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Autonomic regulation of organ vascular resistances during hypoxemia in the cat

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Abstract

This study aimed to dissect the roles played by the autonomic interoreceptors, the carotid bodies (cbs) and the aortic bodies (abs) on the vascular resistances of several organs in anesthetized, paralyzed, artificially ventilated cats challenged by systemic hypoxemia. Two 15 min challenges stimulated each of 5 animals in two different groups: (1) In the intact group hypoxic hypoxia (10% O₂ in N₂; HH) stimulated both abs and cbs, increasing neural output to the nucleus tractus solitarius (NTS); (2) In this group carbon monoxide hypoxia (30% O₂ in N₂ with the addition of CO; COH) stimulated only the abs, increasing neural output to the NTS. (3) In the second group in which their bilateral aortic depressor nerves had been transected only the cbs increased neural output to the NTS during the HH challenge; (4) In this aortic body resected group during COH neither abs nor cbs increased neural traffic to the NTS. CO and 10% O₂ reduced Hb saturation to the same level. With the use of radiolabeled microspheres blood flow was measured in a variety of organs. Organ vascular resistance was calculated by dividing the aortic pressure by that organ's blood flow. The spleen and pancreas revealed a vasoconstriction in the face of systemic hypoxemia, thought to be sympathetic nervous system (SNS)-mediated. The adrenals and the eyes vasodilated only when cbs were stimulated. Vasodilation in the heart and diaphragm showed no effect of chemoreceptor stimulated increase in SNS output. Different chemoreceptor involvement had different effects on the organs.

Keywords

hypoxemia; arterial chemoreceptors; autonomic nervous system; organ vascular resistance

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1. INTRODUCTION

Cardiopulmonary responses to hypoxemia and to carotid body (cb) stimulation have been studied extensively, mostly between the middle 1970s up to the late 1980s. This very large corpus of reports has been elegantly reviewed more recently by Janice Marshall (1994). Some time ago surgical removal of the cbs had been proposed and performed for the benefit of those suffering from pulmonary disorders (Winter, 1972; Stulberg and Winn, 1989; Severinghaus, 1989, Whipp and Ward, 1992). Very recently surgical removal of the cbs has been proposed for the benefit of those suffering from cardiovascular disease (Ponikowski, et al., 1997; Ponikowski, et al., 2001; Paton, et al., 2013). Hence, it seemed appropriate once again, using an animal model, to explore the effects of hypoxemia, acting on arterial chemoreceptors and through the autonomic nervous system (ANS), on cardiovascular responses throughout the organism.

However, as Marshall (1994) has pointed out, multiple factors (Magosso and Ursino, 2001; Ursino and Magosso, 2000) act during hypoxemia and/or cb stimulation to make interpretation of the results difficult. Among such are hyperventilation, hypocapnia, pulmonary stretch receptor/vagal activation, central respiratory drive, blood pressure changes and baroreceptor involvement, extensive systemic tissue hypoxia-induced vasodilation, circulating catecholamines and angiotensin 2.

The purpose of the present study in the anesthetized, paralyzed, open-chested, artificially ventilated cat was to see during the challenge of systemic hypoxemia the role of the cbs and aortic bodies (abs) – acting together, each singly, or not at all --in the control of the vasculature of several organs, while keeping most of the above-mentioned factors constant. Our interpretation of our data will focus on the chemoreceptors, baroreceptors, systemic vasodilation, and the sympathetic nervous system (SNS).

2. MATERIALS AND METHODS

2.1. Animal Model

Two groups of cats of either sex weighing approximately 4 kg were initially sedated with ketamine (35mg/kg, ip), anesthetized (sodium pentobarbital, 30 mg/kg, iv), paralyzed (succinylcholine, 5mg/kg, iv), and artificially ventilated. Anesthesia was renewed when the medial canthal reflex showed a small response, or normoxic blood pressure values became unstable during intervening rest periods, or when the animal appeared to fight the respirator. Occasionally reflex withdrawal from a toe pinch was used. Each group consisted of five cats.

2.2. Preparation

2.2.1. Trachea was cannulated after a midline incision which also exposed the bilateral aortic depressor nerves running alongside/juxtaposed to the cervical vagi. Aortic depressor nerves were isolated, covered with pledgets soaked in Krebs Ringer bicarbonate solution and a layer of mineral oil on top, and warmed with a lamp if necessary. In the aortic body resected group (*abr*) the nerves were sectioned bilaterally to remove centrad directed signals from the aortic bodies.

