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Hypoxic ventilatory response in successful extreme altitude climbers

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ABSTRACT: A very high ventilatory response to hypoxia is believed necessary to reach extreme altitude without oxygen. Alternatively, the excessive ventilation could be counterproductive by exhausting the ventilatory reserve early on.

To test these alternatives, 11 elite climbers (2004 Everest-K2 Italian Expedition) were evaluated as follows: 1) at sea level, and 2) at 5,200 m, after 15 days of acclimatisation at altitude. Resting oxygen saturation, minute ventilation, breathing rate, hypoxic ventilatory response, maximal voluntary ventilation, ventilatory reserve (at oxygen saturation=70%) and two indices of ventilatory efficiency were measured.

Everest and K2 summits were reached 29 and 61 days, respectively, after the last measurement. Five climbers summited without oxygen, the other six did not, or succeeded with oxygen (two climbers). At sea level, all data were similar. At 5,200 m, the five summiters without oxygen showed lower resting minute ventilation, breathing rate and ventilatory response to hypoxia, and higher ventilatory reserve and ventilatory efficiency, compared to the other climbers.

Thus, the more successful climbers had smaller responses to hypoxia during acclimatisation to 5,200 m, but, as a result, had greater available reserve for the summit. A less sensitive hypoxic response and a greater ventilatory efficiency might increase ventilatory reserve and allow sustainable ventilation in the extreme hypoxia at the summit.

KEYWORDS: Altitude, hypoxia, ventilation, ventilatory control, ventilatory efficiency

At high altitude, the reduced partial pressure of oxygen (P_{O_2}) results in arterial desaturation; respiration is then driven by the arterial chemoreceptors, rather than medullary partial pressure of carbon dioxide (P_{CO_2}), and with any physical exertion the necessary increases in ventilation are very large [1, 2].

Previous studies showed that a high hypoxic ventilatory response (HVR) helps in performing work at high altitude [1, 2]. By extension, it is generally believed that extreme altitudes could be tolerated without oxygen support only by subjects with the highest HVR, due to the extreme increase in ventilation required to remove carbon dioxide and increase arterial oxygen partial pressure (P_{a,O_2}). However, even with good acclimatisation, an extreme sensitivity to hypoxia may stimulate minute ventilation (V'_E) close to, or even above, sustainable limits (*e.g.* close to the maximal voluntary ventilation (MVV) defined as the maximal ventilation that can be maintained for 12 s [3]).

Since 1978, several climbers have nevertheless reached the summit of Mt Everest without oxygen, but, to the current authors' knowledge, there is little information (except anedoctal [4]) about the respiratory control in these subjects.

It could be hypothesised that the subjects with a better chance of reaching extreme altitudes without oxygen would be those with the highest HVR, due to their ability to increase P_{a,O_2} through the maximal increase in ventilation. Alternatively, it could be hypothesised that these subjects would approach their limit (*e.g.* the MVV) at relatively lower altitudes, whereas subjects with a brisk but not excessive ventilatory stimulus could maintain sustainable ventilation up to extreme altitudes. This could be possible if a relatively lower ventilation were associated with (or compensated by) a higher ventilatory efficiency.

The opportunity to participate in the recent Italian Everest-K2 expedition (spring–summer 2004) allowed the current authors to test a relatively high number of elite climbers before and during their acclimatisation. The study then tested whether the climbers who could reach the highest summits without oxygen were characterised by a higher or lower ventilatory sensitivity to hypoxia, as compared to those who did not

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succeed or needed supplemental oxygen. The study also tested whether successful climbers had a more efficient respiration, and whether any differences were present even before exposure to high altitude, or became apparent only during acclimatisation.

METHODS

Subjects

The study was approved by the institutional ethics committee, and all subjects gave informed consent to participate. Eleven Italian male elite climbers with previous experience of climbing in the Alps, Himalayas and Andes were studied. All subjects were healthy, nonsmokers, and were not taking any drugs or medications before and during the study. Anthropometric data are shown in table 1.

Protocol

All subjects were studied sitting, in a comfortable position, at ambient temperature and humidity, as follows: 1) at sea level, 1 month before the expedition; and 2) at 5,200 m, after 15 days of total stay at altitude, including 6 days of stay at altitudes between 3,800 and 5,200 m and 9 days from the arrival at North Face Everest Base Camp (5,200 m), *i.e.* when the acclimatisation process should already have begun. After the second evaluation, the climbers reached progressively higher camps, until the Everest summit (8,848 m), 29 days later. Thereafter, they descended to sea level for 2 weeks and left for K2 base camp (5,000 m). After 61 days from the second evaluation, they eventually reached the summit of K2 (8,611 m).

