00, and 2.50 kg of resistance on the cycle ergometer. For females, four work bouts were performed at 0.50, 0.75, 1.00, and 1.25 kg of resistance. Subjects were instructed to maintain a pedal cadence of 60 revolutions per minute (rpm), but rpm were carefully recorded in order to precisely calculate work. External work output was calculated from rpm, the resistance setting on the ergometer over the last 2 min of each work bout, and the circumference of the flywheel.

During testing, subjects inspired room air through a low-resistance breathing valve (Hans Rudolph, Kansas City, MO), and the expired fractions of O_2 and CO_2 were measured continuously from a mixing chamber by gas analyzers calibrated to gas standards before each exercise test: Applied Electrochemistry S-3A O_2 analyzer (AEI Technologies, Pittsburg, PA); Beckman LB-2 CO_2 analyzer (Beckman Instruments, Inc., Schiller Park, IL). Inspired minute ventilation (VE-ATP) was measured by a dry gas meter calibrated with a 3-L syringe and converted to BTPS units (VE-BTPS). These data were processed by an automated O_2 uptake system (Rayfield Electronics, REP-200B) to produce 30-sec interval calculations of oxygen consumption (V_{O_2}) and carbon dioxide production (VC_{O_2}). For all exercise variables, values were determined as the average over the last 2 min of each 5-min exercise period. Data from tests given on separate days were averaged across each of the four workloads to minimize the influence of measurement error.

Calculations of work efficiency

Standard measures of work efficiency, including gross efficiency (GE), net efficiency (NE), and delta efficiency (DE), were calculated according to definitions given by Davis et al. (1982), Gaesser and Brooks (1975), Whipp et al. (1981), and Whipp and Wasserman (1969). To convert V_{O_2} measures into energetic values, a mixed contribution to energy yield of fat and carbohydrate was assumed using standard equivalence assumptions (Brooks et al., 1996) and an average caloric equivalent of 4.92 kcal/L^{-1} V_{O_2}. We opted not to assign different values of the caloric equivalent based on the measured respiratory exchange ratio (RER, V_{CO_2}/V_{O_2}) at each workload. This would assume an equivalence between respiratory gas exchange and the respiratory quotient (RQ), with the latter accurately reflecting underlying metabolic processes. However, RER may not reflect fuel substrate choice, especially during hard exercise, exercise at altitude, or non-steady-state exercise conditions (Brooks et al., 1996). GE was calculated as the ratio of external work output (in kcal/min) to the metabolic EE (in kcal/min). NE was calculated as the ratio of the external work output to the metabolic EE minus the resting EE in kcal/min. DE was calculated from the linear regression of external work on metabolic EE and represents the slope of this relationship, or the unit change in external work per unit change in EE. Only the first three work levels were used in the DE calculation, as it was considered that the final data point (work level 4), for some subjects, might fall on the plateau phase of the V_{O_2}–work rate relationship, reflecting the contribution of non-oxidative energy sources and increasing DE greatly.

Statistics

Group differences in anthropometric measures and DE were tested by analysis of variance (ANOVA) with the Scheffé's correction for multiple comparisons using the GLM procedure of the Systat Statistical Package (Evanston, IL) on a personal computer. Group differences in V_{O_2}, GE, and NE at each work level were tested by analysis of covariance (ANCOVA), controlling for external work rate (watts), with the Scheffé's correction. Mean values are expressed as mean ± standard deviation (SD). Statistical significance criteria was $p < 0.05$ for all tests. Power analysis was conducted using the Pass© Software, version 6.0 (NCSS, 329 North 1000 East, Kaysville, UT).

RESULTS

Subject characteristics are given in Table 1. In general, subject groups were relatively well matched on most traits. Group differences that do exist are either minor or are differences that would be expected based on sex and/or altitude of residence. Despite small but significant age differences between certain study groups, the age range of all subjects was broadly similar because of the study recruitment criteria. Hemoglobin levels were higher in male compared to female groups and higher in HA versus LA resident groups, as expected. In particular, both acclimatized European and deacclimatized Aymara male groups were not significantly different in hemoglobin concentration from other male groups at high and low altitude, respectively. In both cases, this fact confirms the acclimatization–deacclimatization status of these two subject groups. Males were taller and heavier than females, and Europeans were taller and heavier than Aymara. However, the three Aymara and three European male groups were not significantly different from one another in this regard. Males had lower percent body fat compared to women. Within sex, the only significant group difference in percent body fat was between Aymara men at HA (15.2%) and lowland European males (20.2%). The $V_{O_{2max}}$ values, as well as the adaptive interpretation of group differences in $V_{O_{2max}}$, have been reported in a previous publication (Brutsaert et al., 1999). However, $V_{O_{2max}}$ values (ml/min^{-1}/kg^{-1}) are reported here (Table 1), as they may inform interpretation of efficiency measures. Males had higher mass specific $V_{O_{2max}}$ compared to females, and Aymara males tested at HA had significantly higher $V_{O_{2max}}$ compared to all other study groups. Acclimatized European females had lower $V_{O_{2max}}$ compared to all other study groups.

As background data, exercise response variables at each work level are given in Table 2 for males and females. There were no significant within-gender group differences in mean work output at any work level. Nevertheless, there was considerable variability in watts output at a given work level due to differences in pedal cadence. For this reason, statistical testing for group differences in V_{O_2}, V_{CO_2}, and VE-BTPS at any work level is by ANCOVA controlling for external work (watts). For females, there were no significant differences in V_{O_2} and V_{CO_2}, at any work level (Table 2). However, VE-BTPS was significantly lower in Aymara women (group 2) versus acclimatized European women (group 5) at all work levels except the first. In males, there were no significant group differences in V_{O_2}, with the exception of the acclimatized European males (group 4), who had slightly lower V_{O_2} at the highest workload compared to groups 3, 6, and 8. V_{CO_2} was mostly similar between groups at all work levels, although, compared to some groups, Aymara males (group 1) had lower V_{CO_2} at the second, third, and fourth work levels, and acclimatized European males (group 4) had lower VCO_2 at the third work level. VE-BTPS was not significantly different between groups tested at similar altitudes. Aymara males (group 1) tended to have lower VE-BTPS compared to other groups tested at HA, although, unlike the Aymara females, this diffference was not statistically significant. As expected, VE-BTPS was significantly higher in all male groups tested at HA versus those tested at sea level.