2.2.2. Catheters were inserted into the:

2.2.2.1. Left femoral artery for measuring blood pressure and for drawing blood samples.

2.2.2.2. Left femoral vein for further injections of anesthetic, NaHCO₃, and glucose.

2.2.2.3. Right femoral artery, advanced into the descending aorta for withdrawing the reference sample.

After these general procedures were completed a left lateral thoracotomy was performed at the fifth interspace with the animal ventilated on 100% oxygen. The pericardium was cut and the ascending aorta was gently separated from the pulmonary artery. An electromagnetic flow probe (Biotronex Laboratory Inc., 6.0mm; connected to Biotronex Flowmeter, BL 620) was placed around the root of the aorta. In three previous pilot studies tests had been performed to show that this placement did not modify the aortic nerve activity. Proper calibration of the probe was made using a dog's femoral artery through which blood was pumped at differing rates and at various pressures; outflow into a graduated cylinder was timed. A straight line graph was created having a correlation coefficient of 0.99.

2.2.2.4. Left atrium via the appendage for injection of radiolabeled microspheres to determine blood flow to several organs.

e. All pressures were referenced to the level of the right atrium.

2.2.3. Temperature was monitored and kept constant between 37-39° C with a rectal probe and heating pads.

2.3. Recordings

2.3.1. Variables being recorded from the preparation were led to a polygraph (Electronics for Medicine).

2.3.2. Arterial blood samples (0.5-1.0mL) were collected periodically during the preparation phase and during the control/challenge phases of the protocol. Partial pressures of oxygen and carbon dioxide, and hydrogen ion concentration were measured on the Radiometer BMS3MK2 blood gas analyzer. Oxygen saturation, hemoglobin concentration, and carboxyhemoglobin were measured with a CO-oximeter B (Instrumentation Laboratories #182). After blood samples were taken, 0.5-1.0 mL of Dextran 40 (10% Dextran) was infused to preserve normovolemia.

2.4. Preparation and Administration of Radiolabeled Microspheres

2.4.1. Standard procedures were followed in the preparation of four groups of radiolabeled microspheres (Diameter: $15 \pm 3 \mu\text{m}$) with Cerium-141 (Ce-141), Tin-113 (Sn-113), Strontium-85 (Sr-85), and Scandium-46 (Sc-46). Each of these isotopes can be easily distinguished from the others by their principal gamma emission spectra. Precautions and procedures were taken to factor out counts measured at energies differing from their principal peaks.

2.4.2. Each of the four groups of carbonized labeled microspheres was subjected to sonication for 20 minutes before use. The container of microspheres was removed from the sonicator and vigorously shaken for 45 seconds. Then 0.2 mL (8×10^5 spheres) was drawn into a disposable plastic syringe and diluted up to 3 mL with saline. This syringe was shaken for one minute.

2.4.3. The entire content was then injected into the left atrium over 20 seconds. Proper flushing/washing of syringe and catheter followed.

2.4.4. Reference arterial blood samples were taken with a Harvard syringe pump (constant flow: 1.36 ± 0.2 mL/min) beginning 20-40 seconds prior to the injection of spheres and continuing for at least 90 seconds after injection and flushing were completed.

2.5. Measurement of Tissue Blood Flow for each Organ

2.5.1. Fundamental Equation: $(\text{Flow})_i = A_i/A_r \times ([\text{Flow}]_r/\text{Wt}) \times 100$ where $(\text{Flow})_i$ is tissue blood flow (mL/min per 100g tissue), $(\text{Flow})_r$ is withdrawal rate of reference sample (mL/min); A_i and A_r are total tissue counts and reference counts, respectively; Wt is weight of the organ of interest in grams.

2.5.2. Each organ was removed at the completion of the protocol, and weighed fresh. It was then divided into small pieces and placed in counting vials, which were always filled to a height of 3 cm or less to avoid counting distortions.

2.5.3. Standards for the injected isotopes, reference blood samples, and samples from the organs were counted at the same time for the same duration (1 minute). Values were then plugged into the above equation for determining the organ blood flow.

2.5.4. Calculation of the organ vascular resistance was achieved by noting the aortic pressure at the time of the injection and dividing that number by the organ's blood flow.

2.6. Experimental Design

2.6.1. Background studies (Fitzgerald, et al., 1979; Fitzgerald and Traystman, 1980; Lahiri, et al., 1981) showed that both carotid bodies and aortic bodies increased their neural output to the nucleus tractus solitarius (NTS) in response to lowered partial pressures of oxygen in the arterial blood (P_aO_2); this also lowered arterial oxygen saturation (S_aO_2). However, the carotid bodies (cbs) did not respond to a lowering of S_aO_2 with carbon monoxide, whereas the aortic bodies (abs) did respond with increased neural output.

2.6.2. This behavior of the arterial chemoreceptors allowed a design in which the animal could be challenged with 10% O_2 in N_2 (hypoxic hypoxia, HH) and have both cbs and abs sending increased neural output to the NTS. The animal could then be challenged with carbon monoxide hypoxia (COH) with a normal P_aO_2 and only the abs would increase their output to the NTS. This was the one group of cats (*intact*; $n=5$) which generated results labeled HHint and COHint. To make the measurements of control and experimental phases for each challenge required the use of four labeled microspheres.

