Maximum oxygen consumption and heat loss facilitation in small homeotherms by He-O₂

MARIO ROSENMMANN AND PETER MORRISON
Institute of Arctic Biology, University of Alaska, Fairbanks, Alaska 99701

 abstract
Although animals in nature spend the majority of their time resting or at low levels of activity, some functions critical for survival such as fighting, escaping, or predation greatly increase the energy demand. The maximum capability to increase metabolism is the main factor in limiting the intensity of such physical activity and, as well, sets the limit for cold tolerance. Evaluations of maximum oxygen uptake (M_mₐₓ) in mammals have been made by cold exposure in air or water, by exercise on treadmills, by swimming, or by a combination of these. These methods may require extended training sessions for running (as long as 1 mo), cutting off the tail, and elimination of inept performers (32). Another serious reservation is that these procedures may directly modify the character under study. Exposures to subfreezing temperatures risk peripheral cold injury or lethal hypothermia (23). Removal of the natural insulation can increase metabolism greatly but, again, is traumatic and results in irreversible change.

To avoid such extreme cold exposure and the injuries reported during exercise (32, 16), we have developed the use of a helium-oxygen atmosphere to raise the heat output of small homeotherms to maximum levels at more modest ambient temperatures (Tₘ). The effect of He-O₂ in increasing metabolism has been known for some time (3, 36), and although once in some question its action is now generally ascribed to the increased thermal conductance of the gas (5, 25, 34). Since the insulative quality of fur or feathers depends on the slow transfer of heat through the enclosed air spaces, the substitution of a 4 times more conductive medium such as 80% He-20% O₂ (26) should greatly facilitate heat transfer. However, the actual metabolic increases reported in small mammals are so much more modest, e.g., <25% in rats (34) or <30% in mice (3, 10), that the exact nature of the effect is still very much in question.

METHODS
Tests were conducted on two laboratory species, the white mouse and the white rat, previously assessed for M_mₐₓ by various other procedures. Three further strains of Mus musculus, a hairless mutant (HRS/J), and feral house mice from 15,000 feet at Morrococha, Peru and from Arkansas were also compared. In addition, measurements were made on wild species native to different habitats: arctic (Microtus oeconomus from Fairbanks), alpine (Calomys ducilla from 13,000 feet near Puno, Peru), and subtropical (Calomys callosus from San Joaquim, Beni Province, Bolivia), and the pygmy mouse Baiomys taylori. The final species was a small arctic bird, the redpoll (Acanthis flammea), also native to Fairbanks. We are indebted to Dr. Oliver P. Pearson and Dr Karl M. Johnson for the respective Calomys, to Dr. Hermann Pohl for the redpolls, and to Dr. John Seelander for the lowland Mus. These rodents were maintained in our animal facility at a neutral Tₘ of 20–24°C. Three to eight individuals of each type were tested at 735–750 torr.

O₂ consumption was measured in a closed-circuit manometric respirometer (28). Since the oxygen consumed by the animal is replaced by successive aliquots, the inert component maintains its concentration as established. The metabolic chambers of stainless steel were submerged in a thermoregulated water-glycol bath. After a variable length of time (1–3 h) in which the metabolic rate in air was measured, the chambers were flushed with 5–6 times their volume of an 80% He-20% O₂ mixture from a proportioning gas mixing pump or from a gas tank. Use of the gas tanks with premixed He-O₂ reduced the purging time to only 2 min as compared with 7–9 min with the mixing pumps. To avoid temperature changes, the He-O₂ mixture was admitted through a submerged copper coil.
Food as apple, carrot, and sunflower seed was generally available during the tests. Regardless of the duration and temperature of the metabolic measurements, the animals were tested about 4 times a week, and generally 2 days were allowed between consecutive tests at high submaximal rates.