As a point of reference, Fig. 1A shows the expected values of V_{O_2} as a function of external work on a cycle ergometer from sea-level data published by Brooks et al. (1996). GE can be derived at any point along this V_{O_2}–work line by converting V_{O_2} to EE and computing the ratio of external work to metabolic EE when both are expressed in the same units. Figure 1B shows the expected GE values as a function of external work when the caloric equivalent is assumed to be a constant at 4.92 kcal/L^{-1} V_{O_2}. The nonlinearity of this GE–work rate relationship results from the fact that the V_{O_2}–work line does not pass through the origin (zero). Also, different GE reference curves are possible, as the caloric equivalent is not a constant over all exercise intensities. In fact, fuel substrate choice depends in a complex way on exercise intensity, the environment, and various individual factors, including aerobic fitness level. However, the caloric equivalent can only range from 4.69 to 5.05 kcal/L^{-1} V_{O_2}. This means that the reference line in Fig. 1B is a good

Table 1. Characteristics of Study Groups

Study group	*Birth place*	*Altitude tested (m)*	*Age (yr)*	*[HB] g/dL^{-1}*	*Ht (cm)*	*Wt (kg)*	*Body fat (%)*	*$V_{O_{2max}}$ (mL/min^{-1}/kg^{-1}*	*Delta efficiency(%)*
1. Aymara males	HA	3850	23.3 ± 4.4	17.5 ± 0.9 (5–8)	162.8 ± 7.5 (2–7)	56.4 ± 5.1 (2–7)	15.2 ± 4.6 (2,5,7)	51.0 ± 8.1 (2–8)	26.3 ± 2.5
2. Aymara females	HA	3850	22.0 ± 5.3 (4)	16.4 ± 1.2 (3,4,6–8)	149.1 ± 5.4 (1,3–8)	48.3 ± 5.3 (1,3–8)	29.3 ± 4.8 (1,3,4,6–8)	37.6 ± 6.0 (1)	26.7 ± 5.2
3. European migrant males	HA	3600	23.5 ± 6.0	17.8 ± 1.2 (2,5–8)	175.3 ± 7.6 (1,2,5,6,8)	67.8 ± 10.3 (1,2,6,8)	19.2 ± 5 (2,5)	42.2 ± 9.9 (1,5)	27.1 ± 5.2
4. Acclimatized European males	LA	3600	26.8 ± 4.7 (2,7,8)	17.6 ± 1.1 (2,5–8)	175.8 ± 6.9 (1,2,5,6,8)	70.3 ± 7.5 (1,2,5,6,8)	19.6 ± 4.3 (2,5)	41.8 ± 7.5 (1,5)	27.1 ± 3.9
5. Acclimatized European females	LA	3600	25.7 ± 3.6 (8)	15.4 ± 1.2 (1,3,4)	165.4 ± 9.2 (2–7)	60.8 ± 9.9 (2,4)	33.3 ± 7.1 (1,3,4,6–8)	30.4 ± 5.3 (1,3,4,6–8)	28.5 ± 4.7
6. Deacclimatized Aymara males	HA	420	25.7 ± 6.3 (8)	14.8 ± 1.4 (1–4)	161.0 ± 5.6 (2–4,7)	59.0 ± 6.3 (2–4,7)	19.8 ± 5.3 (2,5)	41.3 ± 6.3 (1,5)	25.9 ± 3.4
7. Lowland European males	LA	420	22.4 ± 3.5 (4)	15.2 ± 1.2 (1–4)	175.0 ± 6.8 (1,2,5,6,8)	68.3 ± 6.9 (1,2,6,8)	20.2 ± 5.1 (1,2,5)	42.9 ± 7.9 (1,5)	25.9 ± 3.4
8. Aymara migrant males	LA	420	19.3 ± 3.0 (4–6)	14.2 ± 1.6 (1–4)	164.7 ± 7.2 (2–7)	60.7 ± 8.9 (2–7)	17.2 ± 5.2 (2,5)	43.2 ± 6.9 (1,5)	26.0 ± 3.3

All values presented as mean ± SD.
[1]Significantly different from group 1, $p < 0.05$.
[2]Significantly different from group 2, $p < 0.05$.
[3]Significantly different from group 3, $p < 0.05$.
[4]Significantly different from group 4, $p < 0.05$.
[5]Significantly different from group 5, $p < 0.05$.
[6]Significantly different from group 6, $p < 0.05$.
[7]Significantly different from group 7, $p < 0.05$.
[8]Significantly different from group 8, $p < 0.05$.

