

## HYPOXIA AND ITS INFLUENCES ON THE CARDIOVASCULAR AND RESPIRATORY SYSTEMS OF SPONTANEOUSLY BREATHING CATS

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### ABSTRACT

Effects of acute systemic hypoxia on the cardiovascular system (CVS) and respiration of spontaneously breathing cats were studied in two conditions. 1): Hypoxic air (6-8% O<sub>2</sub> in N<sub>2</sub>) was given to the animal to induce systemic hypoxia for 20 minutes. Hyperventilation at this condition lowered arterial CO<sub>2</sub> tension (PaCO<sub>2</sub>; hypocapnia). 2): In the second run, induction of hypocapnia was prevented by adding 3-5% CO<sub>2</sub> to hypoxic air. Comparison of the results of this study indicated that hypoxia, independent of the presence of hypocapnia, caused a significant increase in respiratory rate, aortic flow and arterial blood pressure. However, in the presence of hypocapnia, the increased respiratory rate was 10% less and a general arterial vasoconstriction was observed.

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**Keywords:** hypocapnia; arterial chemoreceptors; cardiovascular system.

### INTRODUCTION

Previous reports have shown that systemic hypoxia increases neural discharge of aortic and carotid chemoreceptors of the cat.<sup>5</sup> Furthermore, the integrity of these receptors is essential in order for the CVS to overcome the direct depressing effects of hypoxemia.<sup>3</sup> Previous reports have shown that stimulation of arterial chemoreceptors during systemic hypoxia in artificially breathing cats produced an increase in myocardial contractility, cardiac output and arterial blood pressure,<sup>6,7</sup> whereas in the dog this maneuver had an opposite response.<sup>1,7</sup> In normally breathing dogs the usual circulatory responses to systemic hypoxia were tachycardia, increased cardiac output, and peripheral vasodilation.<sup>2</sup> Because of these discrepancies which exist between the reports presented in the literature in one species and the above mentioned examples between dogs and cats, we can not say if arterial chemoreceptors and cardiovascular system of these two species act identically during systemic hypoxia.

It has been shown that exposure of the cat to systemic

hypoxia stimulated aortic and carotid chemoreceptors.<sup>5</sup> Stimulation of carotid bodies is strongly under the influence of PaCO<sub>2</sub>, whereas aortic chemoreceptor responses to this stimulation were not affected that much.<sup>5</sup> Stimulation of these receptors during systemic hypoxia,<sup>3</sup> or by chemical agents during systemic normoxia induced an increase in the heart rate and vasoconstriction.<sup>8</sup> Again in the dog these effects were totally the opposite.<sup>1,2</sup> On the basis of these observations we tried to see if hypocapnia which changes the sensitivity of carotid chemoreceptors to hypoxia interacts with direct and reflex responses of the CVS to systemic hypoxia.

Hence the purpose of this study was to determine the influences of systemic hypoxia on the systemic vasculature and the heart of the spontaneously breathing cat. In this study we tried to see: 1) What influences systemic hypoxia has on the CVS of the cat, especially when the animal's respiration is regulated centrally in response to the need of the body, 2) and whether hypocapnia alters these responses as it does with chemoreceptors.

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**Table I: Arterial pH, carbon dioxide and O<sub>2</sub> tensions during control and during hypoxic-hypocapnia\***

Time	pHa	PaCO <sub>2</sub> (mmHg)	PaO <sub>2</sub> (mmHg)
CONT. 1	7.422 ± 0.001	22.7 ± 1	75 ± 4
MIN. 5	7.493 ± 0.010	17.0 ± 1*	46 ± 3*
MIN. 10	7.507 ± 0.10*	15.8 ± 1*	46 ± 1*
MIN. 15	7.502 ± 0.010	15.2 ± 1*	43 ± 1*
MIN. 20	7.508 ± 0.009*	14.7 ± 0*	43 ± 1*

