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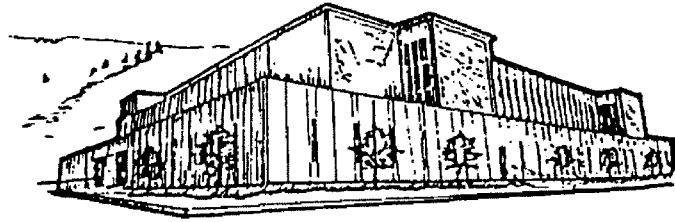
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VENTILATORY AND METABOLIC RESPONSE OF THE LESSER
SPEAR-NOSED BAT, <u>PHYLLOSTOMUS DISCOLOR</u>, TO
HYPERCAPNIA AND HYPOXIA

by

John P. Walsh

B.S., Northeastern University

Presented in partial fulfillment of the requirements
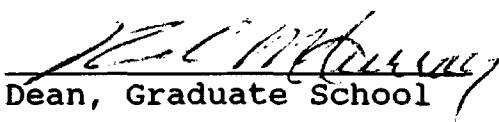
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Ventilatory and metabolic response of the lesser spear-nosed bat, __Phyllostomus__ __discolor__, to hypercapnia and hypoxia.

Directors: Dona F. Boggs & Delbert L. Kilgore

The mean ventilatory response ($\%\Delta\dot{V}_E$) of lesser spear-nosed bats (N = 9) to 3%, 5%, and 7% CO_2 was 30% (SEM = 4.4), 72% (SEM = 8.3) and 107% (SEM = 9.5), respectively. Ventilatory responses of the bats to each of the hypercapnic treatments differed significantly from ventilation on air and each other. Change in metabolic rate ($\%\Delta\dot{V}_{O2}$) showed no pattern and was not significantly different from the air value for any of the hypercapnic treatments.

The mean ventilatory response of these bats (N = 9) to 12%, 10% and 8% inspired O_2 was -4% (SEM = 9.4), -8% (SEM = 10.7) and -25% (SEM = 8.4), respectively. Among the hypoxic treatments only the ventilatory response to 8% O_2 differed significantly from ventilation on air or the other treatments. Metabolic rate did differ significantly from zero and the other hypoxic treatments at 10% and 8% inspired O_2, however, being -30% (SEM = 8.6) and -54% (SEM = 6.1) respectively.

The ventilatory response of the bats to 5% inspired CO_2 is consistent with the prediction of a smaller ventilatory response to hypercapnia in small mammals than in large ($\%\Delta V \propto M_B^{0.130}$). Such a reduced response may minimize the inhibition of ventilation resulting from excessive loss of CO_2 during periods of increased ventilation in response to hypoxia.

While the ventilatory response of these bats does not support the prediction of a larger hypoxic ventilatory response in small mammals than in large ($\%\Delta\dot{V}_E \propto M_B^{0.273}$), their metabolic response is consistent with the depression of metabolism in response to hypoxia typical of many small mammals and suggests that convection requirement ($\dot{V}_E / \dot{V}_{O_2}$) may be a more appropriate measure of the respiratory response to hypoxia in small mammals. The small hypoxic depression of metabolism of these bats relative to the hypoxic depression of metabolism observed in other small species, however, suggests that lesser spear-nosed bats may be adapted to prolonged hypoxia.

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Introduction

Elevated levels of inspired carbon dioxide (hypercapnia) and decreased levels of inspired oxygen (hypoxia) disrupt normal gas exchange and are potent stimuli to ventilation. Limited data on the variation among mammals in the extent of the increases in their ventilation caused by hypercapnia and hypoxia suggest that both may be accounted for by a systematic relationship to either body size or adaptation to habitats with unusual gas compositions. The comparative data on ventilatory responses to hypoxia and hypercapnia upon which these suggested relationships are based is insufficient at the small end of the body size range and only rodents are represented. Also, bats typically roost in confined places where hypercapnic or hypoxic conditions can occur. It is of interest, therefore, to investigate the response of the lesser spear-nosed bat (<u>Phyllostomus</u> <u>discolor</u>) to both of these ventilatory stimuli.

Effect of Body Size on the Hypercapnic and Hypoxic Ventilatory Response

When exposed to elevated levels of inspired CO_2 (F_{ICO_2}), mammals have three compensatory mechanisms for maintaining normal body fluid and tissue pH: 1) an increase in ventilation, which lowers alveolar and arterial P_{CO_2};

2) blood and tissue buffer systems; and 3) renal acid-base regulation via the excretion of H^+ and reabsorption of HCO_3^-.

Mammals that encounter elevated $F_{I_{CO_2}}$ (burrowers and some divers) often typically employ one or both of the latter two mechanisms for dealing with hypercapnia. Most species, however, encounter elevated $F_{I_{CO_2}}$ only briefly, if ever, and for them the ventilatory response to hypercapnia, taking advantage of the tremendous capacity of the lungs to rapidly excrete CO_2 (in the form of 10,000 mEq of carbonic acid per day compared with less than 100 mEq of fixed acids by the kidneys; West, 1985), is sufficient for maintaining homeostasis.

The ventilatory response to hypercapnia of non-burrowing, non-diving mammals has been examined in humans (Heller et al., 1929; Lambertson, 1960; Haywood and Bloethe, 1969), the western australian pseudo-rat (Pseudomys shortridgei; Withers, 1975), laboratory rats (Pappenheimer, 1977; Arieli and Ar, 1979; Birchard et al., 1984; Walker et al., 1985), horses (Klein et al., 1982), laboratory mice (Schlenker, 1985), porcupines (Boggs and Birchard, 1989) and coati mundis (Boggs et al., 1992). Among these species there appears to be a relationship between hypercapnic ventilatory response and body size. An allometric equation for the ventilatory response (in $\%\Delta\dot{V}_E$) of these seven species to 5% CO_2 indicates that

ventilatory response to hypercapnia scales with body mass (M_B) to the 0.130 power ($\%\Delta\dot{V}_E \propto M_B^{0.130}$; B.R. Williams et al., pers comm.); thus, small mammals have a reduced responsiveness to inspired CO_2 compared with that of large mammals.

The reduced response of small mammals to CO_2 may be associated with their increased sensitivity to hypoxia ($\%\Delta\dot{V}_E$ in response to breathing 12% $O_2 \propto 26.9M_B^{-0.273}$, Boggs & Tenney, 1984). A reduced response to CO_2 would allow small mammals to respond more to hypoxic conditions because they would experience less inhibition of ventilation caused by a hyperpneic hypocapnia. The allometric equations of both hypercapnic and hypoxic ventilatory responses, however, are based on data which include only a few small species (mostly rodents), suggesting the possibility of phylogenetic factors influencing the observed slopes.

To date, the big brown bat (Eptesicus fuscus, 20 g), is the only chiropteran species for which hypercapnic ventilatory response has been measured (Szewczak & Jackson, 1992). In response to 5% inspired CO_2, continuously ventilating big brown bats with body temperatures (T_B) of 30°C increased their respiratory frequency over normoxia by 95% (Szewczak & Jackson, 1992). Tidal volume was assumed to remain constant. If tidal volume indeed remained constant and frequency was

representative of ventilation, then this response is close to the increase in ventilation predicted for a 20 gram mammal (75.4%, using the allometric equation above; Williams et al., in prep.). While a constant tidal volume might be a valid assumption in an animal breathing discontinuously at a low body temperature, as appears to be the case for columbian ground squirrels which change the duration of the non-ventilatory period as the primary means of altering ventilation upon exposure to hypercapnia and hypoxia (Milsom, 1988), a constant tidal volume in response to CO_2 in a continuous breather is a less certain assumption. Furthermore, a body temperature of 30°C is well below euthermia for big brown bats, raising the possibility that at this body temperature these bats may have a depressed response to elevated inspired CO_2, as has been demonstrated of other hibernators (Milsom et al., 1986).

There are numerous adaptations employed by mammals inhabiting hypoxic environments to compensate for decreased levels of atmospheric oxygen and ensure adequate oxygenation of the tissues. As is the case with hypercapnia however, most species encounter hypoxic environments only transiently and rely on essentially two compensatory mechanisms for maintaining homeostasis: 1) increasing ventilation, which increases alveolar PO_2 facilitating diffusion of O_2 into the

blood; and 2) decreasing metabolism and thus O_2 demand.

The ventilatory response to acute hypoxia has been measured in some 37 species of non-burrowing, non-diving, lowland mammals (see reviews by Boggs and Tenney, 1984; Frappell et al., 1992) and a relationship to body size may exist. Percent change in ventilation in response to 12% inspired O_2 has been found to scale with body mass to the -0.270 power (10 species, ranging in body mass 0.030kg to 400kg; Boggs and Tenney, 1984), indicating a greater response to hypoxia in small species than in large species. This exponent does not seem to hold, however, when the allometric equation is limited to small species (< 50kg). In a recent survey of the ventilatory response to 10% O_2 in 27 mammalian species ranging in size from 0.008 kg to 47 kg, the allometric relationship of $\dot{V}_E$ during hypoxia was found to have the same slope as that during normoxia, indicating that the ventilatory response to hypoxia (%$\Delta \dot{V}_E$) is unaffected by body size among small mammals (Frappell et al., 1992). These results were attributed to the marked decrease (> 20%) in metabolic rate observed in 21 of the 27 species (Frappell et al., 1992). Previous studies have documented this hypo-metabolic response to hypoxia in small rodents, as well as newborns (Morrison and Rosenmann, 1975; Faleschini & Whitten, 1975; Lechner, 1977; Mortola et al., 1989), and it may be a widespread mammalian phenomenon. The

21 species in which Frappell et al. (1992) measured large drops in oxygen consumption represent 5 mammalian orders (including six species of marsupials).

Data for the ventilatory response of bats to hypoxia (without metabolism measured) are available for the big brown bat (Szewczak & Jackson, 1992), and data for both the ventilatory and metabolic response to hypoxia are available for the broad-nosed bat (Scotorepens balstoni - a microchiropteran, Frappell et al., 1992) and the Liukiu Island flying fox (Pteropus dasymullas - a megachiropteran, Frappell et al., 1992). In response to breathing an air mixture containing 10% O_2, ventilation decreased by 17% (compared with that during normoxia) in hibernating big brown bats at a body temperature of 20°C (Szewczak & Jackson, 1992). This decrease was not significant and it was only at low levels of inspired O_2 (6%) that the bat's ventilation significantly increased (+ 39%, again based only on changes in respiratory frequency). Though Szewczak and Jackson (1992) reported no changes in metabolic rate in the big brown bats during the hypoxic treatments, it may be assumed that their metabolic rate was already greatly reduced as their body temperature ranged between 5°C and 20°C for all measurements. Frappell et al. (1992) observed a 25% increase in ventilation in the broad-nosed bat (T_B 33°C) and a 29% decrease in ventilation in the

Liukiu Island flying fox (T_B 37°C) in response to 10% O_2 (based on frequency and tidal volume). Metabolism, however, decreased by 66% and 91% in the broad-nosed bat and the Luikiu Island flying fox, respectively, the third largest and largest depressions in metabolic rate of the 27 species included in their study. The small hypoxic ventilatory responses and large reductions in metabolism of each of these species demonstrates the importance of the hypo-metabolic response to hypoxia for these and possibly many other species of bats.