Recordings were taken during: 1) spontaneous breathing (4 min without a pneumotachograph and 4 min with the pneumotachograph); 2) slow breathing at 6 breaths·min^{-1} (2 min); 3) 12-s MVV; 4) a slow vital capacity manoeuvre; and 5) progressive isocapnic hypoxia (arterial oxygen saturation (S_{a,O_2}) from resting values to 70%). This was obtained by a re-breathing circuit, in which a variable part of the expired air was passed into a reservoir containing soda lime prior to return to the re-breathing bag, in order to maintain end-tidal carbon dioxide pressure (P_{ET,CO_2}) clamped at 4.8 kPa (36 mmHg; a value that could be reached both at sea level and altitude). The HVR was evaluated as the slope of the linear regression line relating the increase in ventilation to the drop in oxygen saturation [5]. During recordings 2 to 5, the expiratory flow was monitored by a heated Fleish pneumotachograph (Metabo, Epalinges, Switzerland) connected to a mouthpiece. During all recordings, oxygen saturation (3740 Ohmeda Pulse Oximeter; Ohmeda, Englewood, CO, USA) and expired CO_2 (COSMOplus; Novametrix, Wallingford, CT, USA; connected to the mouthpiece, or to nasal tubes during recording 1) were monitored, as well as the electrocardiogram (by chest leads) and blood pressure (by sphygmomanometer). During the first recording, respiration was monitored by inductive belts [6] around the chest, in order to measure the respiratory rate without possible artefacts induced by the pneumotachograph [7]. The pneumotachograph was recalibrated after each re-breathing manoeuvre by a 3-L syringe. The capnograph was calibrated before and after each subject by a known gas reference (5% CO_2 gas mixture). The saturimeter was calibrated by breathing 100% O_2 mixture. All signals were acquired on a Macintosh G3 at 300 samples·s^{-1}. Interactive software analysis written by one of the current authors (L. Bernardi) calculated mean heart rate, tidal volume (V_T), V'_E, mean expiratory CO_2, P_{ET,CO_2}, and S_{a,O_2}, for each breath, according to previous formulae [3], for each sequence. During the sea-level recording session, the subjects underwent simple haematological examinations by standard methods to evaluate haemoglobin content, red blood cell count and haematocrit.

Ventilatory reserve

Since hypoxia stimulates ventilation, one could assume that for a given level of hypoxaemia, each subject ventilates at a given per cent of MVV. According to reports indicating that oxygen saturation at the summit of Mt Everest is in the range of 70% [2], the present authors defined the ventilatory reserve as $=100 \times (MVV - V'_{E(S_{a,O_2}=70)})/MVV$) (fig. 1). This is based on the same formula commonly used to define the ventilatory reserve during exercise at sea level (breathing reserve $=100 \times (MVV - V'_E)/MVV$) [3]. In addition, the reserve was also reported as the difference $MVV - V'_{E(S_{a,O_2}=70)}$, in L·min^{-1}.

Ventilatory efficiency

Ventilatory efficiency could be defined in different ways. At sea level, an established marker of ventilatory efficiency can be obtained by the dead space/tidal volume ratio (V_D/V_T), by

TABLE 1 Anthropometric and baseline haematological data

	Summiters without oxygen	Other climbers	p-value
Subjects n	5	6	
Age yrs	38±5	39±7	NS
Height cm	176±5	176±5	NS
Weight kg	69.3±5.5	72.3±6.2	NS
Body mass index kg·m^{-2}	22.2±1.4	23.1±1.4	NS
Body surface area m^2	1.85±0.09	1.88±0.10	NS
Red blood cell count 10^6·mm^{-3}	5.09±0.25	5.00±0.18	NS
Haemoglobin g·dL^{-1}	15.5±1.0	14.8±0.4	NS
Haematocrit %	45.4±2.8	43.7±1.2	NS

Data are presented as mean±SD, unless otherwise stated. NS: nonsignificant.