RESULTS

Immediately after the substitution of He-O2 for air, O2 consumption increased well above the resting levels in air, as shown in Fig. 1 for *M. oeconomus*. Of interest also is the suppression in He-O2 of the metabolic cycles reflecting changes in activity or posture, an effect also seen at lower Ta in air. These relations are shown in Fig. 2 for a series of Ta between 26 and 7°C again for *M. oeconomus*. The respective values in air and in He-O2 lay along two straight lines which extrapolate to the Tb at 39°C to fit the relations:

\[
M = C(T_b - T_a) = C\Delta T \\
M = C^{He}\Delta T
\]

The constant C usually designated as the (minimum) conductance actually includes a component of evaporative/respiratory heat loss, but at these Ta below thermal neutrality this represents a constant (small) fraction of the thermal loss through the surface—a cost of "chemical" thermoregulation. Accordingly, C is a measure of the overall facility for heat loss from the body and will reflect changes in the properties of the insulative layers. In this example the substitution of He-O2 increased conductance from 0.178 to 0.377 mlO2 (g·h·°C)-1, a factor of 2.12 (C^{He}/C).

At temperatures below the thermoneutral zone, heat production more than doubled in He-O2 until at about 6°C (in this species) a limit was reached, indicating maximum metabolic capability for temperature regulation (M_{max}). In fact, at 1°C in He-O2 the maximum heat production could only be maintained for approximately 5 min, and longer exposure under these conditions resulted in decreased O2 consumption and hypothermia. Exposure to lower temperatures in He-O2 did not seem to modify their maximum response, but the highest rates were held for a shorter time. The quotient, M_{max}/C, provides an estimate of the maximum temperature differential tolerable by the animal, in this case -70°C. This has been shown graphically by extrapolation of M = C\Delta T to the value M_{max} = 12.5 mlO2 (g·h)-1 at -31°C. It may be noted that we have observed limiting values of cold tolerance of this species (neutral acclimation) at -25 to -30°C (unpublished observations).

A somewhat lower ratio was observed in white rats (Fig. 3). Maximum rates in He-O2 were attained within 6-10 min at -3°C. Exposure at -10°C in He-O2 resulted in reduced O2 consumption and hypothermia.

The effects of He-O2 on highland house mice and white mice are shown in Fig. 4. The ratio C^{He}/C was 2.3 in the house mice as compared to 2.1 in white mice and M_{max} was 24% higher, 13.8 vs. 11.1 mlO2 (g·h)-1. In lowland...
house mice the $M_{\text{max}}$ was intermediate at 12.3 mlO$_2$ (g·h)$^{-1}$.

To gain insight into the relation between the surface insulation and the effects of He-O$_2$, hairless mice were also tested (Fig. 5). The ratio of the thermal conductance in air of hairless versus normal mice was 1.9, close to a previously reported ratio of 2.2 for these strains (29). However, in He-O$_2$, the conductance ratio hairless versus normal was only 1.3 due to the much smaller response of the hairless mice to helium (C$^{\text{He}}$/C = 1.40). $M_{\text{max}}$ in hairless mice was 13% higher than in the normal white mice (12.5 vs. 11.1 mlO$_2$ (g·h)$^{-1}$) but still 10% lower than in the feral mice. Similarly, the metabolic expansivity of the hairless mice (10.5 mlO$_2$ (g·h)$^{-1}$) lay between those of the two other strains. $M_{\text{max}}$/M$_{\text{min}}$ ratios were 6.3 in both the white and the hairless mice as compared with 7.2–7.3 in both feral groups.

Results of He-O$_2$ exposure in Calomys ducilla, a highland species, and Calomys callosus, a tropical species, are shown in Fig. 6. $M_{\text{max}}$ of 14 mlO$_2$ (g·h)$^{-1}$ was found in the 16-g C. ducilla and 6.8 mlO$_2$ (g·h)$^{-1}$ in the 3 times larger C. callosus.

Redpolls (Acanthis flammia) were treated in a similar way to the rodents with the exception of a wooden perch in the cages and an aluminum cover to maintain a dark environment and so diminish spontaneous activity. O$_2$ consumption values in air and in He-O$_2$ are shown in Fig. 7. The highest ratio, C$^{\text{He}}$/C = 2.6, was observed in the redpoll and a $M_{\text{max}}$ of 21.8 mlO$_2$ (g·h)$^{-1}$ was elicited at $-5^\circ$C.