TABLE 2. MEAN EXERCISE RESPONSE VARIABLES FOR MALES AND FEMALES

Study group	*Work level 1*	*Work level 2*	*Work level 3*	*Work level 4*
Aymara males (group 1)				
Watts	53.7 ± 5.6	84.7 ± 8.8	108.2 ± 11.5	137.2 ± 14.0
V_{O_2}(L/min^{-1})	1.00 ± 0.11	1.34 ± 0.11	1.58 ± 0.16	1.93 ± 0.19
V_{CO_2} (L/min^{-1})	0.90 ± 0.11	1.23 ± 0.12 (6)	1.51 ± 0.18 (3,6–8)	1.93 ± 0.27 (3)
VE (L/min^{-1}) BTPS	33.5 ± 4.7 (6–8)	45.4 ± 5.9 (6,8)	54.0 ± 7.6 (6–8)	70.4 ± 12.1 (6)
European migrant males (Group 3)				
Watts	59.4 ± 8.3	94.7 ± 12.3	121.2 ± 15.6	152.7 ± 23.0
V_{O_2}(L/min^{-1})	1.12 ± 0.17	1.52 ± 0.20	1.76 ± 0.21	2.14 ± 0.26
V_{CO_2} (L/min^{-1})	1.06 ± 0.20	1.46 ± 0.20	1.83 ± 0.22	2.42 ± 0.54
VE (L/min^{-1}) BTPS	39.0 ± 11.5 (6–8)	53.3 ± 13.2 (6–8)	62.6 ± 11.3 (6–8)	81.7 ± 16.7 (6,8)
Acclimatized European males (group 4)				
Watts	57.4 ± 11.8	87.8 ± 17.4	111.8 ± 22.1	142.6 ± 32.4
V_{O_2}(L/min^{-1})	1.02 ± 0.15	1.36 ± 0.23 (6)	1.59 ± 0.27	1.92 ± 0.36 (3,6,8)
V_{CO_2} (L/min^{-1})	0.95 ± 0.13	1.31 ± 0.24	1.61 ± 0.28 (6,8)	2.04 ± 0.42
VE (L/min^{-1}) BTPS	35.5 ± 5.2 (6–8)	49.8 ± 10.4 (6–8)	58.7 ± 11.7 (6–8)	77.2 ± 19.3 (6,8)
Deacclimatized Aymara males (group 6)				
Watts	55.1 ± 8.9	88.8 ± 13.2	108.5 ± 14.4	132.5 ± 21.8
V_{O_2}(L/min^{-1})	1.00 ± 0.14	1.45 ± 0.20	1.57 ± 0.18	1.92 ± 0.29
V_{CO_2} (L/min^{-1})	0.97 ± 0.15	1.39 ± 0.20	1.71 ± 0.22	2.06 ± 0.37
VE (L/min^{-1}) BTPS	27.5 ± 4.8	41.4 ± 7.4	47.0 ± 8.4	63.1 ± 14.4
Lowland European males (group 7)				
Watts	58.1 ± 10.2	86.9 ± 11.2	109.6 ± 13.0	134.1 ± 20.8
V_{O_2}(L/min^{-1})	1.09 ± 0.15	1.44 ± 0.14	1.64 ± 0.15	2.0 ± 0.23
V_{CO_2} (L/min^{-1})	1.04 ± 0.20	1.34 ± 0.15	1.68 ± 0.19	2.07 ± 0.31
VE (L/min^{-1}) BTPS	29.6 ± 5.7	38.8 ± 5.5	45.5 ± 6.6	58.1 ± 10.7
Aymara migrant males (group 8)				
Watts	58.0 ± 9.9	85.4 ± 8.2	109.9 ± 11.9	135.6 ± 16.7
V_{O_2}(L/min^{-1})	1.05 ± 0.14	1.39 ± 0.15	1.62 ± 0.14	1.97 ± 0.20
V_{CO_2} (L/min^{-1})	1.02 ± 0.20	1.33 ± 0.16	1.72 ± 0.21	2.13 ± 0.26
VE (L/min^{-1}) BTPS	29.5 ± 4.7	38.8 ± 5.1	47.5 ± 6.5	61.2 ± 9.7
Aymara females (group 2)				
Watts	38.5 ± 5.1	52.6 ± 6.4	63.2 ± 7.3	75.9 ± 11.1
V_{O_2}(L/min^{-1})	0.79 ± 0.10	0.95 ± 0.13	1.06 ± 0.12	1.24 ± 0.20
V_{CO_2} (L/min^{-1})	0.71 ± 0.10	0.85 ± 0.12	1.00 ± 0.12	1.15 ± 0.19
VE (L/min^{-1}) BTPS	27.0 ± 4.3	33.2 ± 5.1 (5)	37.9 ± 4.7 (5)	46.1 ± 9.2 (5)
Acclimatized European females (group 5)				
Watts	39.3 ± 6.6	55.3 ± 7.9	64.5 ± 10.0	80.3 ± 12.2
V_{O_2}(L/min^{-1})	0.79 ± 0.09	0.96 ± 0.11	1.04 ± 0.12	1.24 ± 0.16
V_{CO_2} (L/min^{-1})	0.73 ± 0.09	0.92 ± 0.12	1.06 ± 0.15	1.30 ± 0.20
VE (L/min^{-1}) BTPS	29.3 ± 4.8	38.6 ± 7.9	42.8 ± 8.3	55.3 ± 13.3

All values presented as mean ± SD.
[3]Significantly different from group 3, $p < 0.05$.
[5]Significantly different from group 5, $p < 0.05$.
[6]Significantly different from group 6, $p < 0.05$.
[7]Significantly different from group 7, $p < 0.05$.
[8]Significantly different from group 8, $p < 0.05$.

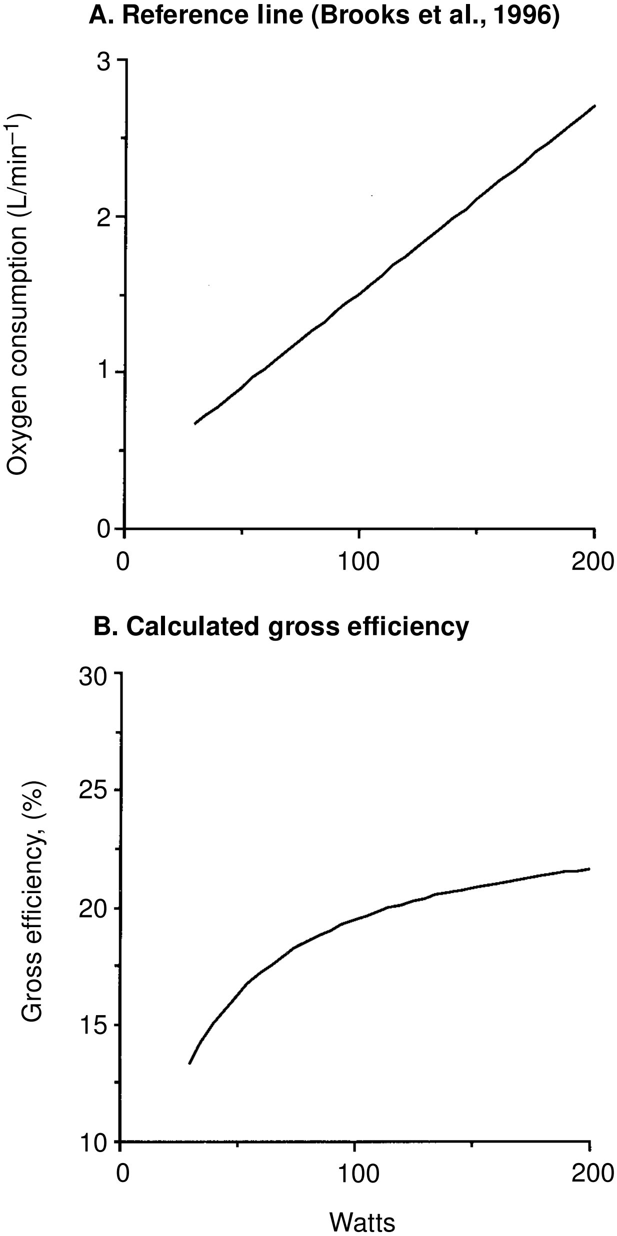

FIG. 1. Reference oxygen consumption as a function of external work on a cycle ergometer from sea-level data given in Brooks et al. (1996) (A), and the calculated gross efficiencies (external work in kcal/min divided by metabolic work in kcal/min) based on the same data (B).

representation of possible GE reference curves and is sufficient when one considers the relatively large intersubject variability in calculated GE values.