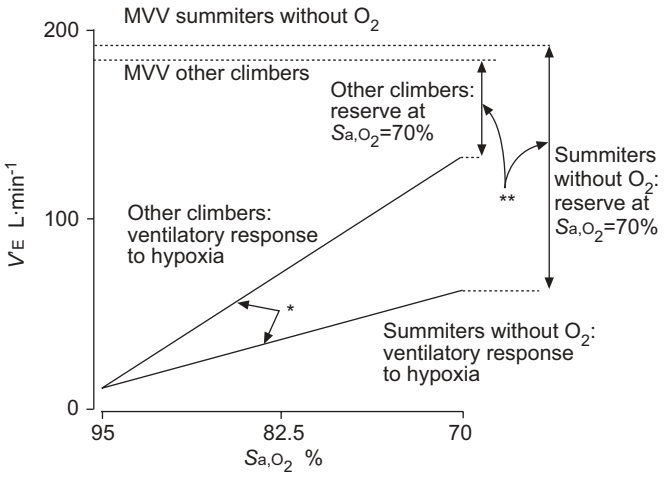

FIGURE 1. Schematic diagram showing the relationship between the ventilatory response to hypoxia and the ventilatory reserve. Data were obtained after 15 days at altitude (9 days at 5,200 m). The significances reported refer to the difference in hypoxic ventilatory response (HVR) mean slopes between the two groups (which were drawn from 95% oxygen saturation (S_{a,O_2}) down to 70%), and to the mean ventilatory reserve between the two groups. Complete numerical data are reported in table 3. The ventilatory reserve was calculated by subtracting the ventilation reached at S_{a,O_2}=70% from maximal voluntary ventilation (MVV). The value of 70% was chosen because this is an average value found on the summit of Mt Everest [2]. The subjects who eventually reached the summit of Mt Everest or K2 without oxygen were characterised by a lower ventilatory response during acclimatisation, allowing them to maintain a ventilatory reserve at rest of 66.6% when S_{a,O_2}=70%, whereas those who could not had a reserve of only 26.7%, as a consequence of a higher HVR. *: $p<0.05$; **: $p<0.01$. V'_E: minute ventilation.

measuring the CO_2 levels in the arterial blood and expired air [3, 8]. The current authors obtained a simple indirect estimate of this variable, similar to standard commercial methods, by the single breath test ''SBT-CO_2'' and Bohr formula [8]: $V_D/V_{Testimated}=(P_{a,CO_2}-P\bar{E},CO_2)/P_{a,CO_2}$ (where P_{a,CO_2} is the non-invasive estimate of arterial P_{CO_2}, based on end-tidal P_{CO_2}, and $P\bar{E},CO_2$ is mixed expired CO_2). In addition, the current authors defined a simple, global and noninvasive estimate of ventilatory efficiency, relative to a particular level of ambient hypoxia, as the amount of ventilation required to achieve a given level of oxygen saturation. This was evaluated as the simple ratio $S_{a,O_2}/V'_E$.

Statistical analysis

Data are presented as mean±SD and analysed by mixed design ANOVA (repeated measures in two groups [9]), to test for differences between groups and between sea level and altitude. Due to the 2×2 comparisons (two groups and two conditions), exact significance levels could be obtained by unpaired (between groups) and paired (between conditions) t-test, when overall significances were ascertained by ANOVA.

RESULTS

Five of the 11 subjects studied reached one (Everest n=2, K2 n=2) or both (n=1) summits without oxygen supplementation. Two of the remaining six subjects reached the Mt Everest summit but needed oxygen supplementation. The present authors thus divided the climbers into two groups: ''summiters without oxygen'' (five subjects) and ''other climbers'' (six subjects). The main anthropometric and haematological characteristics of the groups were not different (table 1). At sea level, no significant differences between the two groups were found in any of the variables (table 2).

After 15 days of stay at altitude, all subjects increased their resting ventilation and hypoxic ventilatory response, and decreased their P_{ET,CO_2} and S_{a,O_2} levels, as compared to sea level. However, the ''summiters without oxygen'' showed significantly lower V'_E, lower respiratory rate, lower HVR and higher P_{ET,CO_2} levels (table 3). The differences in ventilatory variables remained, even after correction for body surface area (table 3). Correction for height, body mass index and body weight gave similar results (not reported in the tables). The ventilatory reserve was markedly higher in the ''summiters without oxygen'' group (fig. 1). The ratio $S_{a,O_2}/V'_E$ was also higher in the ''summiters without oxygen'' group, and the V_D/V_T ratio was lower. There were no significant differences in vital capacity and maximal voluntary ventilation. At altitude, a significant correlation between the ventilatory reserve and $S_{a,O_2}/V'_E$ (fig. 2) was found.

Compared to spontaneous breathing, slow breathing increased the $S_{a,O_2}/V'_E$ ratio and decreased the V_D/V_T ratio in the ''other climbers'' group, so that values were no longer different from the ''summiters without oxygen'' group. As expected, exposure to hypoxia tended to increase heart rate and blood pressure, but the increase was less marked in the ''summiters without oxygen'' group (tables 2 and 3).

