Correlations between heart rate and oxygen consumption in rodents

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MORHARDT, J. EMIL, AND SYLVIA S. MORHARDT. Correlation between heart rate and oxygen consumption in rodents. Am. J. Physiol. 221(6): 1580-1586. 1971.—Heart rates (fh) transmitted by surgically implanted radiotelemetry transmitters and oxygen consumption (VO₂) were measured simultaneously from a series of rodents. Large ranges of fh and VO₂ were obtained by allowing spontaneous activity and by changing the temperature within the metabolism chambers. There were highly significant direct correlations between fh and VO₂ in all instances, and additional regressions were calculated for other small mammals from data in the literature. The physiological significance of the shapes and slopes of the regression lines is discussed, as is the utility of the regressions for predicting VO₂ from fh in animals not in metabolism chambers.

THE RELATIONSHIP BETWEEN energy expenditure and heart rate has been examined systematically in man (1, 5, 6, 9, 10, 12, 16), sheep (25), and the blue-winged teal (20) with the intention of determining whether the heart rate could be used as a means of indirect calorimetry. The relationship has not been examined using simultaneous recordings of heart rate and metabolic rate in small mammals, probably because the maintenance of hard-wire recording leads to small active mammals, while simultaneously measuring oxygen consumption, involves disturbance of the animal and is difficult to accomplish (17). The sheep and human subjects were not disturbed by the recording apparatus and the data from the blue-winged teal were transmitted by radiotelemetry transmitters which, although attached externally, presumably did not disturb the birds. In all of these studies there was a positive correlation of the metabolic rate with the heart rate that was judged sufficiently good to be of utility as a form of indirect calorimetry.

In this study we employed radiotelemetry transmitters that were implanted surgically to minimize disturbance, and we measured simultaneously the heart rates (fh) and oxygen consumption (VO₂) of a series of small rodents. Some of the data presented here have appeared previously in abstract form (18, 19).

In addition, we compared our results with data from other small mammals from which both VO₂ and fh were recorded at a number of ambient temperatures, but not simultaneously.

MATERIALS AND METHODS

The Belding ground squirrel (Spermophilus beldingi beldingi), California ground squirrel (S. beecheyi parvulus), golden-mantled squirrel (S. lateralis chrysodurus), and bushy-tailed woodrat (Neotoma cinerea acraia) used in this study were trapped in the wild and experiments were begun within one week of capture. The California mice (Peromyscus californicus insignis) were from a colony started from wild-trapped animals in 1967, the golden hamster (Mesocricetus auratus) was purchased from a local pet store, and the albino laboratory rats were purchased from the Holtzman Co. All of the animals were given food and water ad libitum throughout the study.

The initial procedure was the surgical implantation of the radiotelemetry transmitters. Each transmitter was constructed of discrete electronic components. When ready for implantation, each transmitter was coated with a beeswax-paraffin mixture over which was applied a thin layer of medical grade silicon rubber (Dow Corning 382). The completed transmitter weighed approximately 6 g, had a volume of approximately 3.5 cm³, a transmission range of less than 6 m, and a battery life of 3-5 weeks. The 100 MHz carrier frequency was frequency modulated by the cardiac biopotential. Each transmitter had one stainless steel electrode on the body of the transmitter, and a second electrode 4-6 cm long insulated, except at the tip, with silicon rubber tubing (Dow Corning 602 135).