+ = Values are expressed in mean ± SE

\* = Vales are significantly different from control values at P≤0.05

**Table II: Arterial pH, carbon dioxide and O<sub>2</sub> tensions control and during hypoxic-normocapnia†**

Time	pHa	PaCO <sub>2</sub> (mmHg)	PaO <sub>2</sub> (mmHg)
CONT. 2	7.418 ± 0.003	21.6 ± 1	81 ± 2
MIN. 5	7.424 ± 0.010	21.1 ± 1	45 ± 3*
MIN. 10	7.428 ± 0.010	21.5 ± 1	45 ± 1*
MIN. 15	7.425 ± 0.012	22.7 ± 1*	46 ± 1*
MIN. 20	7.420 ± 0.010	21.6 ± 1	43 ± 1*

† = Values are expressed in mean ± SE of mean

\* = Vales are significantly different from control values at P≤0.05

### METHODS

**Preparation:** Experiments were carried out on 18 cats. Anesthesia was produced by intraperitoneal injection of 30 mg/kg sodium pentobarbital. Two catheters were placed into right femoral artery and vein for taking arterial blood samples and infusion of dextrose saline during surgery. Arterial blood pressure was measured with a Statham (p-23 Db) pressure transducer connected to arterial cannula. Blood samples (1 ml) were collected to measure arterial PO<sub>2</sub>, PCO<sub>2</sub> and pH (PaO<sub>2</sub>, PaCO<sub>2</sub>, and pHa) with a blood gas analyzer and pH electrode (Radiometer pH M 72 MK2). Left femoral vein was cannulated for continuous recording of central venous pressure. Animal's core temperature was maintained between 36-38°C with the use of an electric plate.

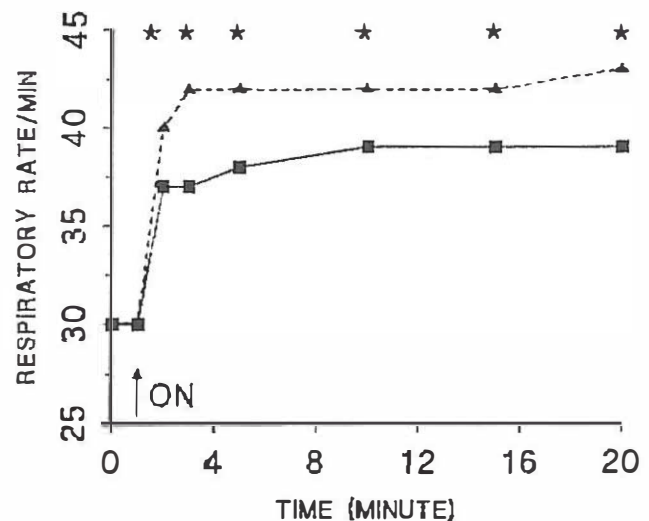
Trachea was intubated for artificial ventilation during surgery and to control animal's breathing gas mixture as stated in the text. Left lateral thoracotomy was performed at fifth interspace as described earlier.<sup>3,6,7</sup> Pericardium was cut and ascending aorta was separated from pulmonary artery. An electromagnetic flow probe (No. 5) was placed about the root of aorta to record aortic flow (Q<sub>ao</sub>). After placing the probe the chest was closed airtight and respiratory pump disconnected to let the animal breath regularly by itself. The animal was left at rest for three hours to reduce the effects of surgical stress.

All of the recordings were made on a seven channel Grase polygraph. Mean arterial blood pressure (Pa) was recorded by electronically damping arterial blood pressure trace. Aortic flow was recorded by a Carolina electromagnetic flow meter. Total peripheral resistance (TPR), excluding coronary resistance, was calculated by dividing Pa minus central venous pressure (mmHg) by Q<sub>ao</sub> (ml/min) and reported as resistance units.

**Experimental procedure:** Before the start of the experiment an arterial blood sample was taken (CONT, Tables I and II). Then the animal was exposed to hypoxic air for 20 minutes and all parameters mentioned above were recorded. After giving the exposed animal room air for one hour to bring blood gas values back to normal and eliminate hypoxic stresses, the same level of hypoxia was induced in the second run as mentioned above but hypocapnia was eliminated by adding 3-5% CO<sub>2</sub> to the hypoxic air.

### Statistical analysis

All results were expressed as mean and standard error of the mean. The data were analyzed using analysis of variance. Duncan's new multiple range test was used to find statistical



**Fig. 1.** Respiratory rate as a function of time during control (0 time) systemic hypoxia with (■) and without hypocapnia (▲). ON= start of the experiment. (\*=significantly different from control, P≤0.05).