In Fig. 2 (for males) and Fig. 3 (for females), V_{O_2} by external work (watts) is plotted against the reference line of Brooks et al. (1996) for each study group. In general, measured V_{O_2} values were not significantly different from the Brooks reference line. Work levels 1 through 4 are indicated by different plot symbols. As described in Table 2, no significant differences were detected in V_{O_2} at any work level between the two female groups (Fig. 3) or between the six male groups (Fig. 2), with the following exception. Acclimatized European men (group 4, Fig. 2B) had significantly lower V_{O_2} at work level 4 compared to European migrant men born at HA and tested at 3600 m (group 3, Fig. 2C), deacclimatized Aymara men tested at 420 m (group 6, Fig. 2E), and Aymara migrant men born at LA and tested at 420 m (group 8, Fig. 2F).

In Fig. 4 (for males) and Fig. 5 (for females), calculated GE values as a function of external work are plotted against the reference curve that was generated in Fig. 1B using the reference data of Brooks et al. (1996). GE values tend to fall slightly below the GE reference curve, but recall that this curve is meant only to represent a family of possible curves depending on the caloric equivalent. Again, group differences in GE at any work level are best evaluated by ANCOVA, holding constant the variation in work output (watts) and work output squared as covariates. The squared term in this analysis accounts for the nonlinearity of the GE–external work relationship. As above, there were no significant differences in GE at any work level between the two female groups (Fig. 5). Similarly, there were no differences in GE between the six male groups (Fig. 4), with the following exception. Acclimatized European men (group 4, Fig. 2B) had significantly higher GE at work level 4 compared to European migrant men born at HA and tested at 3600 m (group 3, Fig. 4C) and deacclimatized Aymara men tested at 420 m (group 6, Fig. 4E).

Differences between groups in NE were also evaluated using the same approach as above, but NE results were not qualitatively different from GE results and thus are not presented here. That is, there were no significant group differences in NE between the two female groups or between the six male groups, with the exception of the acclimatized European men, who had significantly higher NE at work level 4 compared to (some) other male groups. The similarity of GE and NE results is to be ex-

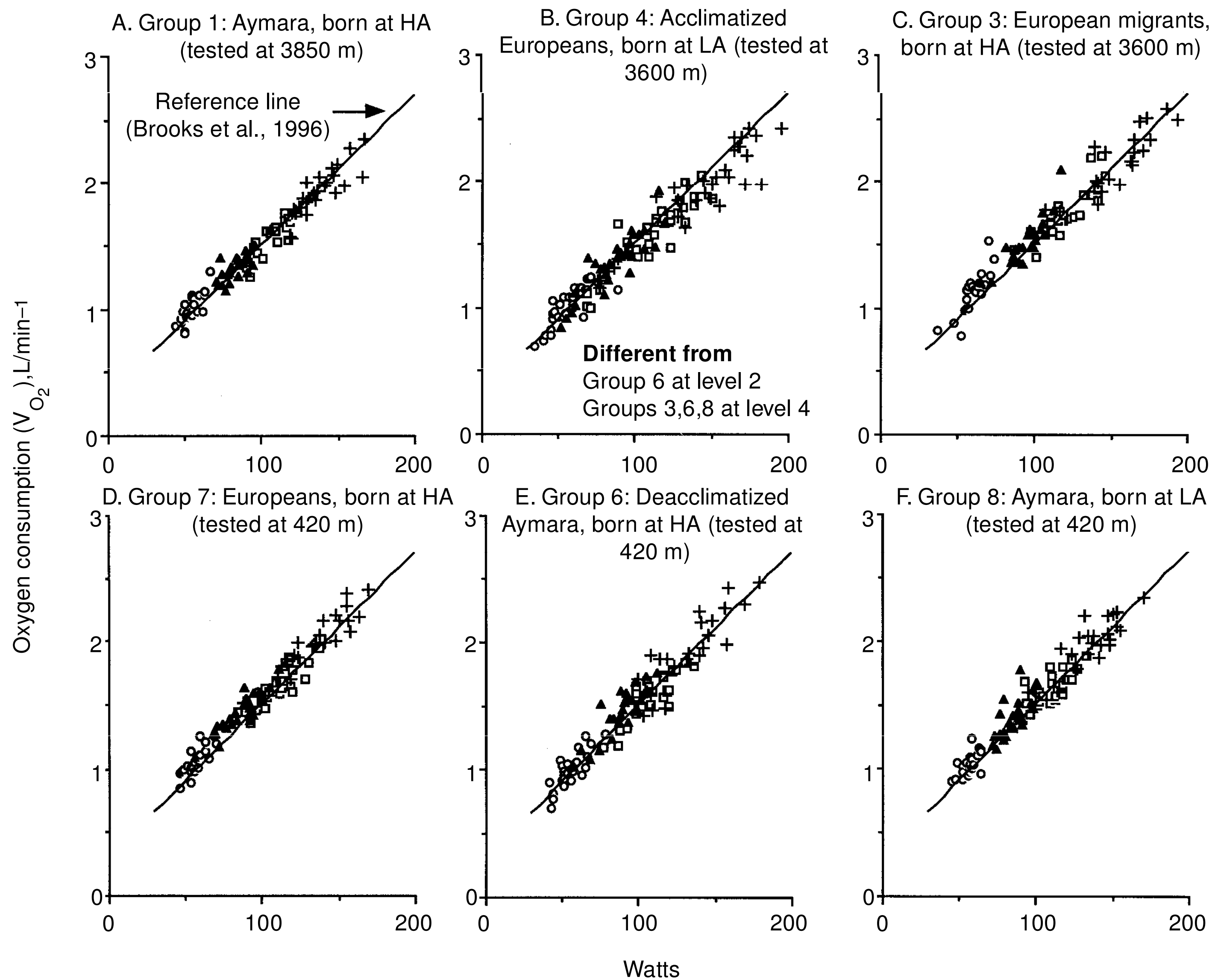

FIG. 2. Oxygen consumption (V_{O_2}, L/min^{-1}) by work rate (W) against the reference line of Brooks et al. (1996) in the six male study groups (A to F). The altitude where each of these groups was tested is given in parentheses. Work levels are identified by different plot symbols: open circles are work level 1, closed triangles are work level 2, open squares are work level 3, and plus signs (+) are work level 4. HA = high altitude, LA = low altitude.