DISCUSSION

Main findings

The climbers who could reach the highest summits without oxygen were characterised by a lower ventilatory sensitivity to hypoxia, as compared to those who did not succeed or needed supplemental oxygen. They also showed a slower breathing rate, lower V'_E, more efficient respiration, and a higher ventilatory reserve. All these differences became apparent only during acclimatisation, probably suggesting the result of an adaptive (rather than constitutive) response to prolonged hypoxia.

Possible explanations

Lower sensitivity to hypoxia increases ventilatory reserve for extreme altitudes

Ventilation cannot increase indefinitely and subjects with very high ventilatory response to hypoxia may reach their ventilatory limits at lower altitudes. The current authors have set this limit at MVV, and calculated a ventilatory reserve as the difference between this value and the ventilation relative to the level of S_{a,O_2} (70%) found at the summit of Mt Everest [2]. Figure 1 shows that in subjects with higher HVR (''other climbers'' group) the ventilation was rather close to MVV when S_{a,O_2} reached 70%. Therefore, during the ascent to extreme altitudes, they might have increased ventilation close to their individual limits (by exhausting their reserve) already at an altitude well below the summit, then being forced to either descend or to use supplemental oxygen.

Conversely, the ''summiters without oxygen'' (due to their relatively lower sensitivity to hypoxia) could increase their

TABLE 2 Data obtained at sea level

	Summiters without oxygen	Other climbers	p-value
Subjects n	5	6	
Spontaneous breathing			
Resp. rate (pneumotach.) breaths·min^{-1}	8.1±3.9	9.9±3.1	NS
Resp. rate (inductive belt) breaths·min^{-1}	10.2±4.9	12.3±3.6	NS
V_T mL	1237±481	1005±292	NS
V'_E L·min^{-1}	8.5±1.1	9.5±3.1	NS
P_{ET,CO_2} mmHg	40.7±2.4	39.4±3.9	NS
S_{a,O_2} %	98.6±0.4	98.1±0.83	NS
V_T/BSA mL·m^{-2}	673±262	528±137	NS
V'_E/BSA L·min^{-1}·m^{-2}	4.64±0.74	4.99±1.40	NS
6 breaths·min^{-1} controlled breathing			
Resp. rate breaths·min^{-1}	6.1±0.2	6.0±0.1	NS
V_T mL	1631±240	2153±908	NS
V'_E L·min^{-1}	9.9±1.7	13.1±5.5	NS
P_{ET,CO_2} mmHg	38.8±3.9	36.8±5.8	NS
S_{a,O_2} %	98.4±0.4	98.4±0.7	NS
V_T/BSA mL·m^{-2}	891±178	1121±441	NS
V'_E/BSA L·min^{-1}·m^{-2}	5.43±1.20	6.83±2.66	NS
Maximal parameters			
MVV L·min^{-1}	165.6±22.7	155.2±29.6	NS
VC mL	5143±756	5173±813	NS
MVV/BSA L·min^{-1}·m^{-2}	89.6±10.3	81.9±15.8	NS
VC/BSA mL·m^{-2}	2796±446	2716±303	NS
Ventilatory control			
HVR L·min^{-1}/% S_{a,O_2}	-0.73±0.36	-1.25±1.31	NS
Ventilatory efficiency			
$S_{a,O_2}/V'_E$ sp. br. %/L·min^{-1}	11.73±1.63	11.32±4.29	NS
$S_{a,O_2}/V'_E$ 6 breaths·min^{-1} %/L·min^{-1}	10.13±1.63	9.10±4.93	NS
V_D/V_T sp. br.	0.196±0.072	0.187±0.048	NS
V_D/V_T 6 breaths·min^{-1}	0.165±0.079	0.133±0.095	NS
Ventilatory reserve			
100×(MVV–$V'_{E(S_{a,O_2}=70)}$)/MVV %	81.4±6.1	68.4±15.4	NS
MVV–$V'_{E(S_{a,O_2}=70)}$ L·min^{-1}	134.9±22.4	105.6±31.2	NS
Cardiovascular parameters			
Heart rate beats·min^{-1}	58.2±6.1	59.5±8.1	NS
Systolic blood pressure mmHg	120.1±10.1	110.8±14.4	NS
Diastolic blood pressure mmHg	69.4±8.2	70.3±14.8	NS

Data are presented as mean±SD, unless otherwise stated. NS: nonsignificant; resp.: respiratory; pneumotach.: pneumotachograph; V_T: tidal volume; V'_E: minute ventilation; P_{ET,CO_2}: end-tidal carbon dioxide pressure; S_{a,O_2}: oxygen saturation; BSA: body surface area; MVV: maximal voluntary ventilation; VC: vital capacity; HVR: hypoxic ventilatory response; V_D/V_T: dead space/tidal volume; sp. br.: spontaneous breathing. 1 mmHg = 0.133 kPa.

ventilation more gradually while ascending to higher altitudes, and thus reach very high levels of ventilation only at the summit, but still remain below their limits.