Prior to implantation, the animals were deeply anesthetized with 50-70 mg/kg sodium pentobarbital (Nembutal) or ether, and a midventral incision 1-2 cm long was made through the abdominal wall. The transmitter was placed in the peritoneal cavity and the insulated electrode was guided subcutaneously to the sternal region ventral to the heart, where it was sutured to the underlying muscles. The incision was then closed with silk thread. This arrangement produced excellent electrocardiograms with clearly distinguishable R waves. After recovery from anesthesia, the animals appeared to be unaware of the presence of the transmitters, and over the course of a month there was seldom any evidence of adverse tissue reaction to the transmitters. The radio signal was received by a commercial home-entertainment FM receiver (KLH 18 or Sony 7F-81W) connected to an oscillograph (E & M Physiograph) or a tachometer (E & M Biotachometer BT-1200). The heart rate was determined either directly from the tachometer or by counting the R waves during a 30-sec period. The two methods produced comparable results.
Oxygen consumption was measured using a paramagnetic oxygen analyzer (Beckman E-2) and an open-flow system. The animal was placed in a glass or acrylic chamber, the volume of which was normally no more than 20 times the volume of the animal, and which, with the exception of the 900-ml glass chamber in which the Peromyscus were measured, contained a small fan blade to mix the air. The chamber was then placed in a stirred water bath for temperature control. Outdoor air was adjusted to the temperature of the water bath, and passed through the chamber at the highest rate which allowed accurate recording of the oxygen consumption (1,000 ml/min for the small animals, up to 3,000 ml/min for the larger animals). A sample of the air, after it had passed through the chamber, was dried, the carbon dioxide removed, and the concentration of oxygen remaining measured by the oxygen analyzer. The oxygen consumption was calculated according to the open-flow method of Depocas and Hart (11). The \( f_h \) and \( \dot{V}_O_2 \) were recorded at 30- or 60-sec intervals. Changes in \( f_h \) and \( \dot{V}_O_2 \) occurred as a result of spontaneous activity and in response to changes in the temperature of the water bath. Water bath temperatures ranged between 0°C and 40°C and these temperatures along with the forced convection by the fan in the chamber resulted in a wide range of \( \dot{V}_O_2 \) values.

Each of the individual measurements of \( f_h \) and \( \dot{V}_O_2 \) is plotted in the accompanying Figs. 1-5 and each incorporates a lag time of 30-60 sec (depending on the flow rate) between recording of the \( f_h \) and recording of the \( \dot{V}_O_2 \). The data from \( S. \) lateralis differ from the other data in that the \( f_h \) and \( \dot{V}_O_2 \) values were averaged over 10-min periods at the time of collection.

RESULTS

There were direct correlations between the \( f_h \) and \( \dot{V}_O_2 \) for each animal examined in this study. Where the relationships were relatively linear, as they were for the Belding ground squirrels (Fig. 1), four of the five albino rats (Fig. 2), the woodrat (Fig. 4), and the golden-mantled squirrel (Fig. 5), least-squares regression lines were fitted. There are strong linear correlations in most of these data (\( r > 0.9 \); see Figs. 1-5 for actual values of \( r \)) and all correlations are highly significant (\( P < 0.01 \)). Two regression lines and correlation coefficients were calculated for different portions of the data from the California ground squirrel (Fig. 4) because the regression appeared to change slope at \( f_h \) near 250 beats/min.

The relationships between \( f_h \) and \( \dot{V}_O_2 \) were clearly not linear for one albino rat (Fig. 2, no. 6), the California mice (Fig. 3), or the hamster (Fig. 5). They were not easily transformed to linear relationships either. To establish some indication of statistical variability, the \( \dot{V}_O_2 \) measurements were grouped over ranges of 25 or 50 heart beats/ min, and the 95% confidence intervals (\( y \pm t \sigma_y \)) were plotted at the midpoints of the ranges of \( f_h \).

Data were collected on more than 1 day from the hamster, the California ground squirrel, three Belding ground squirrels, two albino rats, and the four California mice. For the ground squirrels and the albino rats, the data from different days resulted in least-squares regression lines which had slightly different slopes, but which rotated about a common point in the midrange of \( f_h \) values, so that at all but extremely high or low \( f_h \)'s the regression lines were not significantly different at the 95% confidence level. The data from different days were therefore pooled for the fitting of the final least-squares line, even though some were slightly different statistically at extreme \( f_h \)'s. The grouped data which describe the curves for the hamster and the California mice overlap on different days and are not significantly different at the 95% confidence level.

The relationship between \( f_h \) and \( \dot{V}_O_2 \) for each individual animal usually was not identical to those of other individuals of the same species and body weight.