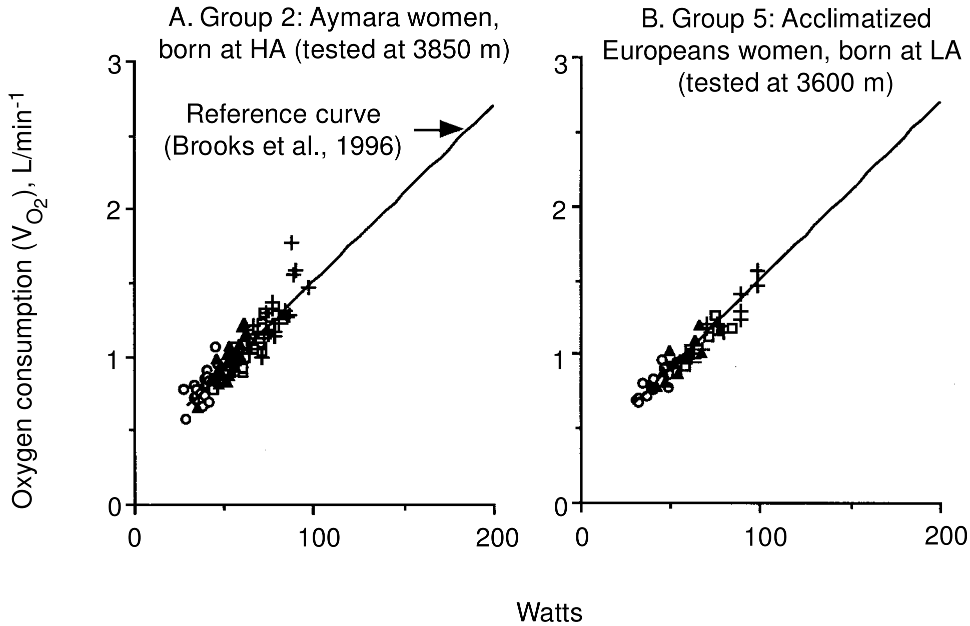

FIG. 3. Oxygen consumption (V_{O_2}, L/min^{-1}) by work rate (W) against the reference line of Brooks et al. (1996) in the two female study groups (A and B). The altitude where each of these groups was tested is given in parentheses. Work levels are identified by different plot symbols, as described for Fig. 2. There were no significant V_{O_2} by work-level differences between these two study groups.

pected, given that NE is an adjusted GE (subtracting a resting EE value from the EE denominator). In this regard, NE values contribute little to the overall efficiency analysis and have the drawback that they incorporate the additional error associated with measurement of the resting EE. Delta efficiency (DE) values are given in Table 1. DE values show relatively high variation within study groups, with values ranging from approximately 17% to 40%. There were no significantly different pairwise comparisons of DE between study groups. Power analysis reveals sufficient study power to detect group differences in V_{O_2} of about 9% at $\beta = 0.90$, $\alpha = 0.05$, and $n = 25$ subjects per group. This translates directly to a ~9% difference in GE or NE, which is equivalent to a 1.5 to 2 percentage point difference in GE or NE as these values are in the 15% to 20% range.

To further investigate the issue of work efficiency, a literature review was conducted searching for published values of V_{O_2} and external work from cycle ergometry exercise in highland native populations in the Andes and Himalayas. In some studies, data were presented in graphic form only. In such cases, these graphic images were digitized, and numeric values were approximated using the public-domain NIH Image program (developed at the U.S. National Institutes of Health and available from the Internet by anonymous FTP from zippy.nimh.nih.gov). Literature data were again plotted against the reference line of Brooks et al. (1996) from studies conducted with Andean natives (Fig. 6) and Himalayan natives (Fig. 7). In the Andes, only four previous studies provide the requisite data, and of these only two give data for multiple workloads. However, in the Himalayas, at least eight previous studies provide the requisite data comprising nine distinct study groups, and all but one of these studies provides multiple data points. No formal statistical testing was conducted, but in the Himalayas, at least, Fig. 7 gives the impression of substantial between-study variation in the V_{O_2}–work relationship distributed randomly around the reference line of Brooks et al.