This study of the ventilatory and metabolic response of lesser spear-nosed bats to hypercapnia and hypoxia broadens the phylogenetic range of species and adds data from another small species to the database from which the allometric equations of mammalian hypercapnic and hypoxic response may be derived. The response of lesser spear-nosed bats to low O_2 is also of interest in the context of the suggested increased importance of the metabolic compared with the ventilatory response to hypoxia in small mammals.

Effect of Habitat on the Hypercapnic and Hypoxic Ventilatory Response

The response of lesser spear-nosed bats (and bats in general) to hypercapnia and hypoxia is also of interest from

the standpoint of physiological ecology. Bats often roost in confined places such as caves and mine tunnels that have altered gaseous atmospheres. Noxious or even deadly gases, reduced levels of O_2, elevated levels of CO_2 or combinations thereof occur frequently in these places (Constantine, 1992). Perhaps bats, like residents of high altitude or burrows, have adaptations that have allowed them to exploit such habitats.

Species chronically exposed to high levels of inspired CO_2, such as burrowing mammals, often display a reduced ventilatory responsiveness to hypercapnia, since increasing ventilation in response to chronically elevated inspired CO_2 is of little value. Species exposed to chronic hypercapnia may also have either elevated blood buffering capacities (e.g., pocket gophers; Chapman & Bennett, 1975; several diving mammals, Lenfant et al., 1970) increased renal retention of HCO_3^- (e.g., the echidna, Bentley et al., 1967; groundsquirrel, Baudinette, 1974), or both (chipmunks, Maclean, 1978), but these mechanisms are not consistently observed in hypercapnia tolerant species. In some cases burrowers appear able to tolerate exceptionally low blood and tissue pH (woodchucks; Boggs & Birchard, 1989; and molerats, Ar et al., 1977), suggesting some adjustment or adaptation of central or peripheral chemoreceptor sensitivity (Boggs, 1991). Adjustments in peripheral chemoreceptor sensitivity are also

suggested by differences in the pattern of the ventilatory response in these species. Most mammals shorten expiratory time (T_E) as part of the carotid chemoreceptor response to CO_2, but burrowing mammals do not. Thus differences in the pattern of the ventilatory response to CO_2 (tidal volume, ventilatory frequency, and inspiratory time and expiratory time), as well as its magnitude can provide clues to the components of the control system that have been altered in the adjustment to chronic hypercapnia.

Species chronically exposed to low atmospheric O_2 (e.g., burrowers, divers, and residents of high altitude) often display a decreased sensitivity to hypoxia and have adaptations facilitating gas exchange. Some of these adaptations include increased blood O_2 carrying capacity (Bartels et al., 1969; Chapman & Bennett, 1975; Withers, 1975; Ar et al., 1979), increased cardiac output and tissue perfusion (Ar et al., 1977; Arieli & Ar, 1981; Boggs et al., 1983), increased hemoglobin-O_2 affinity (Hall et al., 1936; Parer & Metcalfe, 1967; Ar et al., 1977; Boggs et al., 1984; Weber et al., 1986), decreased tissue diffusion distance (Arieli & Ar, 1981), increased Bohr effect (Boggs et al., 1984), increased muscle myoglobin (Lechner, 1976; Hochachka, 1984) and an altered breathing pattern and dead space to tidal volume ratio (Tenney & Boggs, 1986).

Bat lungs have been found to show morphological adaptations distinguishing them from non-flying mammals, including increased total lung volume, increased alveolar surface area, increased pulmonary diffusing capacity and decreased blood gas barrier thickness (Maina & King, 1984; Thomas, 1987; and Maina, 1993). Also, the *in vitro* blood respiratory properties (hematocrit, hemoglobin concentration, and blood O_2 affinity) and cardiac output of some species have also been found to be considerably elevated compared with similarly sized terrestrial mammals. Though these adaptations have traditionally been interpreted as being associated with the high metabolic requirements of flight, they may also serve to improve gas exchange for bats under hypoxic conditions.

The purposes of the present study were 1) to determine the ventilatory and metabolic response of lesser spear-nosed bats to hypercapnia and in so doing broaden the phylogenetic range of species tested for hypercapnic response; 2) to measure the ventilatory and metabolic response of these bats to hypoxia and thereby determine the relative importance of the two primary compensatory options available to them when confronted by a reduction in O_2; and 3) observe the extent and components of the ventilatory response of lesser spear-nosed bats to hypercapnia and hypoxia and compare those with data from other species to determine whether or not lesser spear-nosed bats are adapted to either elevated CO_2 or decreased O_2.

Materials and Methods

Experimental Animals

Eleven lesser spear-nosed bats, Phyllostomus discolor (4 males and 7 females, mean body mass 43.1 ± 2.5 grams), were used in this study. They were kept in a large flight cage and given food and water ad libitum. Experiments began in the morning and continued until mid to late afternoon. Though this is not the time of day when the bats are most active, they seldom eat during daylight hours and were in a post-absorptive state at this time.

Measurements

Measurements obtained during each experiment included tidal volume (V_T), respiratory frequency (f), oxygen consumption $(\dot{V}_{O2})$, body mass (M_B), body temperature (T_B), and ventilatory pattern (T_I, T_E, T_{TOT}). Ventilatory measurements were acquired by whole body Plethysmography (Bartlett & Tenney, 1970). The physiologic chamber used for these measurements was an approximately one liter, clear acrylic cylinder. The chamber was covered with black plastic during experiments to minimize disturbance to the animals. Chamber temperature was held at 27°C to 28°C for all measurements. Gas mixtures were warmed and humidified before passing through the plethysmograph. Pressure changes induced by the warming and humidification of

inspired air as the animal breathed within the closed chamber were detected with a differential pressure transducer (Validyne; Model DP45-16) and recorded simultaneously on a chart recorder (Gould 2200) and computer. After obtaining measurements a calibration was performed by injecting 0.05 ml of air into the chamber with a syringe and recording the pressure change. During calibration a rubber stopper of the same volume as a 41 gram bat was placed in the chamber. Incurrent and excurrent air O_2 and CO_2 concentrations of the dried gas mixtures were measured with Applied Electrochemistry (Models S-3A and CD-3A, respectively) gas analyzers at constant pressure and flow (800 ml/min). Oxygen consumption was calculated using equation 1(d) from Withers (1977), which assumes a respiratory quotient of .85. This value gives an error of + or - 3% when the actual value is 0.7 or 1.0. The bat's colonic temperature was monitored during experiments using a copper-constantan thermocouple calibrated with a thermometer traceable to a National Bureau of Standards thermometer.

Experimental Procedure

Prior to placing a bat in the plethysmograph, a temperature probe was inserted 5mm into the bat's colon and taped to the interfemoral membrane. The bat was then placed in the plethysmograph, where it hung unrestrained, and allowed to

breathe room air for at least one hour prior to taking measurements. When a steady-state (in terms of T_B and ventilation) was reached, the chamber was ventilated with one of six treatment gases, and after a fifteen minute exposure, measurements were made of oxygen consumption ($\dot{V}O_2$), ventilation ($\dot{V}$), tidal volume (V_T), respiratory frequency (f), and inspiratory and expiratory time (T_I and T_E). The six treatment gases were 3, 5, and 7% CO_2 (21% O_2, balance N_2), and 8, 10, and 12% O_2 (with 0% CO_2 and the balance N_2). Bats were exposed to hypercapnic and hypoxic gas mixtures on different days. The order in which the bats were exposed to treatment gas mixtures was randomized and the bats were allowed to breathe air for twenty minutes between each treatment. Room, chamber, and body temperature along with barometric pressure were recorded continuously.

Data Analysis

To account for non-independence of measurements obtained from each animal, a repeated measures design was used to test for differences in respiratory frequency, tidal volume, ventilation, ventilatory pattern, body temperature and oxygen consumption among the various treatments (room air, hypercapnic and hypoxic mixtures)(Wilkinson, 1988). A univariate repeated measures ANOVA was performed on each parameter (for each treatment) to detect significant

differences between treatment and room air measurements and a Tukey post-hoc test was performed to determine differences among the treatment parameter means. A Bonferroni adjustment of overall error rate was used in making multiple comparisons of sample means. A P-value < 0.05 was considered significant in all statistical tests. Only data from bats for which measurements were obtained for all treatments were included in the analysis.

Results

Effects of Hypercapnia on Ventilation, $\dot{V}_{O_2}$ and T_B

Respiratory measurements (f, V_T, $\dot{V}_E$, T_I, T_E, and T_{TOT}), body temperature and oxygen consumption varied considerably among the eleven bats; therefore, all measurements have been expressed as the percent change from the average of room air values taken immediately before and after each treatment. Figure 1 shows the mean percent changes in ventilation, oxygen consumption and convection requirement exhibited by the bats in response hypercapnia. The ventilatory response

of the bats (N=8) to 3%, 5% and 7% was 29.9%, 71.7% and 107.5% respectively (Figure 1A). Repeated measures analysis of variance (ANOVA) with a Tukey Post Hoc test revealed that ventilatory responses to all three of the elevated CO_2 levels differed significantly (P≤.002) from zero (i.e., the air

value) and each other. Oxygen consumption (Figure 1B) remained unchanged and body temperature (Table 1) decreased slightly at 3% CO_2 (P≤.038), but not at 5% or 7% CO_2. Convection requirement (CR = $\dot{V}_E$ / $\dot{V}_{O_2}$) increased progressively at higher levels of hypercapnia (Figure 1C), primarily as a result of increases in ventilation.