Indeed, measurements of ventilation during the first 15 days of acclimatisation at 3,800–5,200 m, even during a hypoxic stimulus, do not accurately reflect the ventilations reached at extreme altitude. Rather, further adaptation will continue to take place as a function of time and altitude, with the result of increasing the ventilatory sensitivity to hypoxia and further decreasing the ventilatory reserve in all subjects. However, those with the lowest reserve will be more prone to exhaust their reserve at lower altitudes.

Despite lower V'_E, subjects in the ''successful climbers'' group had similar S_{a,O_2} levels, suggesting that lower V'_E could be compensated by a higher ventilatory efficiency.

Lower sensitivity to hypoxia and high ventilatory reserve are associated with higher ventilatory efficiency

After 15 days of acclimatisation, both indices of ventilatory efficiency were better in the ''successful climbers'' than in the ''other climbers'' group. As well as the V_D/V_T ratio (a well-known index of efficiency), the present authors have also calculated another index (the $S_{a,O_2}/V'_E$ ratio), which expresses how much ventilation is required to increase oxygen saturation to a given value. At sea level, due to the high values of ambient

TABLE 3 Data obtained after 15 days of exposure to high altitude (9 days at 5,200 m)

	Summiters without oxygen	p-value (*versus* sea level)	Other climbers	p-value (*versus* sea level)	p-value (between groups)
Subjects n	5		6		
Spontaneous breathing					
Resp. rate (pneumotach.) breaths·min-1	10.7±4.3	NS	20.2±1.9	<0.0025	<0.001
Resp. rate (inductive belt) breaths·min^{-1}	10.8±5.9	NS	18.7±4.3	<0.002	<0.05
V_T mL	1391±505	NS	973±134	NS	NS
V'_E L·min^{-1}	13.3±1.8	<0.01	19.2±1.5	<0.0005	<0.0002
P_{ET,CO_2} mmHg	28.2±1.4	<0.0001	24.2±2.4	<0.001	<0.01
S_{a,O_2} %	87.3±1.8	<0.0005	88.7±2.3	<0.0001	NS
V_T/BSA mL·m^{-2}	750±252	NS	511±52	NS	<0.05
V'_E /BSA L·min^{-1}·m^{-2}	7.21±0.78	<0.01	10.13±0.74	<0.001	<0.0001
6 breaths·min^{-1} controlled breathing					
Resp. rate breaths·min^{-1}	6.0±0.5	NS	6.2±0.7	NS	NS
V_T mL	2383±247	<0.025	2428±1060	NS	NS
V'_E L·min^{-1}	14.4±1.4	<0.025	15.1±0.62	NS	NS
P_{ET,CO_2} mmHg	28.1±2.4	<0.005	26.6±2.7	<0.01	NS
S_{a,O_2} %	88.4±1.9	<0.0005	87.9±1.5	<0.0001	NS
V_T/BSA mL·m^{-2}	1291±111	<0.025	1285±582	NS	NS
V'_E /BSA L·min^{-1}·m^{-2}	7.81±0.62	<0.025	8.01±3.44	NS	NS
Maximal parameters					
MVV L·min^{-1}	191.4±35.5	NS	183.0±17.3	NS	NS
VC mL	5258±581	NS	5494±367	NS	NS
MVV/BSA L·min^{-1}·m^{-2}	103.4±15.0	NS	96.3±4.7	NS	NS
VC/BSA mL·m^{-2}	2847±229	NS	2897±166	NS	NS
Ventilatory control					
HVR L·min^{-1}/% S_{a,O_2}	-2.14±1.13	<0.025	-5.09±2.53	<0.025	<0.05
Ventilatory efficiency					
$S_{a,O_2}/V'_E$ (sp. br.) %/L·min^{-1}	6.66±0.86	<0.005	4.64±0.32	<0.025	<0.0005
$S_{a,O_2}/V'_E$ (6 breaths·min^{-1}) %/L·min^{-1}	6.19±0.66	<0.025	6.64±2.51	NS	NS
V_D/V_T sp. br.	0.092±0.035	NS	0.162±0.047	NS	<0.025
V_D/V_T 6 breaths.min^{-1}	0.062±0.078	NS	0.047±0.084	NS	NS
Ventilatory reserve					
100 × (MVV–$V'_{E(Sa,O_2=70)}$)/MVV %	66.6±14.2	NS	26.7±21.3	<0.002	<0.01
MVV– $V'_{E(Sa,O_2=70)}$ L·min^{-1}	129.3±44.2	NS	47.6±38.9	<0.01	<0.01
Cardiovascular parameters					
Heart rate beats·min^{-1}	72.9±9.5	NS	72.6±11.3	<0.05	NS
Systolic blood pressure mmHg	127.2±16.2	NS	130.3±9.6	NS	NS
Diastolic blood pressure mmHg	85.4±11.9	<0.05	90.4±8.3	<0.01	NS