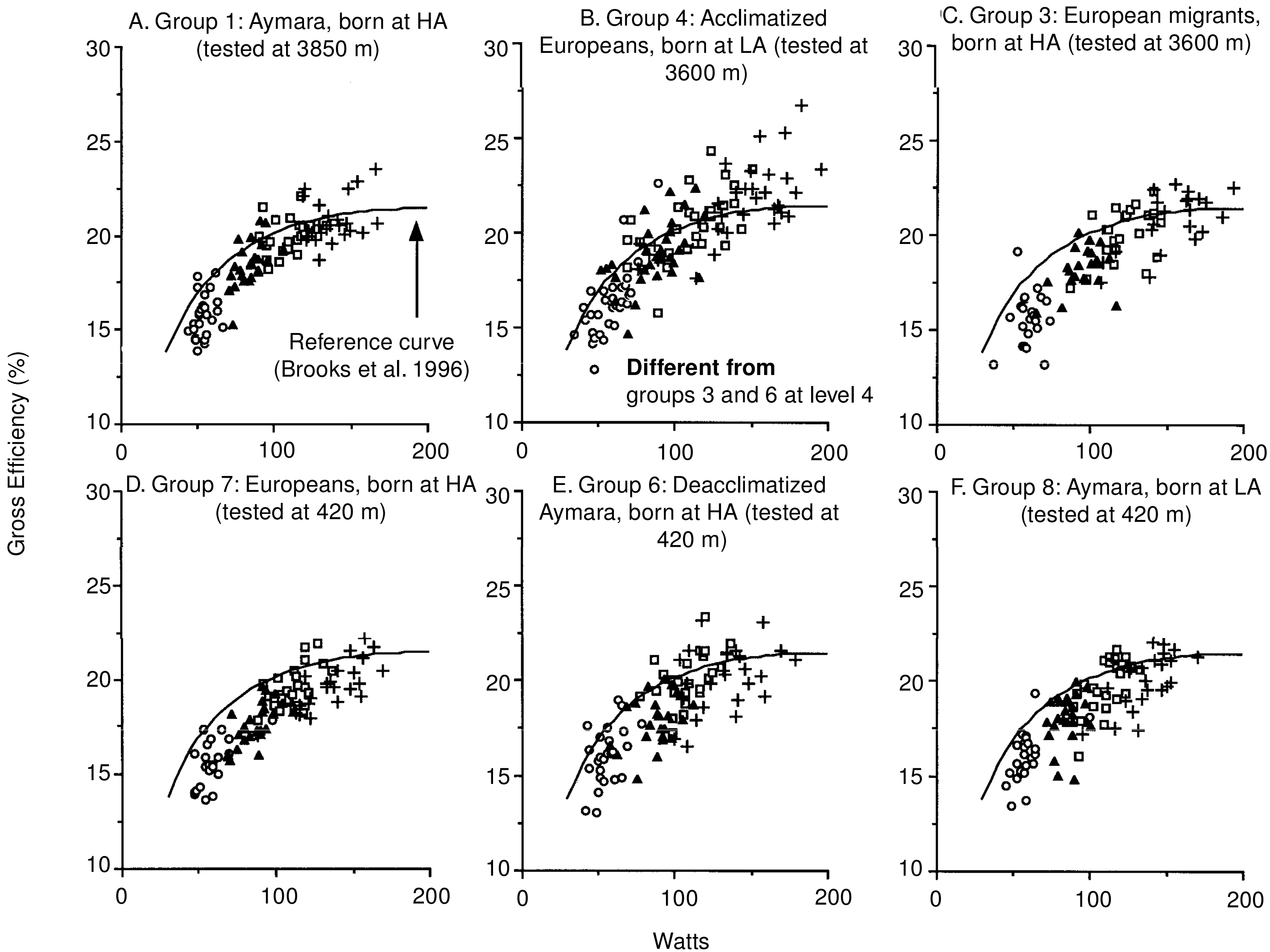

FIG. 4. Gross efficiency (GE, %) by work rate (W) against the reference GE values using data from Brooks et al. (1996) in the six male study groups (A to F). The altitude where each of these groups was tested is given in parentheses. Work levels are identified by different plot symbols, as described for Fig. 2. HA = high altitude, LA = low altitude.

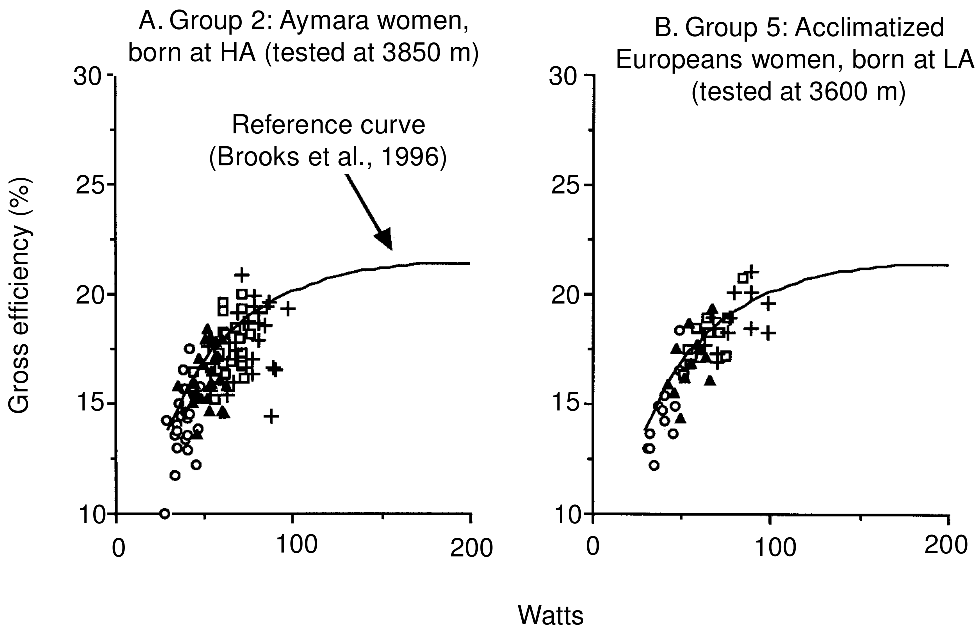

FIG. 5. Gross efficiency (GE, %) by work rate (W) against the reference GE values using data from Brooks et al. (1996) in the two female study groups (A and B). The altitude where each of these groups was tested is given in parentheses. Work levels are identified by different plot symbols, as described for Fig. 2. There were no significant GE values by work-level differences between these two study groups.

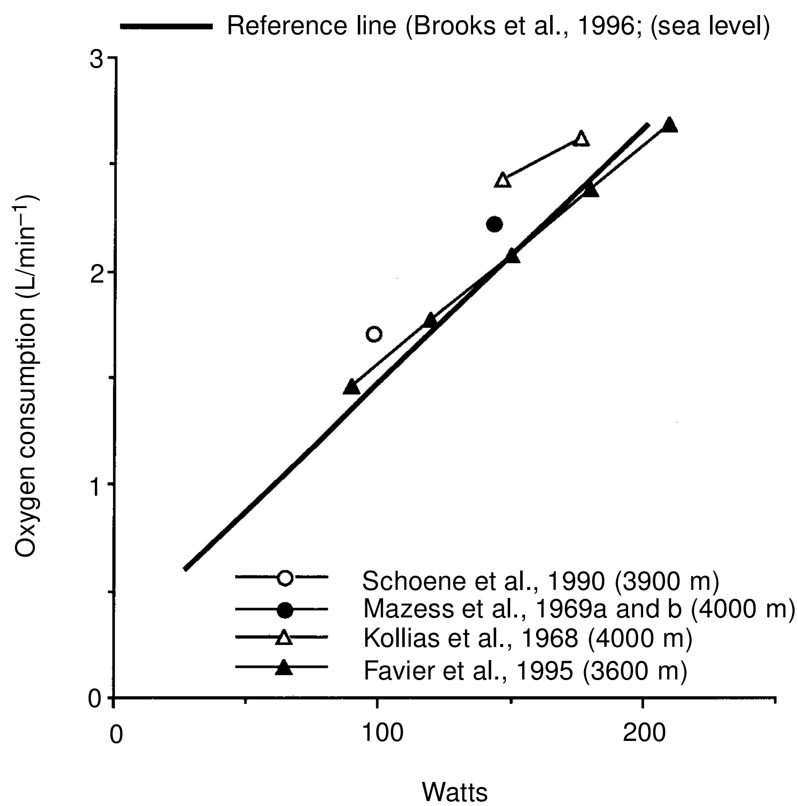

FIG. 6. Cycle ergometer oxygen consumption (V_{O_2}, L/min^{-1}) and work rate (W) data from the Andean literature against the reference line of Brooks et al. (1996) (solid line with no plot symbols). The altitude where each study was conducted is given in parentheses in the figure legend. Studies are by Schoene et al. (1990), Mazess et al. (1969a; 1969b), Kollias et al. (1968), and Favier et al. (1995).