Figure 2 and Table 2 show the mean ventilatory response (%$\Delta\dot{V}_E$, Figure 2A) of the bats to the three hypercapnic treatments, along with the components of that response in percent change in ventilatory frequency (%Δf), percent change in tidal volume (%ΔV_T), percent change in inspiratory time (%ΔT_I) and percent change in expiratory time (%ΔT_E). The elevation of ventilation in response to hypercapnia resulted from increases in both respiratory frequency and tidal volume (Figure 2B & 2C). In response to 3% CO_2, frequency and tidal volume increased similarly, 14.3% and 13.4% respectively. However, in bats breathing 5% and 7% CO_2, the increase in respiratory frequency was nearly twice the increase in tidal volume, being 49.3% at 5% and 63.1% at 7%, compared with increases in tidal volume of only 20.9% and 31.0%, respectively. Despite increases in ventilation at all levels of hypercapnia, ventilatory pattern was significantly affected only at $F_{I_{CO_2}}$'s of 5% and 7%. At 5% CO_2, expiratory time decreased by 34.6% (P≤.001) (Figure 2E & Table 2). At 7% CO_2,

both inspiratory and expiratory time decreased, T_I by 17% and T_E by 46% (P≤.011) (Figure 2D & 2E).

Effects of Hypoxia on Ventilation, $\dot{V}_{O_2}$ and T_B

As shown in Figure 3 and Table 3, lesser spear-nosed bats do not respond significantly, with changes in ventilation or metabolism, to 12% O_2. In bats exposed to 10% O_2, ventilation was not significantly different from that on room air (20.93% O_2), but metabolism was reduced significantly by 29.7% (P≤.005) (Figure 3A & 3B). Bats breathing 8% O_2 significantly reduced ventilation and metabolism; ventilation was reduced by 25.1% (P≤.016) and metabolism was reduced by 53.6% (P≤.005). The relatively small reductions in ventilation and large reductions in metabolism at 10% and 8% O_2 resulted in significant (P≤.001) increases in convection requirement at both of these levels of hypoxia; convection requirement increased by 49.6% at 10% O_2 and by 91.3% at 8% O_2 (Figure 3C). Body temperature was reduced significantly at each level of hypoxia (P≤.001) (Table 3), by 1.1°C at 12% O_2, 2.2°C at 10% O_2 and 3.6°C at 8% O_2.

As shown in Figure 4A and 4B, the ventilatory response of the bats was primarily effected by a significant (P≤.017) decrease in ventilatory frequency at all levels of hypoxia, 21.7% at 12% O_2, 20.4% at 10% O_2 and 34.5% at 8% O_2 (and Table

4). Tidal volume changed significantly in response to 12% O_2 (P≤.011), it increased 19.6%, but did not change significantly in response to either 10% or 8% O_2 (Figure 4C). Inspiratory time and expiratory time increased with each level of hypoxia (Figure 4D & 4E). However, these increases were significant (P≤.029) only at 10% O_2 (being 44.8% for T_I and 35.8% for T_E) and at 8% O_2 when T_I increased by 73.4%. Though the mean increase in T_E was the greatest at 8% O_2, it was not statistically significant because of the large variance in these measurements.

Discussion

Effect of Body Size on the Hypercapnic and Hypoxic Ventilatory Response of Lesser Spear-Nosed Bats

The 72% increase in ventilation in response to 5% CO_2 observed in the lesser spear-nosed bats is close to the allometric prediction and similar to that observed in other small non-fossorial mammals. The equation of Williams et al. (unpublished) describing the response of non-fossorial mammals to 5% inspired CO_2, $\%\Delta\dot{V}_E \propto 51.05 M_B^{0.130}$ (body mass in grams), predicts an 83% increase in ventilation over normocapnia for a 40 gram mammal. Figure 5 is a plot of this relationship with the species used to generate the curve indicated. Lesser

spear-nosed bats are represented by the open circle and it is clear that the 72% increase observed in these bats is well within the 95% confidence limits of the log-log regression equation fit to these data.

The similarity of the hypercapnic ventilatory response of lesser spear-nosed bats to that of other non-fossorial mammals lends support to the idea that this species and other small mammals have a reduced sensitivity to CO_2 compared with large mammals. The bats represent not only another small species but also another mammalian order that can be added to the lower end of the size range of mammals used to derive the allometric equation of Williams et al. (unpublished, Figure 5).

Nevertheless, it is still possible, if not probable, that environmental and phylogenetic factors are influencing the observed slope (0.130) of the allometric equation for the mammalian ventilatory response to 5% $F_{I_{CO_2}}$ rather than size alone. Many small mammals may have historically lived in confined spaces where CO_2 accumulates or is typically elevated. For instance, the hypercapnic responses of laboratory rats, which comprise the majority of points at the low end of the mammalian hypercapnic response scale (Figure 5), are well below those of some smaller non-fossorial (albino

mice) and semi-fossorial species (Djungarian hamsters) (Schlenker, 1985; Boggs & Birchard, 1989). This is not as would be predicted and possibly due to the semi-fossorial habits of the wild-type ancestors of present day laboratory rats (Boggs & Birchard, 1989), or perhaps common descent of murids and other fossorial rodents from a CO_2 insensitive ancestor.

Lesser spear-nosed bats also have a reduced ventilatory response to hypoxia. As shown in Figure 4 and Table 4, the ventilation of the bats was unchanged in response to 12% or 10% O_2, and when ventilation did change in response to 8% O_2, $\dot{V}_E$ decreased by 25% rather than increasing as would be predicted (Boggs & Tenney, 1984). This type of response is similar to that reported for several species of small non-fossorial mammals by Frappell et al. (1992). One bat, three rodents and two species of marsupial were found to show a drop or no change in $\dot{V}_E$ in response to hypoxia. Frappell et al. (1992) observed a 28% reduction in ventilation in the Liukiu Island flying fox, a 23% decrease in $\dot{V}_E$ in the hopping mouse (Notomys alexis) and a 34% drop in $\dot{V}_E$ in the fat-tailed dunnart (a marsupial, Sminthopsis maniculatus) in response to 10% $F_{I_{O_2}}$. Gerbils, hamsters, and the kowari (another marsupial) showed slight but insignificant increases in ventilation (5%, 1% and 9%, respectively) in response to the

same mixture (Frappell et al., 1992). Another bat included in the Frappell et al. (1992) study, the broad-nosed bat, increased $\dot{V}_E$ by just 25%. Clearly, the ventilatory response to hypoxia is not the primary compensatory strategy employed by these small species. What appears to be the primary hypoxic response of the lesser spear-nosed bats and these other species is a drop in metabolism accompanied by a reduction in body temperature. The six species mentioned above from Frappell et al. (1992) decreased $\dot{V}_{O_2}$ by an average of 62% and T_B by an average of 2.2°C when exposed to 10% O_2. In addition, as previously mentioned, 21 of 27 species from five mammalian orders included in the study by Frappell et al. (1992) showed large (>20%) reductions in $\dot{V}_{O_2}$ and corresponding reductions in T_B upon exposure to 10% O_2. These data, together with data for 5 other species of rodents (Morrison and Rosenmann, 1975), guinea pigs (Hill, 1959), and rats (Adolph and Hoy, 1960; Olson & Dempsey, 1978), support the contention of Frappell et al. that hypometabolism in hypoxia is a general characteristic of many species of small mammals from different mammalian orders.

The advantage of a hypometabolic response to hypoxia is two-fold. First, the drop in $\dot{V}_{O_2}$ reduces the amount of O_2 required by the organism. However if $\dot{V}_{O_2}$ drops more than $\dot{V}_E$, which it uniformly does since an increase in $\dot{V}_E$ usually occurs

in response to hypoxia even in species that drop $\dot{V}_{O_2}$ (the average $\%\Delta\dot{V}_E$ of Frappell et al.'s (1992) 27 species was +23%), it also produces an increase in the convection requirement ($\dot{V}_E$ / $\dot{V}_{O_2}$) and a second benefit. An increase in convection requirement serves to increase alveolar and therefore arterial P_{O_2}, and decrease alveolar and arterial P_{CO_2}, and results in improved tissue oxygenation (Mortola and Rezzonico, 1988).

It has been suggested that the critical measurement for the respiratory control system is convection requirement and not ventilation (Boggs, 1991: Frappell et al, 1992). While changes in $\dot{V}_E$ may vary substantially between species, the control system universally increases convection requirement in response to hypoxia (even the mole rat eventually decreases its $\dot{V}_{O_2}$ in response to hypoxia, at about an $P_{I_{O_2}}$ of 33 torr; Arieli et al., 1977). Figure 6, which includes data for lesser spear-nosed bats, laboratory mice (Boggs, unpublished) and five small species from Frappell et al. (1992) shows the characteristic response of small mammals of increasing convection requirement and reducing body temperature when exposed to hypoxia. The more appropriate measure of physiological response to hypoxia in small species would appear to be convection requirement.

It has also been suggested that the drop in body

temperature associated with the hypoxia-induced hypometabolism observed in small mammals is not the result of a decline in $\dot{V}_{O_2}$ but the cause of it (Mortola et al., 1989). Frappell et al. (1992) proposed that this is the simplest hypothesis for the trend of larger reductions in $\dot{V}_{O_2}$ in small mammals than in large. Small mammals require more energy than large mammals to maintain body temperature and the same hypoxia-induced inhibition of thermogenesis would be expected to have a larger effect on their temperature and $\dot{V}_{O_2}$ than those of larger species. Also, it has been pointed out that decerebrate newborn rats do not show the typical hypoxia-induced depression of metabolism (Martin-Body & Johnson, 1988), implying that pontine connections to the hypothalamus may play a role in the hypothermic-hypometabolic response to hypoxia. The change in T_B of the lesser spear-nosed bats during exposure to 12% O_2 supports these ideas. As can be seen in Table 3, the bats had significantly reduced T_B prior to any change in $\dot{V}_E$ or $\dot{V}_{O_2}$ (neither of which changed significantly at 12% $F_{I_{O_2}}$). This suggests that the hypothermic response to hypoxia is initiated before the hypometabolic response and, if not independent of it, may play some part in causing the subsequent drop in $\dot{V}_{O_2}$.

Effect of Habitat on the Hypercapnic and Hypoxic Ventilatory Response of Lesser Spear-Nosed Bats

There are numerous accounts in the literature of the tolerance of various bat species to altered cave or mine atmospheres, including atmospheres with elevated levels of CO_2 and reduced O_2. For example, Dwyer and Hamilton-Smith reported being unable to enter caves in Australia containing large colonies of the common bent-winged bat (<u>Miniopterus</u> <u>shreibersii</u>) because of high concentrations of CO_2. Also in Australia, James et al. (1975) reported CO_2 concentrations as high as 12% in caves known to be frequented by bats. In Texas, the cave myotis (<u>Myotis</u> <u>velifer</u>) has been reported roosting in caves with CO_2 levels of 2.1%. Increased ambient CO_2 is often accompanied by an equal decrease in O_2 levels (Constantine, 1992), and Fenton (1980) has described triple leaf-nosed bats (<u>Triaenops</u> <u>persicus</u>) inhabiting mines in Tanzania by the thousands with oxygen levels insufficient to sustain the flame of a pressure lamp. Other accounts are similarly anecdotal so it is hard to judge how common an occurrence elevated CO_2 or reduced O_2 might be, but the point remains that some species of bats may show physiological adjustments to elevated $F_{I_{CO_2}}$ and reduced $F_{I_{O_2}}$.