Data are presented as mean±SD, unless otherwise stated. NS: nonsignificant; resp: respiratory; pneumotach.:pneumotachograph; V_T: tidal volume; V'_E: minute ventilation; P_{ET,CO_2}: end-tidal carbon dioxide; S_{a,O_2}: oxygen saturation; BSA: body surface area; MVV: maximal voluntary ventilation; VC: vital capacity; HVR: hypoxic ventilatory response; V_D/V_T: dead space/tidal volume; sp.br.: spontaneous breathing. 1 mmHg=0.133 kPa.

P_{O_2}, the changes in S_{a,O_2} are very small despite large changes in ventilation. However, at high altitude, S_{a,O_2} is much more variable, and depends essentially on the level of alveolar ventilation. An efficient breathing pattern (characterised by a lower proportion of overall dead space/total ventilation) will require a lower total (alveolar+dead space) ventilation to obtain a given level of S_{a,O_2}. Although alveolar ventilation could not be measured directly, both indices of efficiency suggested that the ''successful climbers'' had a higher relative proportion of alveolar/total ventilation during acclimatisation to altitude.

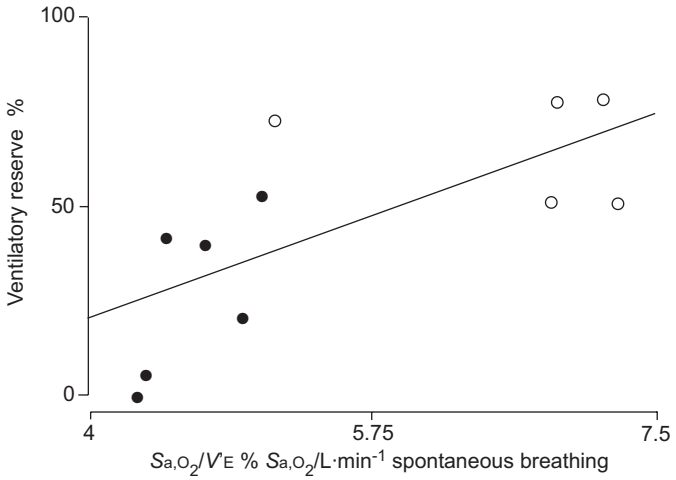

FIGURE 2. Correlation between ventilatory efficiency and ventilatory reserve. The data were obtained after 15 days at altitude (9 days at 5,200 m) for ''summiters without oxygen'' (○) and ''other climbers'' (●) groups. S_{a,O_2}: oxygen saturation; V'_E: minute ventilation. r=0.69; p=0.018.

Slower breathing could link lower HVR and higher respiratory efficiency

The increased efficiency and the higher ventilatory reserve were found to be linked (fig. 2). A common underlying factor could be the breathing rate, which was markedly lower in the ''summiters without oxygen'' group during acclimatisation (table 3). Breathing slowly and/or deeply may improve gas exchange at sea level [6, 8, 10–14], at altitude [15] and in experimental models [16], and, in addition, slower breathing reduces the HVR [17, 18]. The lower respiratory rate in the ''summiters without oxygen'' group was not an artefact caused by the mouthpiece [7]. The difference remained even when recording was carried out with only the inductive belt (tables 2 and 3) and without the mouthpiece.

A confirmation of the importance of slowing breathing rate can be seen by the data obtained when all subjects were forced to breath at a fixed slow respiratory rate (6 breaths·min^{-1}): both indices of ventilatory efficiency (V_D/V_T and $S_{a,O_2}/V'_E$) improved in the ''other climbers'' group and all group differences disappeared even at altitude (table 3). These findings were obviously transitory, but similar effects can be maintained by specific respiratory training [6, 18].