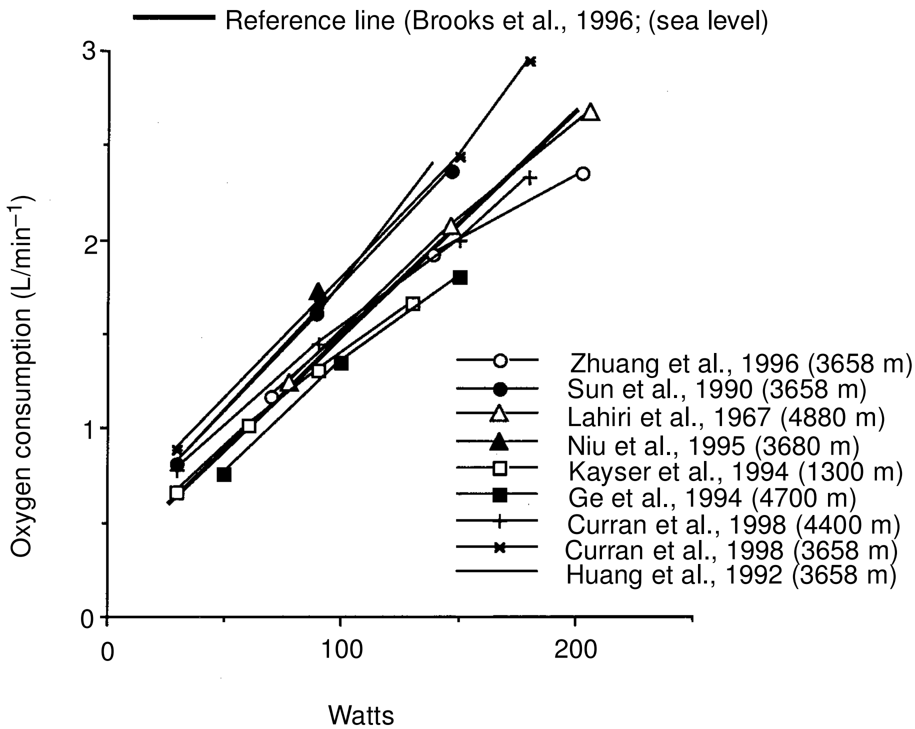

FIG. 7. Cycle ergometer oxygen consumption (V_{O_2}, L/min^{-1}) and work rate (W) data from the Himalayan literature against the reference line of Brooks et al. (1996) (solid line with no plot symbols). The altitude where each study was conducted is given in parentheses in the figure legend. Studies are by Zhuang et al. (1996), Sun et al. (1990), Lahiri et al. (1967), Niu et al. (1995), Kayser et al. (1994), Ge et al. (1994), Curran et al. (1998), and Huang et al. (1992).

DISCUSSION

The results of this study do not support the hypothesis of energetic advantage in Andean highland natives. The study was designed to evaluate the possibility of either genetic and/or developmental adaptation to HA via selected comparisons between study groups. For example, genetic adaptation can be inferred on the basis of differences between Aymara and European study groups born and raised at HA, and developmental adaptation can be inferred on the basis of differences between Europeans born and raised in different environments (Harrison, 1966; Haas, 1980). However, such inferences are not warranted on the work efficiency phenotype, as this study shows a fixed V_{O_2}–work rate relationship and similar values of calculated GE, NE, and DE between nearly all study groups. The one exception was acclimatized European men (group 4), who showed slightly lower levels of V_{O_2} at high work output and thus slightly higher GE (between 150 and 200 W). This difference was not evident in the DE calculation. While statistically significant, the biological significance of a small (~5%) lower V_{O_2} at work level 4 may be questioned relative to the hypothesis of increased energetic efficiency. Furthermore, it may be that this slightly lower V_{O_2} at high work output has to do with the specific rigors of performing exercise in hypoxia in lowland-born individuals, rather than to an altered relationship between steady-state V_{O_2} and work rate in such subjects per se (see below).

All study participants were given the same four sex-specific absolute workloads. These workloads were selected to avoid the plateau phase of the V_{O_2}–work rate relationship. That is, workloads were intended to be submaximal, but not necessarily below the lactate threshold of all subjects. This goal was achieved for the majority of subjects (see Fig. 2), who showed a linear increase in V_{O_2} with increasing external work; but inspection of Fig. 2B suggests that some acclimatized European men tested at

3600 m (group 4) had begun to plateau by work level 4. This plateau could be because some men were approaching a true $V_{O_{2max}}$, or it could be because some were not at a true steady state. The latter seems more likely based on the relative work rate data. At work level 4, the mean value of V_{O_2} in acclimatized European men was at ~73% of $V_{O_{2max}}$, not much different from the other two male groups tested at HA (between 69% and 75% of $V_{O_{2max}}$) or the two female groups tested at HA (between 69% and 71% of $V_{O_{2max}}$). Thus, acclimatized European men were not working harder in a relative sense compared to the other study groups. This suggests that the plateau is a reflection of an earlier and/or greater increase in anaerobic metabolism that results in a nonsteady-state V_{O_2} kinetic. This hypothesis is supported by studies that show increased lactate production (e.g., Hermansen and Saltin, 1967) concomitant with a slowed kinetic of V_{O_2} onset during exercise by nonnative groups in hypoxia (Springer et al., 1991; Ibanez et al., 1993; Engelen et al., 1996). A plateau was not suggested by the data from acclimatized European women (group 5), but only 12 such women were tested and the absolute difference between workloads was relatively small compared to men (i.e., ~25 W between workloads).

Relative to the previous literature on work efficiency in Andean natives, the present study is directly comparable to the studies of Kollias et al. (1968), Mazess et al. (1969a, 1969b), Favier et al. (1995), and Hochachka et al. (1991), as these studies were all conducted using cycle ergometers. In contrast, the original studies of Hurtado (Hurtado, 1932, 1964), as well as subsequent studies by Reynafarje and Velasquez (1966) and Haas et al. (1983), used a treadmill. Although these treadmill studies all report higher work efficiencies in Andean natives, these results must be viewed with caution relative to the hypothesis of energetic advantage because of the inherent problem of measuring external work on a treadmill. Treadmill work depends on body size and on the economy of movement, which makes treadmill work efficiencies difficult to interpret relative to metabolic organization. In this regard, treadmill work efficiencies may be better designated by the term work (or running) economy (Daniels, 1985). A similar problem of interpretation exists for step test exercise, as in the study of Cerretelli (1980), who describes no efficiency differences between Himalayan natives and lowland controls using this exercise modality.

The results of this study are consistent with the early results of Mazess et al. in Peru (1969a, 1969b) and Favier et al. (1995) in Bolivia, who reported no efficiency differences between lowland controls and Andean highland natives, although the relevant population sample described by Favier et al. is perhaps best characterized as Mestizo, comprising an admixed population born and raised at HA. Favier et al. report five workloads on a cycle ergometer (plotted in Fig. 6), and the V_{O_2} data do not differ substantially from the Brooks et al. (1996) reference line. Mazess et al. report only one workload (Fig. 6), and the V_{O_2} value is higher than expected, but this may be due to error in the measurement of external work. The important point of the Mazess studies is that there were no efficiency differences between Peruvian natives and various lowland control groups using the same ergometer.