2.6.3. The second group of cats which had their bilateral aortic depressor nerves transected (*abr*; $n=5$) generated results labeled HHabr and COHabr. Again the control and experimental phases of the two challenges required the use of four labeled microspheres. In this group during the HH challenge only the cbs were sending increased neural output to the NTS; during the COH challenge neither abs nor cbs were sending increased neural traffic to NTS.

2.7. Protocol for Both Intact and Aortic Nerve Transected Groups

2.7.1. Three hours were allowed for the preparation to recover from the surgical procedures.

2.7.2. The experimental procedure started with a control period of normoxia, normocapnia. Measurements of blood gas values, aortic flow, and aortic pressure were made, followed by microsphere injection #1.

2.7.3. A 15 min challenge of hypoxic hypoxia (HH; 10% O₂ in N₂) followed in which all variables were measured, with a blood sample taken at the 15 minute time period. Microsphere injection #2 immediately followed the 15 min blood sample.

2.7.4. A one hour rest period under normoxia/normocapnia followed.

2.7.5. A second control period as in step 2. (above) was established when microsphere injection #3 was made along with a recording of aortic flow and pressure and blood gas values.

2.7.6. The animal was then ventilated for 15 min on carbon monoxide (COH; 2% in air for the first 2 min [reducing S_aO₂ to 50-60%] and then 0.1% for the last 13 minutes [reducing S_aO₂ to 35-40%]). Blood sample values and other variables' values were recorded. Microsphere injection #4 immediately followed the taking of the final blood sample.

2.7.7. Animals were sacrificed with an i.v. injection of Na-pentobarbital (50mg/kg). An absence of heart beat for five minutes signaled the sacrifice was complete. Preparation of the animal and steps in the protocol were approved by the University's Animal Care and Use Committee which follows the National Institutes of Health's norms and guidelines for the care and use of animals.

2.8. Statistical Evaluation Tools

2.8.1. All evaluations within a group (intact or abr) used the Repeated Measures Analysis of Variance (RMANOVA). This was followed by The All Pairwise Multiple Comparison Procedure (Tukey Test). Because of the limited number of experiments we also normalized the challenge value to the control value. Again RMANOVA was used to compare the normalized responses within the intact group and within the abr group. To test values between groups a Student's t-Test was used. This tested, for significance, the difference between two samples from separate populations.

3. RESULTS

3.1. Stimulus

Blood Gas Data are found in Table 1. Note the relative constancy in the pH_a and the P_aCO₂ values. The magnitudes of the hypoxic stimulus were comparable as were the reductions in S_aO₂.

3.2. Responses

3.2.1. *Systemic Responses* in the Five Intact and in the Five Abr cats (Mean±SEM).

3.2.1.1. CARDIAC OUTPUT—Table 2 (top) presents the increases in cardiac output (C.O.) during the control (ctl) and 15 challenge phases (HH, COH) of the five experiments in the two groups of cats.

3.2.1.2. AORTIC BLOOD PRESSURE—Table 2 (middle) presents the increases in aortic blood pressure (P_{ao}) during the control (ctl) and 15 challenge phases (HH, COH) of the five experiments in the two groups of cats.

3.2.1.3. TOTAL PERIPHERAL RESISTANCE—Table 2 (bottom) presents the changes in total peripheral resistance (TPR) during the control (ctl) and 15 challenge phases (HH, COH) of the five experiments in the two groups of cats.

3.2.2. **Organ Vascular Resistances** in the Five Intact and Five Abr Cats. The data presented in the figures show an A panel and a B panel. The A panel records the calculated vascular resistance of the organ from P_{ao} at the time of the injection of microspheres to determine blood flow in the organ divided by the organ's measured blood flow. In panel B we have chosen to normalize each 15 minute (15) value to its respective control value (ctl) in each of the five animals of each group (*int*, *abr*) since there was some variability in the measurements and the number of experiments was small. Again the RMANOVA tool was used within a group, while the Student's t-Test was used to test between groups (*int* vs *abr*).

3.2.2.1. BRAIN—3.2.2.1.1. Brain blood flow increased significantly during HHint (327% of ctl), during COHint (402% of ctl), during HHabr (442% of ctl), and during COHabr (295% of ctl). With respect to vascular resistance, systemic hypoxemia significantly vasodilated the brain vasculature in both the intact (*int*) and in the aortic body denervated (*abr*) groups. RMANOVA shows all four 15 values are significantly less than their corresponding control values. Again RMANOVA shows in the *int* group that the two control (ctl) values do not differ. But the two 15 values also do not differ significantly ($P = 0.306$); this is somewhat curious since all five 15 values during the COHint challenge were less than the corresponding 15 values during the HHint challenge. The two ctl values for the *abr* group differed ($P = <0.001$) while the two 15 values were statistically indistinguishable.