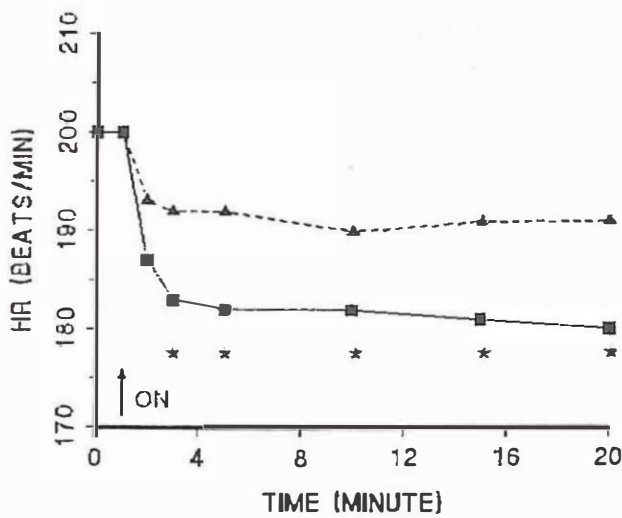


Fig. 2. Heart rate (beats/min.) as a function of time. Other descriptions are as in Fig. 1.

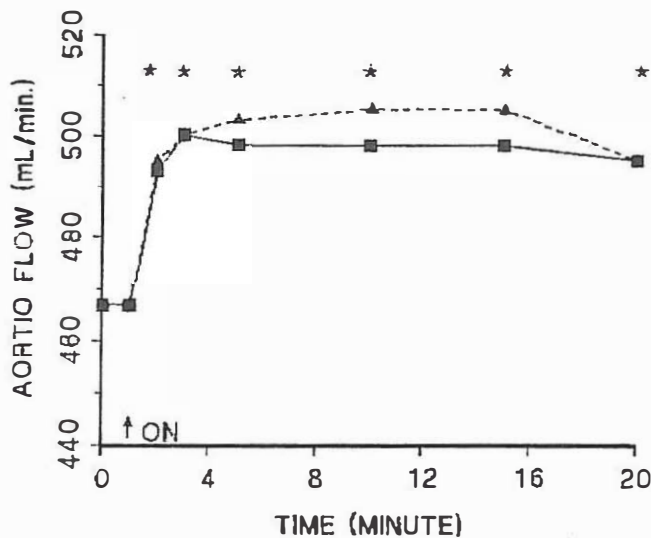


Fig. 3. Aortic flow (ml/min.) as a function of time. For more detail see the legend of Fig. 1.

differences between the means when probability value was equal or less than 0.05 ( $P \leq 0.05$ ).

## RESULTS

Blood gas values and pH are presented in Tables I and II. There was a significant and equal decrease in  $\text{PaO}_2$  in both experiments.  $\text{PaCO}_2$  decreased and pH was elevated significantly in the first experiment and remained normal during the second experiment.

Respiration: There was a significant increase in respiratory rate as shown in Fig. 1. Comparison of the results of the two experiments indicated that elimination of hypocapnia caused a slight increase in respiratory rate.

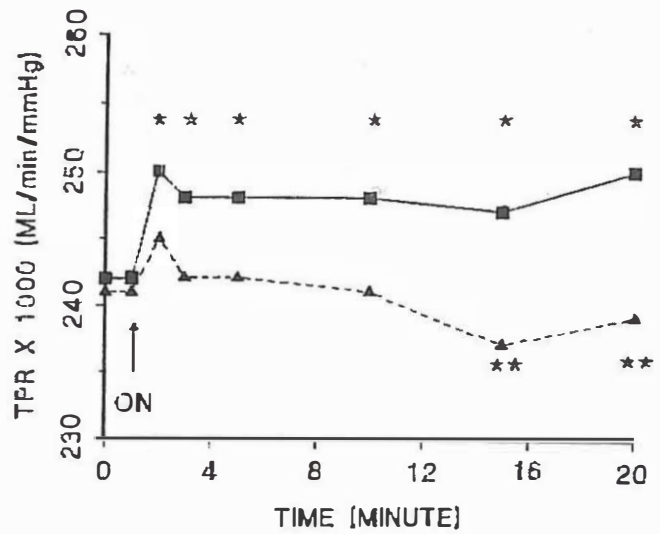


Fig. 4. Total peripheral resistance (TPR) as a function of time. For more detail see the legend of Fig. 1 (\*\*=significantly different from each other at  $p \leq 0.05$ .)