Table 1 summarizes the thermogenetic effects of He-O$_2$ in the experimental species, the temperatures at which $M_{\text{max}}$ was elicited in He-O$_2$, the extrapolated air temperatures for these rates, and the thermal conductance values in relation to the He-O$_2$ atmosphere and to the animal's surface area. In general, $M_{\text{max}}$ in the rodent species was obtained in He-O$_2$ at 13–30°C warmer temperatures than expected in air, but in the hairless mice the difference was only 7°C. In contrast, a 70°C warmer temperature for $M_{\text{max}}$ elicitation in He-O$_2$ was estimated for the redpolls.
A comparison of our data on \( M_{\text{max}} \) of mice, rats, and of the pygmy mouse with reported values for the same species but obtained with different methodologies is shown in Table 2. Our values for white mice are equal or higher than reported values for mice kept at neutral or warm temperatures (21). Ratios of \( M_{\text{max}} \) obtained in \( \text{He-}O_2 \) are only 4% lower than those from cold-acclimated animals (32). Similarly, \( M_{\text{max}} \) values of \( \text{He-}O_2 \) for other species, such as the pygmy mouse and the house mouse, are equal or higher than reported capabilities in normal mice (12). In other species, such as the white rats, \( M_{\text{max}} \) in \( \text{He-}O_2 \) temperatures is up to 8% lower than from cold-acclimated animals (32).

Published data for the rest of our wild species seem to be unavailable, but some values have been reported in references (28-30).

**DISCUSSION**

**HEAT LOSS AND MAXIMUM OXYGEN CONSUMPTION IN HE-\( O_2 \)**

Published data for the rest of our wild species seem to be unavailable, but some values have been reported in references (28-30).

**TABLE 2. Comparison of maximum metabolism and \( M_{\text{max}}/M_{\text{min}} \) ratios obtained with different techniques**

<table>
<thead>
<tr>
<th>Species</th>
<th>Weight, g</th>
<th>Acclim.</th>
<th>( M_{\text{max}} ), ml O_2/g h</th>
<th>( M_{\text{max}}/M_{\text{min}} )</th>
<th>Reference and Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Mus musculus</em> albino</td>
<td>18.3</td>
<td></td>
<td>10.75</td>
<td>3.5</td>
<td>(8) Cold water wetting</td>
</tr>
<tr>
<td></td>
<td>26.5</td>
<td>c</td>
<td>10.10</td>
<td>5.2</td>
<td>(13) Run 6 m/min at 2°C</td>
</tr>
<tr>
<td></td>
<td>26.7</td>
<td>c</td>
<td>12.15</td>
<td>6.5</td>
<td>(12) Run 5 m/min at -10°C</td>
</tr>
<tr>
<td></td>
<td>33.0</td>
<td>c</td>
<td>10.50</td>
<td>4.2</td>
<td>(32) Run 23 m/min at -10°C</td>
</tr>
<tr>
<td></td>
<td>34.0</td>
<td>w</td>
<td>9.30</td>
<td>4.3</td>
<td>(32) Run 19 m/min at -3°C</td>
</tr>
<tr>
<td></td>
<td>33.4</td>
<td>c</td>
<td>7.40</td>
<td>4.2</td>
<td>(18) Noradrenaline, 1.7 mg/kg</td>
</tr>
<tr>
<td></td>
<td>29.5</td>
<td>n</td>
<td>11.10</td>
<td>6.3</td>
<td>(4) He-( O_2 ) at 7°C</td>
</tr>
<tr>
<td>Hairless</td>
<td>21.0</td>
<td>n</td>
<td>12.50</td>
<td>6.3</td>
<td>(1) He-( O_2 ) at 14°C</td>
</tr>
<tr>
<td>Wild, highland</td>
<td>17.3</td>
<td>n</td>
<td>13.80</td>
<td>7.3</td>
<td>(1) He-( O_2 ) at 2-5°C</td>
</tr>
<tr>
<td>Wild, lowland</td>
<td>17.0</td>
<td>n</td>
<td>12.30</td>
<td>7.2</td>
<td>(1) He-( O_2 ) at 10°C</td>
</tr>
</tbody>
</table>