In contrast, the results of this study are different from those of Kollias et al. (1968) and Hochachka et al. (1991). Kollias et al. reported slightly lower GE at two relatively high workloads in Peruvian Quechua compared to both athletic and nonathletic lowland controls tested at HA. However, these differences are difficult to interpret, as the measure reported is not a standard GE construct and incorporates a recovery phase of V_{O_2} into the denominator of the calculation. Perhaps more informative is to consider the direct plot of the V_{O_2} versus work rate data from Kollias et al., as shown in Fig. 6. Only the Peruvian HA natives from this study are plotted, but values confirm a higher than expected level of V_{O_2}. The lowland control groups in the Kollias study fall directly on the Brooks standard line (data not shown in Fig. 6). In this regard, the Kollias study is similar to the present study, that is, slightly lower O_2 consumption in acclimatized Europeans compared to highland natives, but only at higher work levels. Again, this lower V_{O_2} at high workloads may reflect an altered V_{O_2} kinetic, rather than a fundamental change in the V_{O_2}–work relationship.

Hochachka et al. (1991) reported a 1.5 to 2-fold higher GE and NE in Peruvian Quechua compared to lowland controls when both groups were tested in the lowlands under normoxia and hypoxia. The results from this study differ from other studies in several important ways. First, the reported magnitude of the highland versus lowland group difference is much greater than that reported in any other study. Second, the largest efficiency differences are reported at the lowest levels of absolute work, and group differences largely disappear at the highest levels of work. Third, the design focuses on Quechua who were studied after a period of deacclimatization to the lowlands. The rationale for this particular design is that traits that do not deacclimate may represent historically fixed traits in the population. This does not necessarily need to be the case because of irreversible developmental effects (Brutsaert, 2001), but nevertheless the present study has replicated this aspect of the Hochachaka et al. study. Again, the present study shows no efficiency differences between highland Aymara (group 1), deacclimatized Aymara who have been in the lowlands for at least 2 months (group 6), and Aymara who have been born and raised in the lowlands (group 8).

The study of Hochachka et al. (1991) does not directly provide V_{O_2} and work rate data, so it is not possible to plot results on Fig. 6. In addition, most of the efficiency data are presented as a function of external work normalized to body mass (i.e., W/kg), and this may introduce bias. Andean native versus European lowland control male subjects typically differ by 15 to 20 kg. When GE was expressed relative to watts per kilogram in this study, this had the effect of creating an artificially higher GE in acclimatized European men (group 4) versus Aymara (group 1). That is, GE values expressed relative to watts per kilogram in acclimatized European men were left-shifted because of larger body size and consequently lower watts per kilogram work output. The artifact introduced in this manner is especially problematic at low power output (30 to 100 W) because of the nonlinearity of the GE–work rate relationship (Fig. 1B). Similarly, measurement errors would accentuate group differences in GE on this part of the GE–work rate curve, and this is a possibility that should be considered when evaluating the large group differences in GE and NE reported by Hochachka et al. (1991). At 60 W (low power output), Hochachka et al. report mean GE values of ~18% and ~12% in Quechua and lowland controls, respectively. This GE difference disappears at work levels approaching $V_{O_{2max}}$, which is what would be predicted if there were measurement error between study groups in the external work output. The GE value of the Quechua studied by Hochachka et al. at 60 W (~18%) is not different from the reference value presented in this paper (Fig. 2B). Thus, one possibility is error in the measurement of either V_{O_2} or external work in the Hochchacka et al. control group.

The Himalayas are another region of the world where native groups have had a long history of exposure to hypobaric hypoxia (Zhimin, 1982). Some studies report no efficiency differences (or no differences in the V_{O_2} at a given level of work) between HA native and lowland controls (Lahiri and Milledge, 1966; Lahiri et al., 1967; Kayser et al., 1994). However, at least two studies report higher work efficiency in Tibetans versus lowland controls (Ge et al., 1994; Niu et al., 1995), and one study reports higher work efficiency in Tibetans resident at 4440 m versus Tibetans at 3658 m (Curran et al., 1998). In the present study, data on V_{O_2} and cycle ergometer work rate were collected from published studies with Himalayan native populations and plotted against the reference line of Brooks et al. (1996) (Fig. 7). The hypothesis of energetic advantage can be tested via analysis of these existing data on the assumptions that measurement error between studies is random and that there is no systematic bias between studies. If so, then the overall mean V_{O_2} relative to work rate should be an accurate reflection of the true V_{O_2}–work rate relationship in Himalayan groups, provided a sufficient number of independent studies have been conducted. In Fig. 7, there is obvious variation between studies in the V_{O_2}–work relationship, but this variation seems more or less evenly distributed around the reference line of Brooks et al. Four studies report groups with higher than expected V_{O_2}

at all workloads (thus lower efficiency) (Sun et al., 1990; Huang et al., 1992; Niu et al., 1995; Curran et al., 1998). One study reports lower than expected V_{O_2} at all workloads (Ge et al., 1994). Two studies superimpose well with the reference data of Brooks et al. at low work output, but suggest lower than expected V_{O_2} at high workloads (Kayser et al., 1994; Zhuang et al., 1996). Finally, two studies report groups that superimpose closely with the Brooks reference data at all workloads (Lahiri et al., 1967; Curran et al., 1998). In summary, no strong trends are evident, and this analysis also provides little support for the hypothesis of energetic advantage in the Himalayas.

CONCLUSIONS

This study does not support the long-standing hypothesis of high work efficiency in HA natives. We have demonstrated that there are no large work efficiency differences between Andean Aymara and various control populations. In addition, a review and analysis of the literature suggest that the same is true for natives of the Himalayan region. Nevertheless, the negative results of this study do not invalidate the general hypothesis of energetic advantage in HA natives, nor do they diminish the valuable metabolic–evolutionary framework of HA adaptation presented by Hochachka et al. (1991), which is described in the introduction of this paper. It is possible that the hypothesis of energetic advantage is not easily evaluated using simple pulmonary V_{O_2} measures. The present study had sufficient power to detect V_{O_2} (and thus GE and NE) differences between groups of about 9%. However, even smaller differences may be important within an evolutionary or developmental context, although this is a difficult issue to evaluate a priori. Also, it may be argued that an accurate analysis of muscle energetics requires additional measures, such as lactic acid accumulation and V_{O_2} kinetics. This is especially true as one adaptive strategy, like fuel substrate choice, has the potential to confound interpretation of another strategy, like work efficiency. Thus, studies more specifically focused on energy metabolism and fuel substrate use during exercise in HA native groups are indicated.

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Address reprint requests to:
Tom Brutsaert
Department of Anthropology
1400 Washington Ave.
The University at Albany, SUNY
Albany, New York, 12222

E-mail: tbrutsae@csc.albany.edu

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