In order to assess the accuracy with which \( \dot{V}_O_2 \) could be predicted from an observed \( f_h \), the 95% confidence interval for prediction of \( y \) from \( x \) was calculated as (23):

\[
y = bx \pm t \sigma_y x \sqrt{1 + 1/n + x^2 / \Sigma x^2}
\]
where \( \dot{V}_{O_2} \) is milliliters \( O_2 \) per minute, \( SV \) is stroke volume in milliliters blood per heart beat, and \( (A-V)O_2 \) diff is the difference in concentration of oxygen between arterial and venous blood in milliliters \( O_2 \) per milliliter blood. This relationship indicates that changes in \( \dot{V}_{O_2} \) are accompanied by changes in one or more of the variables on the right-hand side of equation 1. The equation can be rearranged to show that the oxygen pulse (OP), which is the amount of oxygen consumed per heart beat, is equal to the \( SV \cdot (A-V)O_2 \) diff:

\[
\text{OP} = \frac{\dot{V}_{O_2}}{f_h} = SV \cdot (A-V)O_2 \text{ diff}
\]  

The OP can be calculated from the data in Figs. 1–5 and is plotted in Fig. 6 as a function of the \( f_h \). This plot provides a clearer indication of the physiological significance of the relationships in Figs. 1–5 than is evident directly.

**DISCUSSION**

**Physiological significance of the regressions.** The observed direct correlations between \( f_h \) and \( \dot{V}_{O_2} \) are to be expected since increased \( \dot{V}_{O_2} \) necessitates increased availability of oxygen to the tissues, and changes in \( f_h \) reasonably would be expected to increase the rate of blood flow. Equation 1 is a simple relationship between \( \dot{V}_{O_2} \) and cardiovascular parameters:

\[
\dot{V}_{O_2} = f_h \cdot SV \cdot (A-V)O_2 \text{ diff}
\]  

This confidence interval is on the order of \( \pm 1 \text{ ml } O_2/(g \cdot \text{hr}) \) at any \( f_h \) for the rats and squirrels. It was calculated only for data to which a linear regression line could be fitted.

**FIG. 2.** Correlations between \( \dot{V}_{O_2} \) and \( f_h \) for 5 albino laboratory rats. Least-squares regression lines are fitted to data from 4 of rats, but for rat 6 a curve is fitted by eye through mean values of \( \dot{V}_{O_2} \) averaged over 25 or 50 beats/min ranges of \( f_h \) (see Methods). Vertical lines on curve indicate 95% confidence intervals for these mean values of \( \dot{V}_{O_2} \). Symbols and terminology are same as for Fig. 1.

**FIG. 3.** Correlations between \( \dot{V}_{O_2} \) and \( f_h \) for 4 California mice. Curves are fitted by eye through mean values of \( \dot{V}_{O_2} \) averaged over 25 to 50 beats/min ranges of \( f_h \). Vertical lines indicate 95% confidence intervals for these mean values of \( \dot{V}_{O_2} \). Symbols and terminology are same as for Fig. 1.
HEART RATE AND OXYGEN CONSUMPTION CORRELATIONS

Bushy-tailed woodrat

\( \text{HEART RATE} \)

FIG. 4. Correlations between \( V_02 \) and \( f_h \) for a bushy-tailed woodrat and a California ground squirrel. Least-squares regression lines are fitted to data. Two lines are fitted to data from ground squirrel because regression more closely approximated two straight lines than one. Symbols and terminology are same as for Fig. 1.

If the regression of \( V_02 \) on \( f_h \) is linear, Fig. 6 shows that the amount of oxygen utilized per heart beat tends to change (either increase or decrease depending on the slope of the regression) at a decreasing rate as the \( f_h \) increases. Thus, the higher the \( f_h \), the smaller is the change in \( V_02 \) with further \( f_h \) increase. If the \( f_h \) remained constant as the \( f_h \) changed, it would mean that changes in the \( f_h \) accounted for all of the increased oxygen transport. Evidently (with the exception of \( S. \) beechey) where the regression of \( V_02 \) on \( f_h \) is linear, the \( f_h \) contributes a progressively larger percentage of the increased oxygen transport as the heart speeds, tending in some cases toward nearly 100% (e.g., \( S. \) beldingi 66, 67, and 68). In other cases (e.g., \( S. \) beldingi 45), changes in \( f_h \) (whether caused by changes in SV, (A-V)O2 diff, or both) remained quite important even at the highest \( f_h \) observed.