With increasing altitude and hypoxia the respiratory rate is expected to increase; however, the advantages of maintaining a relatively lower breathing rate and a proportionally higher V_T remain. This could be anticipated by the lower V'_E at 70% S_{a,O_2}, seen in the ''summiters without oxygen'' (fig. 1).

Together with the slower breathing rate, subjects in the ''summiters without oxygen'' group showed a lower increase in heart rate and blood pressure from sea level to altitude (tables 2 and 3). Due to the reciprocal influences between chemo- and baro-reflexes [19], these findings indicate that, together with a lower increase in ventilation, these subjects had a lower need to increase sympathetic activation, which could help maintain exercise capacity at extreme altitudes. Further studies are necessary in order to examine in deeper detail the cardiovascular control during adaptation to high altitude in similar subjects.

Very high sensitivity to hypoxia may be counterproductive

From the alveolar air equation [1, 2], at extreme altitudes, it is known that very high ventilation is needed in order to drive the P_{CO_2} down to a low enough level to maintain an alveolar P_{O_2} compatible with life. Accordingly, it has been suggested that the higher the ventilatory response, the better the climbing performance should be at moderate–high altitudes [1]. However, it has been found that with increasing ventilation the work of breathing also increases, and there is a critical ventilation level at which the increase in respiratory work blunts the increase in arterial P_{O_2} [20]. Similarly, subjects with very high HVR may incur a greater work of breathing that may be counterproductive at extreme altitude [21]. This was demonstrated in a group of subjects exercising at 5,050 m, where only the subject with the lowest increase in maximal ventilation at high altitude (as compared to sea level) remained below his critical ventilation during exercise [22]. Therefore, a very high HVR is useful at moderate–intermediate altitudes, when the increase in ventilation remains well below critical limits, whereas at extreme altitudes the metabolic cost of excessive breathing may be counterproductive.

The HVR is traditionally evaluated by breathing at constant CO_2 (see Methods). In real life, the hypocapnia resulting from hyperventilation in turn reduces the ventilatory stimulus and, hence, maintains the ventilatory reserve. However, if this effect were determinant, it should have favoured those subjects with higher ventilatory responses. Instead, the current findings indicate that there is little advantage in increasing ventilation without a parallel increase in efficiency.

Conclusions

A key requisite to achieving the highest altitudes without supplemental oxygen seems to be a high ventilatory efficiency, which may limit the stimulus for an excessive increase in ventilation. This may have several important benefits, as follows: 1) it reduces the work of breathing, which, at extreme altitudes, becomes extremely relevant and may cancel the advantages of increased ventilation [20–22]; 2) it reduces the thermal exchanges and, hence, the thermal loss [1]; and 3) it allows a sufficient ventilatory reserve to allow the needed ventilation at altitudes where the extreme hypoxia would otherwise stimulate ventilation beyond sustainable values.

These findings agree with the concept that a well-functioning HVR is necessary [1] to climb to altitude, and a very brisk response is certainly useful to perform work at intermediate altitudes. However, the current findings suggest that HVR should be only moderately increased, in order to allow very high (yet sustainable) ventilation at extreme levels of hypoxia. High ventilatory efficiency is essential to maintain adequate level of arterial P_{O_2} despite a lower increase in V'_E. In this respect, a slower breathing rate could be an important factor, as it combines the increase in efficiency and the reduction in HVR. The differences between climbers became evident only when acclimatisation had begun, suggesting that was the result of a different adaptation strategy.

There are practical implications of these findings. Training in slow breathing may speed up and simplify the adaptation process to high altitude, and help withstand severe levels of hypoxaemia by improving respiratory efficiency, even at sea level. This may apply to relevant cardiovascular and respiratory diseases, like chronic heart failure [6, 23, 24] and chronic obstructive pulmonary disease [25, 26].

In conclusion, summiters without oxygen may have unconsciously adopted a breathing strategy that allowed them to maintain a higher ventilatory efficiency during acclimatisation, and perhaps as a consequence, a lower increase in hypoxic ventilatory response. This could have given them a sufficient ventilatory reserve to climb without oxygen supplementation. Therefore, a very high hypoxic ventilatory response may not be necessary to climb in extreme hypoxia without oxygen supplementation, provided that ventilatory efficiency is optimised.