Ventilatory response and ventilatory pattern data presented

here do not support the notion that lesser spear-nosed bats have an unusual tolerance or adaptation to hypercapnia. Hypoxic ventilatory and metabolic data, however, suggest that the bats are unusually tolerant of hypoxia and may have some degree of adaptation to low O_2.

Lesser spear-nosed bats respond with the predicted magnitude of increase (for a non-fossorial mammal) in ventilation to 5% CO_2. This increase in ventilation is accomplished by increases in both ventilatory frequency and tidal volume, with frequency increasing about twice as much as V_T in bats breathing 5% and 7% CO_2 (Figure 2). This is similar to the response of laboratory rats (Arieli & Ar, 1979; Walker et al., 1985), but different from the response of fossorial species such as syrian hamsters, pocket gophers and echidnas (Schlenker, 1984; Walker et al., 1985; Darden, 1972; Bentley et al., 1967). These fossorial species increase V_T to a greater extent than frequency in response to hypercapnia. A low frequency/large V_T response has the advantage of altering the V_{DS}(dead space volume):V_T ratio and providing more effective alveolar ventilation, resulting in a smaller change in arterial partial pressure of CO_2 (Pa_{CO_2}) with increased inspired CO_2 (Tenney & Boggs, 1986). Such a response may be an adaptation to a chronically high CO_2 burrow environment where increasing ventilation through an increase in

respiratory frequency would not be an effective way of eliminating CO_2 and would only add to the work of breathing (Walker et al., 1985). The point here is that lesser spear-nosed bats, unlike the above fossorial species, do not respond in this way and increase ventilatory frequency as well as V_T in response to increased CO_2. Their response to CO_2 is therefore consistent with that observed in non-fossorial mammals not chronically exposed to CO_2.

The within-breath pattern of lesser spear-nosed bats inhaling hypercapnic gas mixtures is also consistent with that typically observed in non-fossorial mammals: an increase in inspiratory drive (V_T/T_I) accompanied by a decrease in expiratory time (nine species, see Figure 6A., Boggs, 1991). The increase in inspiratory drive is normally produced by an increase in tidal volume with little change in inspiratory time until large tidal volumes are achieved (Boggs, 1991). This was the case for lesser spear-nosed bats. As shown in Figure 2 and Table 2, a significant change in inspiratory time did not occur until the $F_{I_{CO_2}}$ was raised to 7% and the increase in tidal volume reached 31%. Expiratory time, meanwhile, changed to a much greater extent, decreasing significantly by 35% at 5% CO_2 and 46% at 7% CO_2. Such a response can be contrasted with that of two fossorial species, woodchucks and Syrian hamsters, both of whom consistently increase T_E while

also increasing V_T in response to CO_2 (Birchard & Boggs, 1989; Walker et al., 1985).

As can be seen in Figure 2B, the bats did not significantly change oxygen consumption $(\dot{V}_{O_2})$ when exposed to any of the hypercapnic treatments. Similarly, body temperature was not greatly affected by increased CO_2. Though there was a significant drop in T_B while the bats breathed 3% CO_2, 0.3°C (Table 2), this change in T_B was minor and probably not representative of any systemic physiological response since T_B showed contradictory and non-significant changes at 5% and 7% CO_2. A slight drop in T_B when exposed to 5% CO_2 has been reported in Australian pseudo-rats (-.88°C after a 30 minute exposure; Pseudomys albocinereus, Withers, 1975), kangaroo rats (-.02°C after a 20 minute exposure; Soholt et al., 1973) and laboratory rats (-0.6°C after a 15 minute exposure; Soholt et al., 1973), but in each case at least some of the reduction is probably attributable to the increased evaporative heat loss occurring with hyperpnea (calculated to be 40% of hypercapnic heat loss for the pseudo-rats; Withers, 1975)

Lesser spear-nosed bats, like some other small mammals noted previously, show a marked depression of metabolism, along with a small increase in ventilation, in response to hypoxia. This type of response reduces oxygen demand and

provides for improved respiratory gas exchange. Such a response would seem preferable for an animal that encounters extended periods of hypoxia, and simply increasing ventilation would seem less effective. Support for this can be seen in Morrison and Rosenmann (1975), who observed that mammals that are able to reduce their metabolism in response to progressive hypoxia have significantly lower lethal P_{O_2} values than those who are unable to reduce their metabolism, such that a direct correlation between metabolic rate at death (M = % basal metabolic rate) and lethal P_{O_2} (P_C, in torr) exists following the regression equation: $P_C = 27 \ M^{1.0}$. The five species in which Morrison and Rosenmann (1975) observed the largest reductions in metabolism, and also the lowest P_Cs, were four highland species and one burrower, species that would be expected to regularly experience hypoxia. Lesser spear-nosed bats typically roost in tree cavities (in groups of a dozen to more than 100) where they may also experience extended periods of hypoxia, thus their blunted response to low O_2 (little or no ventilatory or metabolic response until 8% $F_{I_{O_2}}$) may represent an adaptation to a low O_2 environment. No data are available, however, for gas concentrations within lesser spear-nosed bat roosts.

It seems reasonable to interpret the blunted hypoxic ventilatory response and large hypoxic metabolic response of

lesser spear-nosed bats and other previously mentioned small species as an adaptation to low O_2. When one compares the magnitude of the percent change in the ratio of these two responses, the convection requirement, of lesser spear-nosed bats (+49%) with all of the species included in Frappell et al. (1992) under 1 kg (n=12, +189%), however, it is evident that these bats are unusual in their greatly reduced combined response to hypoxia (Figure 6). The comparison becomes even more dramatic when limited to just the lesser spear-nosed bats and the chiropteran species included in Frappell et al. (1992). The convection requirements of the broad-nosed bat and the Liukiu Island flying fox increase by 275% and 731% respectively in response to 10% O_2. Compared with lesser spear-nosed bats, all of these other species overventilate substantially in response to hypoxia. It is likely that other factors are playing at least some role in producing the extraordinary hypoxic tolerance of lesser spear-nosed bats, and such a factor may be the high oxygen affinity of their hemoglobin.

Hemoglobin affinity is represented by a P_{50} value, which is the partial pressure of oxygen sufficient to half-saturate the blood of a given animal. The lower the P_{50} value an animal has, the more easily oxygen is taken up by the blood. For a mammal (or even a bat) of their size, lesser spear-nosed bats

have an unusually high affinity hemoglobin. Their P_{50} at normal blood pH (7.4) is 28.6 torr (n=4, mean M_B of 45.2 ± 1.34 grams; Jurgens et al., 1981), compared with a P_{50} of 44 torr in the similarly sized laboratory mouse (M_B = 40 grams; Schmidt-Neilsen & Larimer, 1958), and an average P_{50} of 33.1 torr for 4 other chiropteran species (M_B from 5 - 150 grams; Jurgens et al., 1981) at the same pH and normal body temperature. Figure 6 includes data for the ventilatory and metabolic responses to 10% O_2 for lesser spear-nosed bats and laboratory mice and it can been seen that the ventilatory response of the bats to hypoxia (indicated by the filled circle) is considerably less than that of the mice (indicated by the open triangle; data from Boggs unpublished). The metabolic response of the two mammals, however, is essentially the same. The result of the difference in the extent of the ventilatory hypoxic response between these species is that convection requirement ($\dot{V}_E$ / $\dot{V}_{O_2}$) increases to a much greater extent in the mice than in the bats. This can be seen even more dramatically in Figure 7, in which the percent change in convection requirement (%Δ $\dot{V}_E$ / $\dot{V}_{O_2}$) of the two species is plotted together for different partial pressures of inspired oxygen ($P_{I_{O_2}}$'s). The steep portion of the ventilatory and metabolic response curve of the mice occurs well before that of the bats, which appear to be still on the flat portion of their response curve at a $P_{I_{O_2}}$ of 54.4 torr. This is as would

be predicted by the difference in the P_{50} value between the two species. The higher affinity hemoglobin of lesser spear-nosed bats should provide for improved O_2-saturation of their blood (compared with that of laboratory mice at the same P_{O_2}) and therefore they would not be expected to increase convection requirement (to increase the ampount of O_2 carried in the blood) as much under similar hypoxic conditions.

A reduced responsiveness to hypoxia, in terms of an increase in convection requirement, in an animal with a low P_{50} is a reasonable, if not expected, characteristic since no purpose would be served by increasing the convection requirement at high blood O_2-saturation. This appears to be the case among birds (rheas and pheasants; Boggs & Birchard, 1983), and other mammals thus far studied (llamas, cats, and rats; Van Nice et al., 1980; Boggs & Birchard, 1989), and may be the case for lesser spear-nosed bats. These species have hypoxic thresholds (the highest arterial partial pressure of O_2, P_{aO_2}, at which ventilation is significantly increased over its normoxic value) that coincide roughly with the knee of their hemoglobin O_2 dissociation curves, at about the point where O_2 saturation drops to 85% (Van Nice et al., 1980). A problem with this correlation of hypoxic threshold and the knee of the O_2 dissociation curve, however, is that the sensors that respond to hypoxia, the chemoreceptors of the

carotid bodies, respond to the partial pressure of O_2 in the arterial blood (P_{aO_2}) and not its content (Boggs, 1991). Birchard and Tenney (1986) reported no difference in the hypoxic ventilatory threshold of rats treated with sodium cyanate to lower their P_{50} compared with untreated controls. Thus, though it appears that the actual sensing of hypoxic conditions is independent of the saturation of hemoglobin, natural selection has somehow matched the sensitivity of the O_2 sensors in the carotid bodies with the affinity of the hemoglobin in the blood (Boggs & Birchard, 1983). A mechanism for this matching has remained unclear, however, new information on cellular O_2 sensing mechanisms provides an interesting hypothesis.