Where the regression of \( V_02 \) on \( f_h \) was not linear, the relationship between \( f_h \) and \( V_02 \) became more complex. In all such relationships in the present study, the OP tended to remain constant at lower \( f_h \)’s and to increase at higher \( f_h \)’s, the converse of the previous situation. In these animals, therefore, particularly in the Peromyscus where the effect was most consistent, an increase in the \( f_h \) was of great importance, compared to changes in the SV or (A-V)O2 diff, except at the highest \( f_h \) values.

It seems reasonable that as the \( f_h \) increases there would come a point at which decreased diastolic filling time, and a consequently decreased SV, would offset any advantages of further increase in \( f_h \). Further increases in O2 transport would then have to be met by increased O2 extraction from the blood (i.e., increased (A-V)O2 diff). Rushmer (21) has shown that there is, in fact, very little change in the SV of dogs and humans at any \( f_h \) and that increased O2 transport is met by a combination of increased \( f_h \) and (A-V)O2 diff. The data compiled by Rushmer on humans and the work of Davies (10) indicate that at \( f_h \)’s near the maximum level there are further increases in the \( V_02 \) with only small additional change in \( f_h \). These patterns are similar to those observed in the California mice and the hamster in the present study. In these animals, as maximum \( f_h \) is approached, further increases in \( V_02 \) must depend on increased (A-V)O2 diff. We did not observe this pattern in most of the larger animals we examined, probably because maximum \( f_h \)’s were not achieved in the absence of forced exercise. In the smaller animals, however, environmental changes did result in \( f_h \)’s near maximum. It is tempting to speculate that since larger animals are less closely coupled to environmental changes, the environmental extremes we used were neither great enough nor of sufficient duration to cause maximum \( f_h \). Many of the larger animals were clearly in distress at the extremes of temperature and convection we used; thus, it seems more likely that maximum \( f_h \)’s do not occur in the larger rodents in the absence of exercise.

**Comparison with other species.** Relationships similar to those in our data can be calculated from data in other studies in which the \( f_h \) and \( V_02 \) were measured at different times, but at controlled ambient temperatures and under similar conditions of activity. Figure 7 shows selected regressions...
FIG. 6. Regressions of oxygen pulse (OP) on f$_h$ for all of data in Figs. 1–5. The steeper the slopes of lines, the smaller the contribution of increased f$_h$ to increased oxygen transport.

FIG. 7. Regressions of $\dot{V}_O_2$ on f$_h$ for some animals in Figs. 1–5, and for 10 other mammals from which relationship could be calculated from data in literature. See Table 1 for identification of animals, their body weights, and references to sources of data.