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REFERENCES

1 Ward MP, Milledge JS, West JB. High altitude medicine and physiology. 2nd Edn. London, Chapman & Hall, 1995; pp. 240–263.
2 West JB. Human limits for hypoxia. The physiological challenge of climbing Mt. Everest. *Ann N Y Acad Sci* 2000; 899: 15–27.
3 Wasserman K, Hansen JE, Sue DY, Casaburi R, Whipp BJ. Principle of exercise testing and interpretation. 3rd Edn. Baltimore (MD), Lippincott Williams and Wilkins, 1999.
4 Houston C. Going higher. Oxygen man and mountain. Seattle (WA), Mountaineers, 1998; p. 174.
5 Rebuck AS, Campbell EJM. A clinical method for assessing the ventilatory response to hypoxia. *Am Rev Respir Dis* 1974; 109: 345–350.
6 Bernardi L, Spadacini G, Bellwon J, Hajiric R, Roskamm H, Frey AW. Effect of breathing rate on oxygen saturation and exercise performance in chronic heart failure. *Lancet* 1998; 351: 1308–1311.
7 Askanazi J, Silverberg PA, Foster RJ, Hyman AI, Milic-Emili J, Kinney JM. Effects of respiratory apparatus on breathing pattern. *J Appl Physiol* 1980; 48: 577–580.
8 Fletcher R, Jonson B. Deadspace and the single breath test for carbon dioxide during anaesthesia and artificial ventilation. *Br J Anaesth* 1984; 56: 109–119.
9 Bruning JL, Kintz BL. Computational handbook of statistics. Glenview (IL), Scott Foresman, 1968; pp. 54–61.
10 Al-Saady N, Bennett ED. Decelerating inspiratory flow waveform improves lung mechanics and gas exchange in patients on intermittent positive-pressure ventilation. *Intensive Care Med* 1985; 11: 68–75.
11 Fletcher R, Jonson B. Prediction of the physiological dead space/tidal volume ratio during anaesthesia/IPPV from simple pre-operative tests. *Acta Anaesthesiol Scand* 1981; 25: 58–62.
12 Fletcher R, Jonson B, Cumming G, Brew J. The concept of deadspace with special reference to the single breath test for carbon dioxide. *Br J Anaesth* 1981; 53: 77–88.
13 Cooper EA. Physiological deadspace in passive ventilation. II. Relationships with tidal volume, frequency, age, and minor upsets of respiratory health. *Anaesthesia* 1967; 22: 199–219.
14 Rehder K, Sessler AD, Rodarte JR. Regional intrapulmonary gas distribution in awake and anesthetized-paralyzed man. *J Appl Physiol* 1977; 42: 391–402.
15 Keyl C, Schneider A, Gamboa A, *et al.* Autonomic cardiovascular function in high-altitude Andean natives with chronic mountain sickness. *J Appl Physiol* 2003; 94: 213–219.
16 Bowes CL, Richardson JD, Cumming G, Horsfield K. Effect of breathing pattern on gas mixing in a model with asymmetrical alveolar ducts. *J Appl Physiol* 1985; 58: 18–26.
17 Bernardi L, Gabutti A, Porta C, Spicuzza L. Slow breathing reduces chemoreflex response to hypoxia and hypercapnia and increases baroreflex sensitivity. *J Hypertens* 2001; 19: 2221–2229.
18 Spicuzza L, Gabutti A, Porta C, Montano N, Bernardi L. Yoga and chemoreflex response to hypoxia and hypercapnia. *Lancet* 2000; 356: 1495–1496.
19 Somers VK, Mark AL, Abboud FM. Interaction of baroreceptor and chemoreceptor reflex control of sympathetic nerve activity in normal humans. *J Clin Invest* 1991; 87: 1953–1975.
20 Otis AB, Fenn WO, Rahn H. The mechanics of breathing in man. *J Appl Physiol* 1950; 2: 592–607.
21 Schoene RB. Limits of human lung function at high altitude. *J Exp Biol* 2001; 204: 3121–3127.
22 Cibella F, Cuttitta G, Romano S, Grassi B, Bonsignore G, Milic-Emili J. Respiratory energetics during exercise at high altitude. *J Appl Physiol* 1999; 86: 1785–1792.
23 Narkiewicz K, Pesek CA, Van De Borne PJH, Kato M, Somers VK. Enhanced sympathetic and ventilatory responses to central chemoreflex activation in heart failure. *Circulation* 1999; 100: 262–267.
24 Ponikowski P, Chua TP, Anker SD, *et al.* Peripheral chemoreceptors hypersensitivity. An ominous sign in patients with chronic heart failure. *Circulation* 2001; 104: 544–549.
25 Faling LJ. Pulmonary rehabilitation-physical modalities. *Clin Chest Med* 1986; 7: 599–618.
26 Gigliotti F, Coli C, Bianchi R, *et al.* Exercise training improves exertional dyspnea in patients with COPD: evidence of the role of mechanical factors. *Chest* 2003; 123: 1794–1802.