The type I cells of the carotid bodies respond to a reduced partial pressure of O_2 in the blood and generate action potentials that are transmitted via the carotid sinus nerve to the respiratory centers of the brainstem, regulating respiration and circulation in the body (Acker, 1989). It appears that the P_{O_2} sensor protein on the type I cells is a heme type protein, NAD(P)H oxidase. This heme protein may be a beta-type cytochrome (based on its photometric absorbance signal) similar to the heme in hemoglobin, which is also a beta-type cytochrome (Acker, 1994). Similarly, the cells in the liver that sense P_{aO_2} and stimulate the release

erythropoietin, Hep3b and HepG2 cells, also display a photometric signal indicating the presence of a beta-type cytochrome. This suggests the possibility that the heme proteins in an organism may be genetically determined to have matched affinities for O_2. Thus, an animal with a high affinity hemoglobin would also have a higher affinity heme protein in its O_2 sensors, and therefore a lower threshold to its ventilatory response. Documentation of more species with an apparent matching between their hemoglobin saturation and hypoxic threshold, as well as further investigation of the identities and properties of the heme proteins in O_2 sensing cells, is needed to support this idea.

Summary

The ventilatory and metabolic responses to 3%, 5%, and 7% carbon dioxide and 12%, 10%, and 8% oxygen were determined in lesser spear-nosed bats. The percent changes in ventilation, ventilatory frequency, tidal volume, inspiratory time, expiratory time, oxygen consumption and body temperature were then compared with those of other bats and small terrestrial mammals.

Lesser spear-nosed bats have a reduced ventilatory response (and essentially no metabolic response) to 5% inspired CO_2.

The mean 72% increase in ventilation observed in lesser spear-nosed bats breathing a 5% CO_2 gas mixture is similar to that observed in other small mammals and the expected ventilatory response from the allometric equation of Williams et al (1993, in prep.)

Lesser spear-nosed bats increase tidal volume, increase respiratory frequency, and reduce expiratory time in response to 5% CO_2. This pattern is different from that of hypercapnia-adapted species (e.g., the syrian hamster and woodchuck).

Lesser spear-nosed bats show reductions in ventilation (-8%), in metabolism (-30%) and in body temperature (-2.2 o C) while breathing a 10% O_2 gas mixture that are similar to those of other small mammals. However, the change in convection requirement ($\%\Delta \dot{V}/\dot{V}_{O_2}$ = 49%) suggests that this species is less sensitive to hypoxia than other small mammals. The high affinity hemoglobin of lesser spear-nosed bats may account for or be genetically associated with this reduced sensitivity.

The fitting of the hypercapnic ventilatory response of lesser spear-nosed bats to the allometric relationship of Williams et al. (in prep.) is satisfying, however, the problem of a lack of a number of non-rodent species at the low end of

the size range of the data on mammalian hypercapnic response remains. Data from more species from a broader phylogenetic range are still needed to confirm or refute this allometric relationship. The support of the hypercapnic allometric relationship provided by data from lesser-spear nosed bats also brings up another problem. It has been argued that a reduced sensitivity to hypercapnia may be beneficial in terms of allowing an increased ventilatory response to hypoxia. While lesser spear-nosed bats are consistent with prediction in the extent of their hypercapnic response, they do not have an increased response to hypoxia. The source of this inconsistency is probably the complexity of the combined ventilatory and metabolic response to hypoxia and how it is effected by factors like hemoglobin affinity. With this in mind, it would be of interest to more closely examine the arterial P_{O_2}, blood pH, oxygen dissociation curve and Bohr effect of lesser spear-nosed bats and the relationship of these parameters to the species's ventilatory and metabolic responses to hypoxia.

FIGURE 1. (A) Mean percent change in ventilation (V_E); (B) mean percent change in oxygen consumption (V_O); and (C) mean percent change in convection requirement (V_E/ V_O) with hypercapnia. (*) denotes significant difference from air measurement, (†) denotes significant difference from 3% CO_2, (φ) denotes significant difference from 5% CO_2 and (θ) denotes significant difference from 7% CO_2.

A.

B.

C.

D.

E.