### Table 1. Identification of species, body weights, and references comprising the regression lines in Fig. 7

<table>
<thead>
<tr>
<th>Regression No. on Fig. 7</th>
<th>Body Weight</th>
<th>Name</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>60 kg</td>
<td>Man</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>55 kg (est)</td>
<td>Suffolk wether sheep</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>21.5 kg</td>
<td>Mongrel dog</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>0.5–1.1 kg</td>
<td>Pteropus poliocephalus</td>
<td>4</td>
</tr>
<tr>
<td>5</td>
<td>.33–.55 kg</td>
<td>Pteropus scapulatus</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>962 g</td>
<td>Albino laboratory rat</td>
<td>This study</td>
</tr>
<tr>
<td>7</td>
<td>340 g</td>
<td>Spermophilus beecheyi</td>
<td>This study</td>
</tr>
<tr>
<td>8</td>
<td>160 g</td>
<td>Spermophilus lateralis</td>
<td>This study</td>
</tr>
<tr>
<td>9</td>
<td>150 g</td>
<td>Macroderma gigas</td>
<td>This study</td>
</tr>
<tr>
<td>10</td>
<td>146 g</td>
<td>Spermophilus beldingi</td>
<td>This study</td>
</tr>
<tr>
<td>11</td>
<td>144 g</td>
<td>Neotoma cinerea</td>
<td>This study</td>
</tr>
<tr>
<td>12</td>
<td>65 127 g</td>
<td>Tamias striatus</td>
<td>This study</td>
</tr>
<tr>
<td>13</td>
<td>107 g</td>
<td>Microtus auratus</td>
<td>This study</td>
</tr>
<tr>
<td>14</td>
<td>50–90 g</td>
<td>Ceracrus nana</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>50–65 g</td>
<td>Eumyscus pernici</td>
<td>14</td>
</tr>
<tr>
<td>16</td>
<td>50 g</td>
<td>Peromyscus californicus</td>
<td>This study</td>
</tr>
<tr>
<td>17</td>
<td>22 g</td>
<td>Leptonycrurus sanborni</td>
<td>8</td>
</tr>
<tr>
<td>18</td>
<td>6–9 g</td>
<td>Baiomys taylori</td>
<td>13</td>
</tr>
</tbody>
</table>

From Figs. 1–5 plotted with regressions derived from other publications. Table 1 identifies the animals, their weights, and the sources of the data. For all of the animals represented in Fig. 7, there is a direct correlation between the f$_h$ and the $\dot{V}_O_2$. The types of regressions observed in this study occur for all the small mammals included in Fig. 7. The regressions of $\dot{V}_O_2$ on f$_h$ from very small mammals tend to be curvilinear (the data on $\dot{V}_O_2$ for $L$. sanborni were highly variable at low f$_h$ so that we did not attempt to estimate the nonlinear part of the relationship). At high f$_h$ the slopes of the regressions for very small mammals tend to be more steep than those for medium-sized mammals, and there is considerable variability in the slopes of the regressions lines between species. For all of the species other than sheep, humans, and the rodents in this study, only data from single animals or mean values from groups of animals are available, but it can be anticipated from our results that slopes of regression lines from different individuals of any species would vary. Figure 7 also indicates that smaller mammals tend to have higher f$_h$'s and higher basal $\dot{V}_O_2$'s per gram and larger ranges of $\dot{V}_O_2$ and f$_h$ than large mammals. Standard regressions for basal $\dot{V}_O_2$ (converted from Brody's (7) equation, kcal/day = 70.5 kg$_{0.724}$ to ml O$_2$/ (g·hr) = 3.84 g$^{-0.266}$ using a conversion factor of 1,000 ml O$_2$ = 4.8 kcal), and basal f$_h$ (f$_h$ = 241 kg$^{-0.25}$ (22)) are plotted simultaneously along the bottom of Fig. 7. The fact that the lowest f$_h$'s and $\dot{V}_O_2$'s for most of the animals...
neutral ambient temperatures, and whenever this happened although in two others there was no significant difference. The most obvious applications are those in which the experimenter cannot observe the animal, or cannot detect the effects of various environmental parameters on the animal by observation, but would like to have some index of relative $V_0_2$ and activity. For example, it may be of interest to know if an animal in its burrow is active or resting.

When combined with radiotelemetry of body temperature, the regressions will allow a considerably more precise evaluation of the effects that small changes of the microhabitat have on energy exchange in homeotherms. Analysis of behavioral thermoregulation of birds and mammals in nature is equivocal unless changes of both body temperature and metabolic rate are known, since it is generally characteristic of these animals that body temperatures may be maintained relatively constant at the expense of changes of the metabolic rate. The actual effects of a change in microhabitat on an animal’s energetics are reflected by a combination of changes of the body temperature and changes of the metabolic rate. The technique described in this paper allows observation of qualitative changes in metabolic rate of undisturbed animals in nature.

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