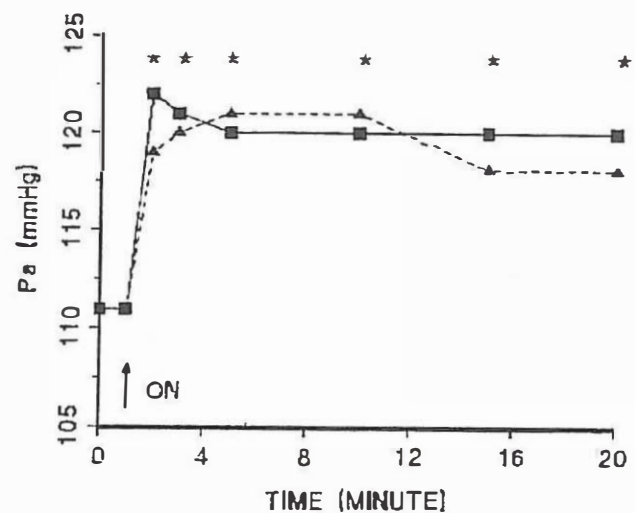


Fig. 5. Mean arterial blood pressure,  $\text{Pa}$  (mmHg) as a function of time. For more detail see the legend of Fig. 1.

Cardiac activity: As shown in Fig. 2, systemic hypoxia only in the presence of hypocapnia caused a significant (11 %) decrease in heart rate. However, it is interesting to note that presence or absence of hypocapnia did not affect the increased levels of aortic flow during hypoxia. (Fig. 3).

Vascular resistance and blood pressure: Changes in TPR are shown in Fig. 4. There was a sharp elevation in TPR two minutes after exposure to hypocapnia but leveled off during normocapnia. Systemic hypoxia independent of the level of  $\text{PaCO}_2$  significantly elevated the  $\text{Pa}$  (Fig. 5).

## DISCUSSION

In this study the influence of systemic hypoxia and



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hypocapnia was assessed by exposing the normal breathing cat to hypoxic air. This is a model of high altitude hypoxia which is seen in mountain climbers. It seems that hypocapnia reduced the reflex sensitivity of the respiratory center to hypoxia (Fig. 1). This is so because earlier reports have indicated that carotid body neural discharge was lower during hypocapnia.<sup>5</sup> The reflex and direct responses of arterial blood vessels to systemic hypoxia in spontaneously breathing cats were similar to what was reported earlier in artificially breathing cats.<sup>4,6</sup> Induction of hypocapnia converts this response to vasoconstriction (Fig. 4). However, Daly et al. indicated that systemic hypoxia even in the presence of hypocapnia in self-breathing dogs produced peripheral vasodilation.<sup>2</sup> It is interesting to note that elevation of cardiac output (not TPR) was the main cause of hypertension in the cat (Fig. 3), whereas in Daly's report, strong vasoconstriction (even cardiac output decreased) was the cause of hypertension.<sup>2</sup> There was a significant reduction in the values of heart rate with the presence of hypocapnia (Fig. 2). Whereas tachycardia was reported in the dog at the same condition.<sup>2</sup> This is another reason to believe that the CVS responses of these two species to systemic hypoxia are totally different.

In summary, results of this study indicated that systemic hypoxia in spontaneously breathing cats increased respiratory activity. Its influences on the CVS seemed to be the same as what was reported earlier in the artificially breathing cat.<sup>5</sup> Induction of hypocapnia due to hyperventilation did not significantly alter the increased levels of aortic flow and blood pressure. However, elimination of hypocapnia curtailed bradycardia and induced arterial vasoconstriction. Finally from these results we strongly believe that responses

of the cardiovascular system of the cat and the dog to systemic hypoxia are totally different.

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