MEAN % Δ $\dot{V}_E$

MEAN % Δ f

MEAN % Δ $\dot{V}_T$

MEAN % Δ T_I

MEAN % Δ T_E
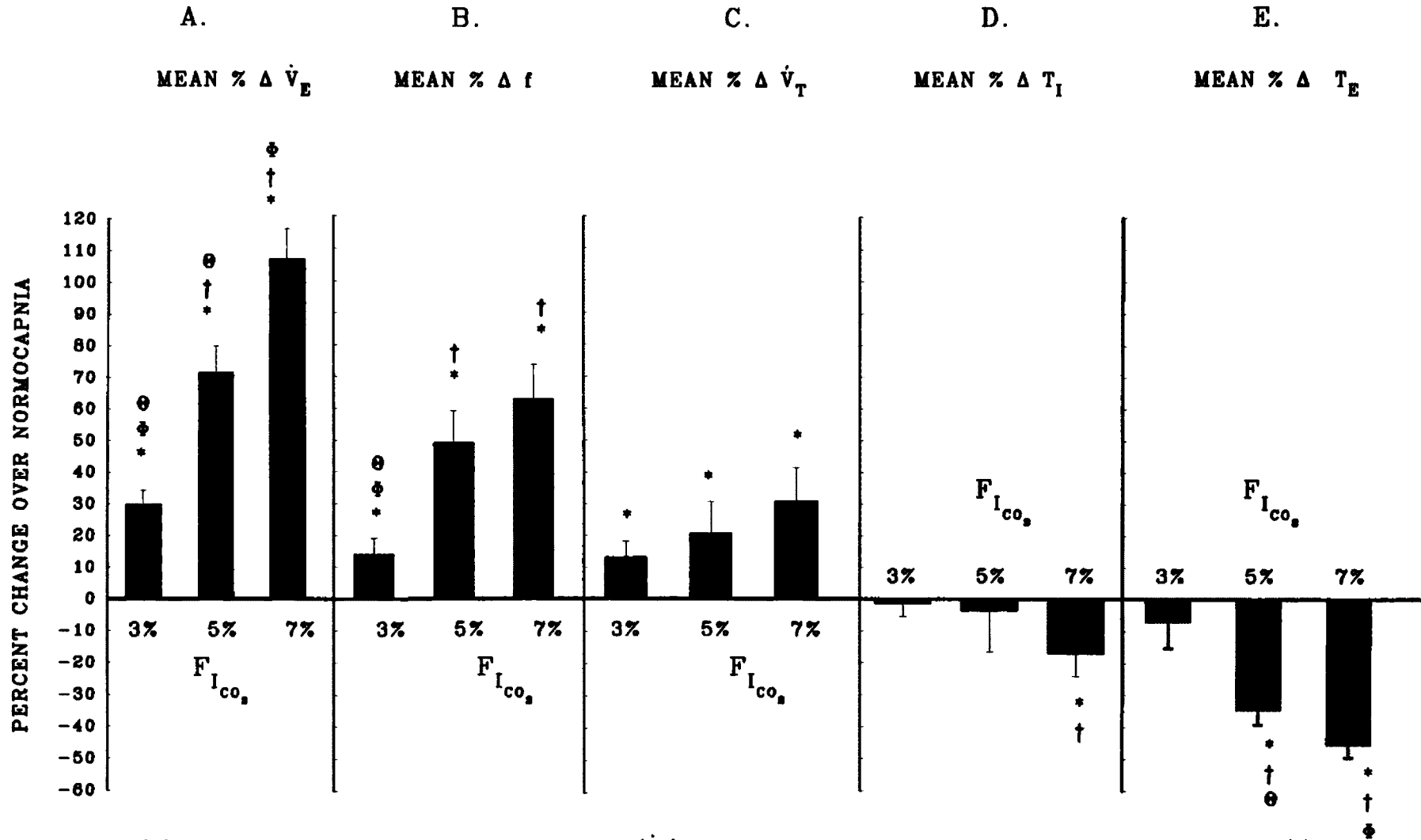
FIGURE 2. (A) Mean percent change in ventilation ($\dot{V}_E$); mean percent change in ventilatory frequency (f); (C) mean percent change in tidal volume (V_T); (D) mean percent change in inspiratory time (T_I); and (E) mean percent change in expiratory ime (T_E) with hypercapnia. Symbols denote significant difference from room air measurement (*), 3% CO_2 measurement (†), 5% CO_2 measurement (◆), and 7% CO_2 measurement (θ).
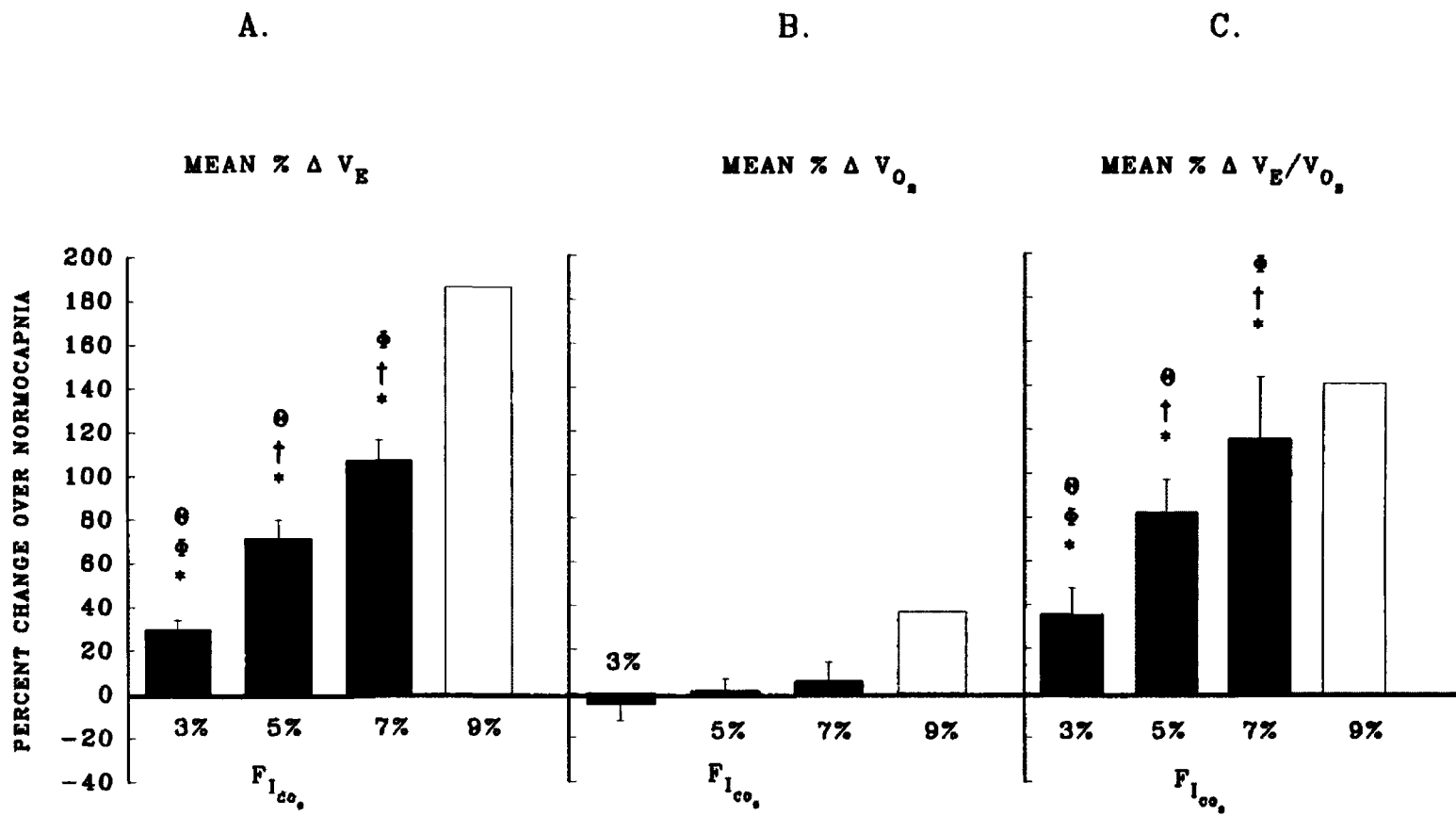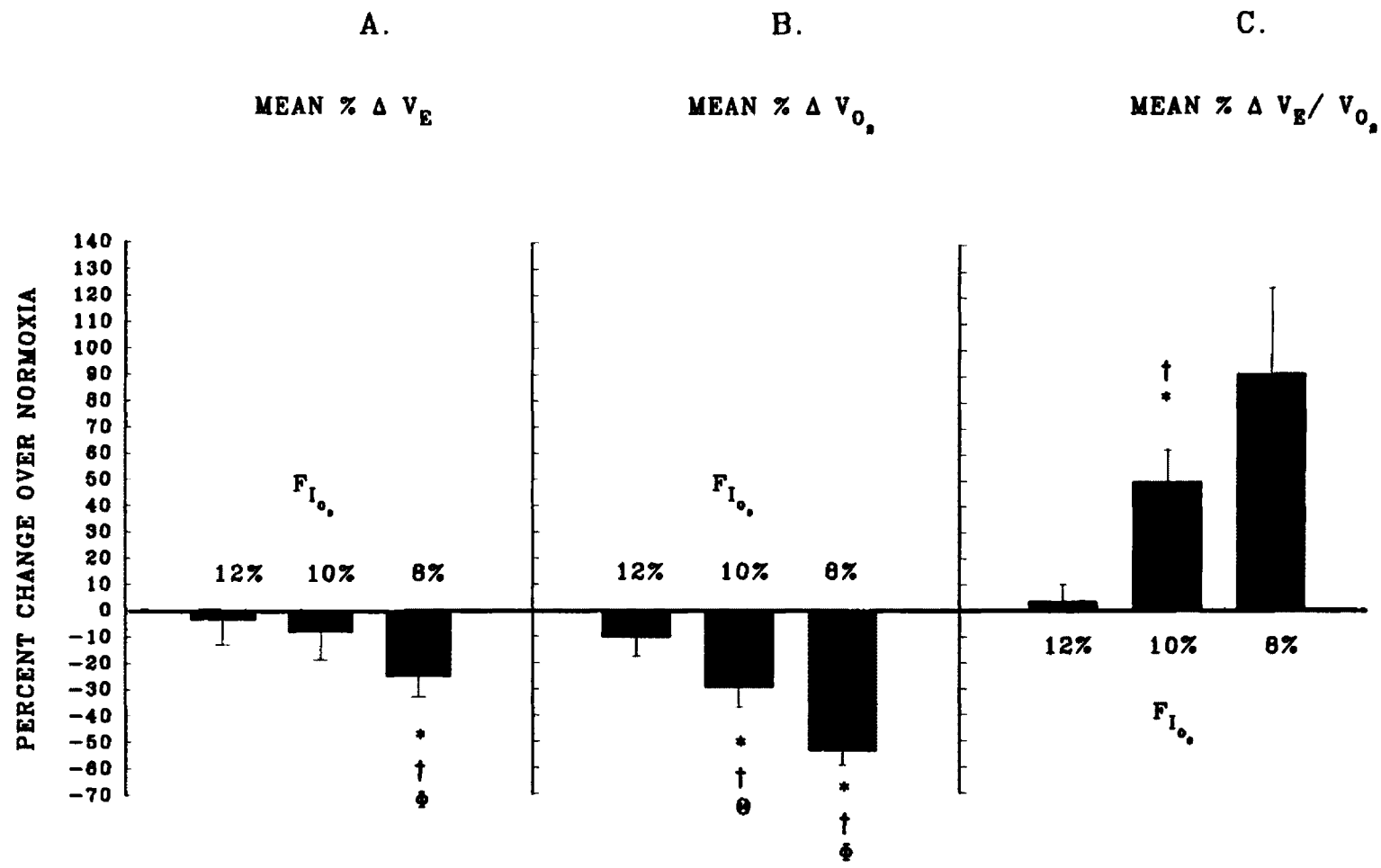
FIGURE 3. (A) Mean percent change in ventilation (V_E); (B) mean percent change in oxygen consumption (V_O); and (C) mean percent change in convection requirement (V_E/V_O) with hypoxia. (*) denotes significant difference from room air, (†) denotes significant difference from 12% O_2. (♦) denotes significant difference from 10% O_2 and (θ) denotes significant difference from 8% O_2.
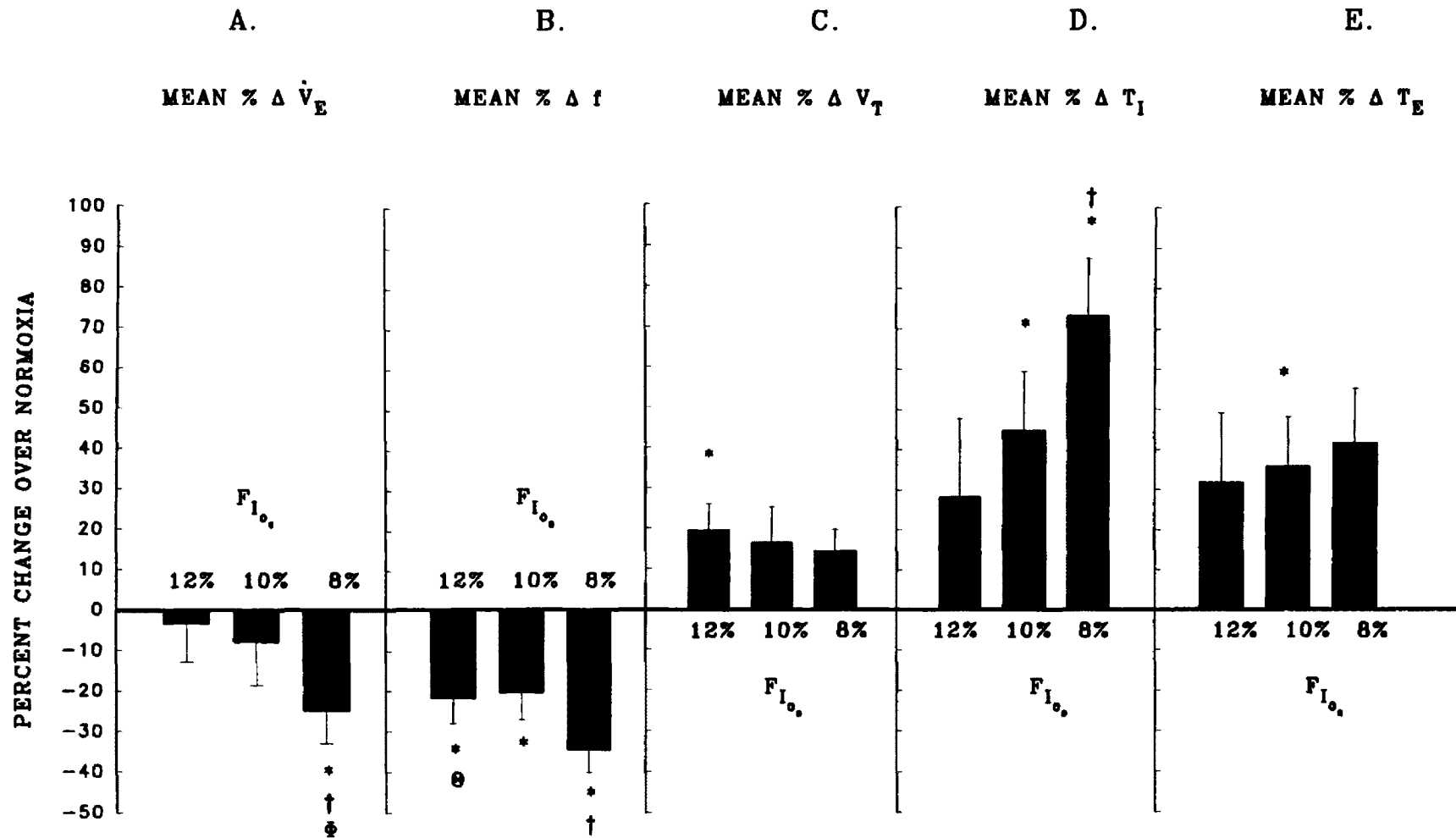
FIGURE 4. (A) Mean percent change in ventilation ($\dot{V}_E$); (B) mean percent change in ventilatory frequency (f); (C) mean percent change in tidal volume (V_t); (D) mean percent change in inspiratory time (T_I); and (E) mean percent change in expiratory time (T_E) with hypoxia. Symbols denote significant difference from room air measurement (*), 12% O_2 measurement (†), 10% O_2 measurement (Φ), and 8% O_2 measurement (θ).

$$\log \% \, \Delta \, V_E \; = \; .134 \, \log \, M_B \; + \; 1.689$$

BODY MASS (GRAMS)