**Rattus norvegicus albino**

<table>
<thead>
<tr>
<th>Weight, g</th>
<th>Acclim.</th>
<th>( M_{\text{max}} ), ml O_2/g h</th>
<th>( M_{\text{max}}/M_{\text{min}} )</th>
<th>Reference and Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>380</td>
<td>w</td>
<td>3.20</td>
<td>2.7</td>
<td>(19) Cold exposure at -35°C</td>
</tr>
<tr>
<td>385</td>
<td></td>
<td>2.76</td>
<td>2.7</td>
<td>(4) Cold exposure down to -33°C</td>
</tr>
<tr>
<td>290</td>
<td></td>
<td>4.89</td>
<td>3.3</td>
<td>(27) Swim with 2% load</td>
</tr>
<tr>
<td></td>
<td></td>
<td>115</td>
<td>3.6</td>
<td>(8) Cold water wetting</td>
</tr>
<tr>
<td>300*</td>
<td>w</td>
<td>3.20</td>
<td>2.7</td>
<td>(17) Run at 0°C or rest at -35°C</td>
</tr>
<tr>
<td>300*</td>
<td>c</td>
<td>5.05</td>
<td>4.2</td>
<td>(17) Run at -30°C or rest at -45°C</td>
</tr>
<tr>
<td>286</td>
<td>w</td>
<td>4.90</td>
<td>3.1</td>
<td>(32) Run 35 m/min at 6°C</td>
</tr>
<tr>
<td>334</td>
<td>c</td>
<td>5.40</td>
<td>3.1</td>
<td>(32) Run 27-37 m/min at -3°C</td>
</tr>
<tr>
<td>253</td>
<td>n</td>
<td>5.20</td>
<td>4.9</td>
<td>(1) He-( O_2 ) at -3°C</td>
</tr>
<tr>
<td>371</td>
<td>c</td>
<td>(5.53)</td>
<td>(5.0)</td>
<td>(22, 23) Cytochrome oxidase activity</td>
</tr>
</tbody>
</table>

**Baiomys taylori**

<table>
<thead>
<tr>
<th>Weight, g</th>
<th>( M_{\text{max}} ), ml O_2/g h</th>
<th>( M_{\text{max}}/M_{\text{min}} )</th>
<th>Reference and Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.3</td>
<td>10.40</td>
<td>5.3</td>
<td>(20) Exposure at 15°C</td>
</tr>
<tr>
<td>6.9</td>
<td>12.30</td>
<td>4.3</td>
<td>(1) He-( O_2 ) at 23°C</td>
</tr>
</tbody>
</table>

* Assumed.  † Acclimation: cold, warm, neutral, T_a.  ‡ This study.
The conductance ratios of 1.83 when the fur was intact, 1.62 when the fur was clipped to 1 mm, and 1.52 when the fur was totally removed.

As heat dissipation is seen to be much more affected by insulation in air than in He-O₂ (>3 times), a simple way of describing the metabolic effects of helium in different species is in terms of the functional removal of the surface insulation, regardless of its degree or quality, the metabolic increase then being proportional to the magnitude of the insulation so "removed." Thus, well-insulated animals, sensitive to small changes of skin temperature (15), would show a larger response.

Among the many applications of inert gases, He-O₂ atmospheres have been used for therapeutic reasons (2, 9), also for prevention of nitrogen narcosis in divers (1), and in recent years for induction of hypothermia in small mammals (6, 30, 31). The elicitation of maximum O₂ consumption in small homeotherms may prove to be another practical application. The rapidly attained Mmax values (3–10 min), the simplicity of operation, the avoidance of extreme cold temperatures and of treadmills and training tests are definite advantages of the present technique over the current conventional methods.

This research was supported in part by National Institutes of Health Grant GM 10102 from the National Institute of General Medical Sciences and Grant RR-00518 from the Division of Research Resources.

Received for publication 9 October 1973.

REFERENCES