% CHANGE IN VENTILATION
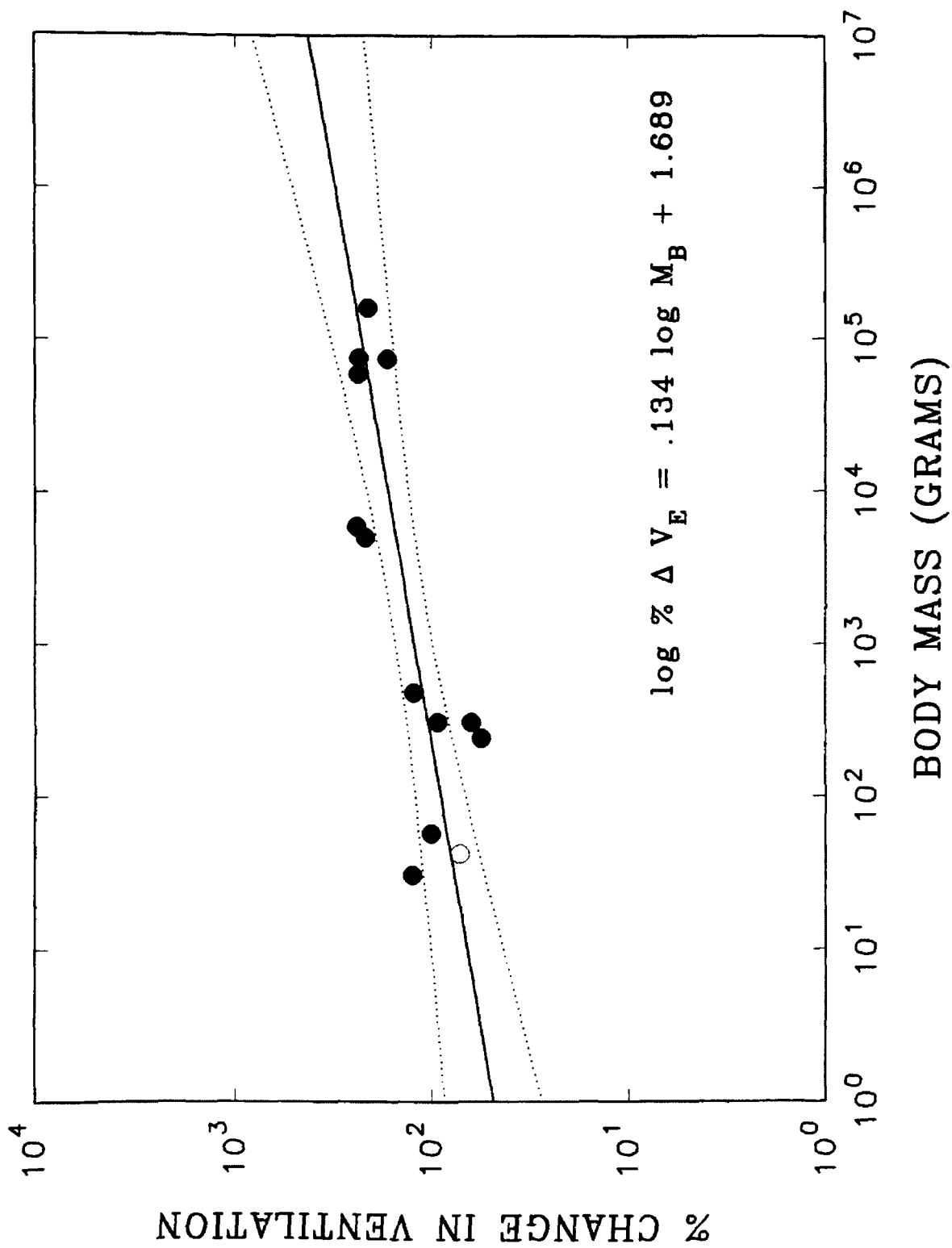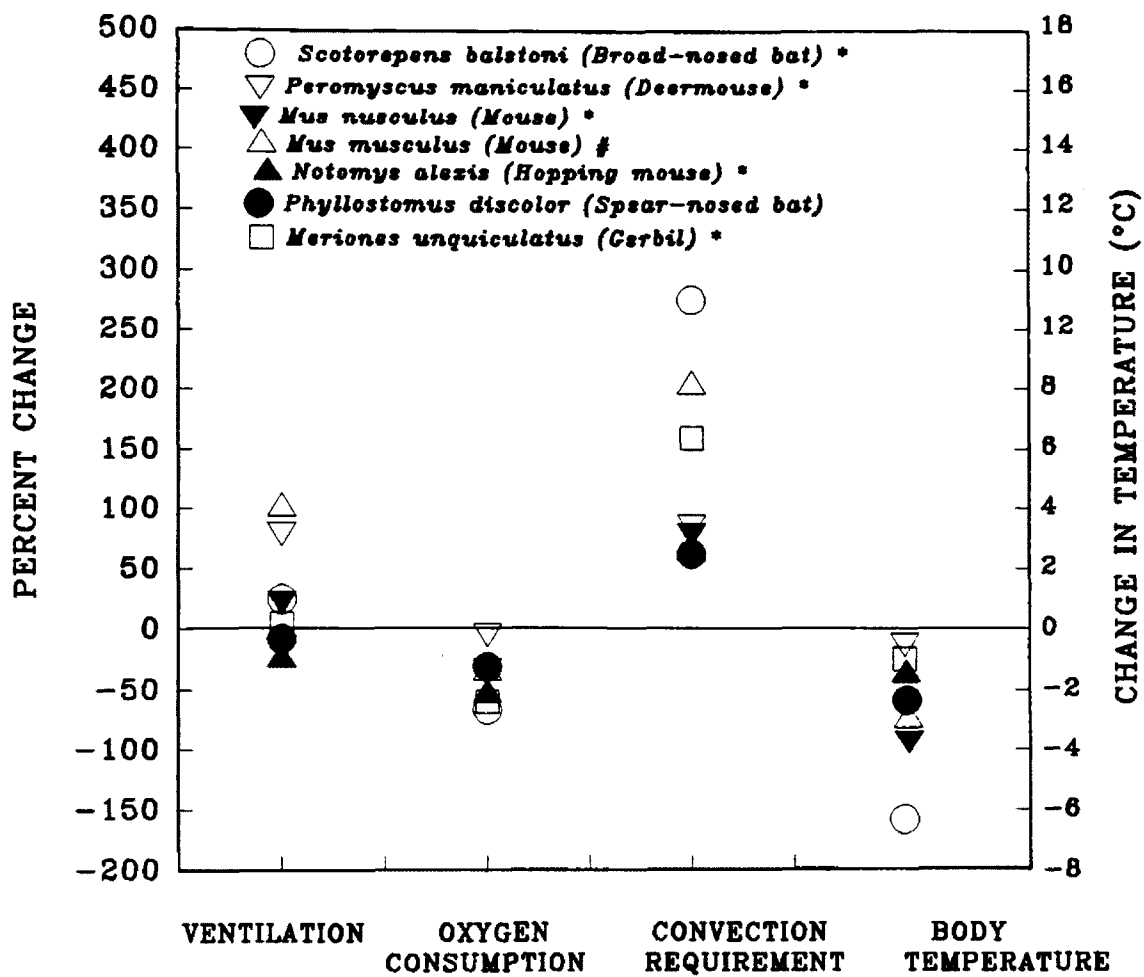
* Data from Frappel et al (Am. J. Physiol. 262:R1040, 1992)
# Data from Boggs (unpublished)

O MICE (mean M_B = 37g)

● LESSER SPEAR-NOSED
BATS (mean M_B = 43g)

350

300

250

P_{50}= 44

200

150

100

50

P_{50}= 28

0

0   20   40   60   80   100   120

PERCENT CHANGE IN V_E / V_{O_2}

$P_{I_{O_2}}$
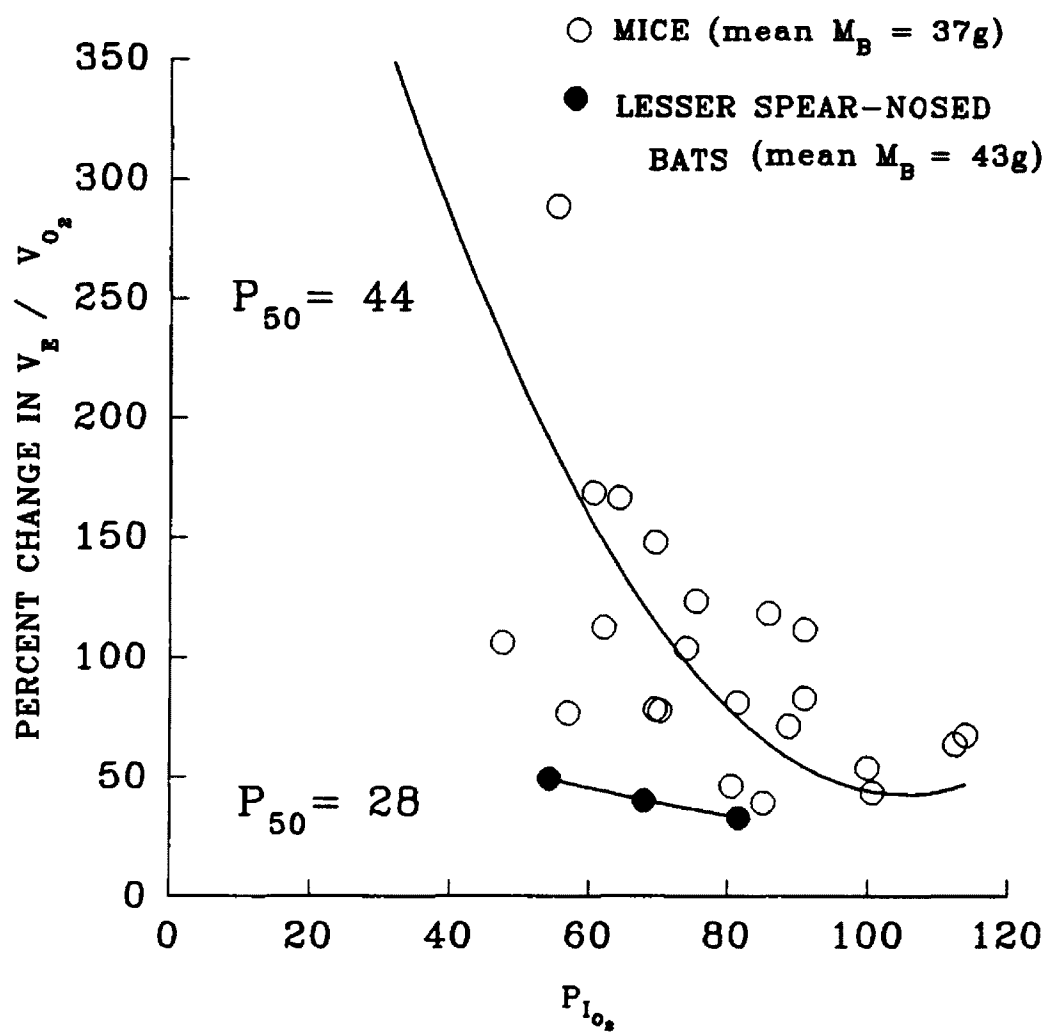
3% CARBON DIOXIDE

	0% V̇E	3% V̇E	%CHANGE	0% V̇O2	3% V̇O2	%CHANGE	0% CR	3% CR	%CHANGE	0% TB	3% TB	TBCHANGE
MEAN	81.971	106.520	29.866	0.061	0.057	-5.196	37.323	49.958	35.900	38.286	37.987	-0.299
STDE	10.981	15.444	4.442	0.008	0.008	7.140	6.627	9.349	11.887	0.319	0.293	0.117
		κπ	P=.002					κπ	P=.009		ж	P=.038

5% CARBON DIOXIDE

	0% V̇E	5% V̇E	%CHANGE	0% V̇O2	5% V̇O2	%CHANGE	0% CR	5% CR	%CHANGE	0% TB	5%TB	TBCHANGE
MEAN	70.810	123.620	71.696	0.057	0.057	1.198	32.394	58.648	82.187	38.176	38.204	0.076
STDE	6.523	14.878	8.313	0.007	0.007	6.326	5.617	10.553	15.836	0.207	0.222	0.226
		επ	P=.002					επ	P=.001			

7% CARBON DIOXIDE

	0% V̇E	7% V̇E	%CHANGE	0% V̇O2	7% V̇O2	%CHANGE	0% CR	7% CR	%CHANGE	0% TB	7%TB	TBCHANGE
MEAN	74.635	164.693	107.497	0.059	0.062	5.659	33.285	68.860	116.283	38.389	38.335	-0.144
STDE	8.275	18.527	9.479	0.007	0.009	8.627	6.207	12.879	27.986	0.224	0.278	0.280
		εκ	P=.000					εκ	P=.001			

STDE = STANDARD ERROR OF THE MEAN   VE IN MLS BTPS / MIN   VO2 IN ML STPD/MIN   TB IN C

Table 1. Ventilatory and metabolic response of lesser spear-nosed bats to hypercapnia. 0% columns contain data for measurements taken while the bats breathed a 0% CO2, 21% O2, balance N2 mixture. 3%, 5% and 7% columns contain data for measurements taken while while the bats breathed 3%, 5% and 7% CO2 mixtures. %CHANGE columns contain percent changes in ventilation (V̇E) oxygen consumption (V̇O2), convection requirement (CR = V̇E/V̇O2) and body temperature (TB) with different levels of hypercapnia. Symbols denote significant difference between the above percent change and 3% CO2 (ε), 5% CO2 (κ) and 7% CO2 (π).

45

3% CARBON DIOXIDE

	0% TI	3% TI	%CHANGE	0% TE	3% TE	%CHANGE	21% f	3% f	%CHANGE	0% TV	3%TV	%CHANGE	0% V̇E	3% V̇E	%CHANGE
MEAN	0.102	0.100	-1.656	0.296	0.290	-7.140	199.890	228.381	14.261	0.477	0.537	13.392	81.971	106.520	29.866
STDE	0.021	0.022	3.844	0.041	0.061	8.031	29.271	33.413	4.797	0.053	0.054	3.354	10.981	15.444	4.442
							K	P=.036				P=.004		$K\epsilon$	P=.002

5% CARBON DIOXIDE

	0% TI	5%TI	%CHANGE	0% TE	5% TE	%CHANGE	21% f	5% f	%CHANGE	0% TV	5%TV	%CHANGE	0% V̇E	5% V̇E	%CHANGE
MEAN	0.189	0.216	-3.761	0.303	0.202	-34.588	166.140	244.760	49.334	0.476	0.564	20.977	70.810	123.620	71.696
STDE	0.056	0.086	12.778	0.034	0.032	4.457	21.251	30.063	9.798	0.048	0.052	8.423	6.523	14.878	8.313
					$\pi\epsilon$	P=.001		π	P=.001			P=.041		$\pi\epsilon$	P=.002

7% CARBON DIOXIDE

	0% TI	7% TI	%CHANGE	0% TE	7% TE	%CHANGE	21% f	7% f	%CHANGE	0% TV	7%TV	%CHANGE	0% V̇E	7% V̇E	%CHANGE
MEAN	0.110	0.086	-17.255	0.310	0.164	-45.611	169.670	263.008	63.052	0.504	0.639	31.043	74.635	154.693	107.497
STDE	0.017	0.013	7.127	0.037	0.018	3.669	27.350	27.368	10.740	0.039	0.048	13.478	8.275	18.527	9.479
		π	P=.011		πK	P=.000		π	P=.000			P=.036		πK	P=.000

STDE = STANDARD ERROR OF MEAN   TI & TE IN SECONDS   TV IN MLS BTPS   f IN BREATHS / MIN

Table 2. Ventilatory response of lesser spear-nosed bats to hypercapnia. 0% columns contain data for measurements made while bats breathed a 0% CO_2, 21% O_2, balance N_2 mixture. 3%, 5% and 7% columns contain data for measurements made while the bats breathed 3%, 5%, and 7% CO_2 gas mixtures. %CHANGE columns represent percent change in in inspiratory time (TI), expiratory time (TE), ventilatory frequency (f), tidal volume (TV) and ventilation (V̇E) with different levels of hypercapnia. P-values denote significant differences between treatment value and normocapnic value. Symbols denote significant difference between the above percent change and 3% CO_2 (π), 5% CO_2 (K) and 7% CO_2 (ϵ).

12%

BAT	21% VE	12% VE	%CHANGE	21% VO2	12% VO2	%CHANGE	21%CR	12% CR	%CHANGE	21% TB	12% TB	TBCHANGE
MEAN	72.748	68.217	-3.654	0.056	0.048	-10.451	33.290	33.417	3.394	37.654	36.526	-1.129
STDE	6.921	7.502	9.433	0.004	0.002	7.177	4.216	3.199	6.592	0.256	0.208	0.269
										ρ ∂	P = .000	

10%

BAT	21% VE	10% VE	%CHANGE	21% VO2	10% VO2	%CHANGE	21% CR	10% CR	%CHANGE	21% TB	10% TB	TBCHANGE
MEAN	67.638	60.828	-8.191	0.057	0.039	-29.657	28.113	40.568	49.552	37.891	35.677	-2.214
STDE	6.549	6.814	10.698	0.003	0.004	7.802	2.636	2.884	13.346	0.273	0.327	0.210
				δ ∂	P = .006		δ	P = .006		δ ∂	P = .000	

8%

BAT	21% AIR	8% VE	%CHANGE	21% VO2	8% VO2	%CHANGE	21%VO2	8%V/VO2	%CHANGE	21% TB	8% TB	TBCHANGE
MEAN	68.430	47.913	-25.112	0.059	0.026	-63.694	26.486	49.573	91.283	38.089	34.521	-3.568
STDE	7.181	3.421	8.448	0.004	0.002	6.690	1.678	8.552	34.806	0.274	0.308	0.210
	δ ρ	P = .015			δ ρ	P = .000				δ ρ	P = .000	

STDE = STANDARD ERROR OF MEAN   VE IN MLS BTPS / MIN   VO2 IN MLS STPD / MIN   TB IN °C

Table 3. Ventilatory and metabolic responses of lesser spear-nosed bats to hypoxia. 21% columns contain data for measurements made while the bats breathed a 21% O2, balance N2 gas mixture. 12%, 10% and 8% columns contain data for measurements made while the bats breathed 12%, 10% and 8% O2 gas mixtures. %CHANGE columns show percent change in ventilation (VE), oxygen consumption (VO2), convection requirement (VE/VO2) and body temperature (TB). P-values denote significant differences between treatment values and normoxia. Symbols denote significant difference between given value and 12% O2 (δ), 10% O2 (ρ) and 8% O2 (∂) value.

12% OXYGEN

	21% TI	12%TI	%CHANG	21% TE	12% TE	%CHANG	21% f	12% f	%CHANG	21% TV	12% TV	%CHANG	21% V̇E	12% V̇E	%CHANGE
MEAN	0.108	0.137	28.232	0.272	0.351	31.915	181.023	140.051	-21.786	0.419	0.497	19.675	72.748	68.217	-3.654
STDE	0.011	0.017	13.954	0.030	0.044	13.638	16.182	15.273	5.533	0.029	0.037	5.501	6.921	7.502	9.433
							Ѱ	P=.002				P=.011			

10% OXYGEN

	21% TI	10% TI	%CHANG	21% TE	10% TE	%CHANG	21% f	10% f	%CHANG	21% TV	10% TV	%CHANG	21% V̇E	12% V̇E	%CHANGE
MEAN	0.123	0.171	44.830	0.312	0.411	35.839	148.652	116.026	-20.412	0.463	0.528	16.416	67.638	60.828	-8.191
STDE	0.011	0.016	14.600	0.026	0.038	12.316	11.254	10.096	5.518	0.026	0.030	8.754	5.549	6.814	10.698
			P=.010				P=.029			P=.017					

8% OXYGEN

BAT	21% TI	8% TI	%CHANG	21% TE	8% TE	%CHANG	21% f	8% f	%CHANG	21% TV	8% TV	%CHANG	21% V̇E	8% V̇E	%CHANGE
MEAN	0.128	0.206	73.416	0.337	0.432	41.602	148.344	91.649	-34.494	0.474	0.535	14.261	68.430	47.913	-25.112
STDE	0.014	0.019	19.403	0.040	0.037	17.198	15.844	6.959	6.089	0.030	0.037	6.478	7.181	3.421	9.448
		β P=.001						β P=.002						βϒ P=.016	

STDE = STANDARD ERROR OF MEAN   TI & TE IN SECONDS   TV IN MLS BTPS   f IN BREATHS / MIN

Table 4. Ventilatory response data for lesser spear-nosed bats exposed to hypoxia. 21% columns contain data for measurements made while the bats breathed a 21% O2, balance N2 gas mixture. 12%, 10% and 8% columns contain data for measurements made while the bats breathed 12%, 10% and 8% O2 gas mixtures. %CHANGE column data represent percent change in inspiratory time (TI), expiratory time (TE), ventilatory frequency (f), tidal volume (TV) and ventilation (V̇E) with different levels of hypoxia. P-values denote significant differences between treatment value and normoxia. Symbols denote significant difference between the above percent change and 12% O2 (β), 10% O2 (ϒ) and 8% O2 (Ѱ).

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