3.2.2.1.2. In Figure 1B the 15 values in Figure 1A were normalized each to its own ctl . Although in Figure 1A RMANOVA showed the 15 HHint value did not differ from the 15 COHint value, normalizing the data showed the components operating during the HHint challenge had a greater effect in overcoming the hypoxemic-induced vasodilation than did the components during the COHint challenge . The drop in vascular resistance during COHint challenge was to a significantly lower percent of its control than during the HHint challenge ($P = 0.003$). The two normalized drops in vascular resistance in the *abr* group did not differ significantly. Evaluation with a Student's t-Test showed the HHint value in the first group to be significantly higher than the HHabr value in the second group ($P = 0.001$); the same test showed the HHint value did not differ from the COHabr value ($P = 0.085$). Nor do the COHint and HHabr values differ. In terms of peripheral chemoreceptor involvement the data suggest that the combination of cbs plus abs attenuates the hypoxia-induced tissue vasodilation more than the cbs acting alone, and there is no difference between the effect of the cbs acting alone and that of the abs acting alone.

3.2.2.1.3. Table 3 presents the increases in blood flow to various parts of the brain during the two challenges as a % of the ctl value. Note that in 10/12 brain areas of the *int* cats the increase in blood flow during the HH challenge is less than the increases during the COH challenge. In the *abr* cats all 12 areas during the HH challenge have a greater blood flow than during the COH challenge (as % of ctl).

3.2.2.2. HEART—Coronary blood flow increased significantly during both challenges in both groups: by 739% (HHint), by 420% COHint), by 469% (HHabr), and by 451% (COHabr) of their respective controls. Figure 2A shows significant reductions ($P = <0.001$) in coronary vascular resistance during all four hypoxic challenges. There are no significant differences among them. Nor are there significant differences when the 15 values are normalized each to its own control value (Figure 2B).

3.2.2.3. KIDNEY(data not shown)—Kidney blood flow increased by 39% (HHint) and 17% (COHint) of their respective ctl values, but decreased by 2% (HHabr), and 6% (COHabr) of their respective ctl values. None of the changes was significant. Though the hypoxemic challenges did reduce the renal vascular resistance in all four challenges, RMANOVA detected no significant differences between the ctl and 15 values during either

of the two challenges in either the *int* group or the *abr* group of cats. This was also true when the 15 values were normalized each to its own control.

3.2.2.4. SPLEEN—HHint, COHint, HHabr, COHabr significantly decreased splenic blood flow to 34%, 35%, 41%, and 38% of their respective ctl values. Figure 3A shows a pronounced vasoconstriction in the face of what must have been the local vasodilatory effect of systemic hypoxia; it was significant in three of the four challenges. RMANOVA showed the constriction during the COHabr challenge not to be significant ($P = 0.108$). But since 5/5 values for 15 were $> \text{ctl}$, a paired t-Test did show significance ($P=0.021$). Figure 3B indicates that the 15 value for the COHint challenge, normalized to its own control, is significantly ($P = 0.041$) less than that for the normalized 15 value for the HHint challenge. But the two normalized values for the *abr* cats do not differ significantly. Between groups evaluations showed HHint differed significantly from COHabr, but not from HHabr. COHint differed from neither HHabr nor COHabr.

3.2.2.5. STOMACH—HHint, HHabr, and COHabr significantly increased stomach blood flow by 66%, 58%, and 90% of their respective ctl values. The 36% increase during COHint was not significant. From the perspective of chemoreceptor impact on the sympathetic nervous system's (SNS) role in offsetting the systemic-wide vasodilation Figure 4A presents an interesting picture. In the *int* group RMANOVA shows the 15 reduction in vascular resistance during the HHint challenge is not significant whereas the reduction during the COHint challenge is significant ($P = 0.033$). Furthermore, in the *abr* group both 15 reductions are significant ($P = 0.001$, $P = <0.001$). Normalizing the 15 value as a percent of its own control (Figure 4B), one finds that in the *int* group the % reductions did not differ significantly. The same held true in the *abr* group. With the use of the Student's t-Test the normalized value for the HHint challenge is significantly greater than either the HHabr challenge ($P = 0.017$) or the COHabr challenge ($P = <0.001$). Further, the normalized reduction with abs acting alone (COHint) did not differ from cbs acting alone (HHabr), but did differ from COHabr ($P = 0.046$).

3.2.2.6. LIVER(data not shown)—Liver blood flow showed an increase during HHint and HHabr, but decreases during COHint and COHabr. None of these changes was significant. With respect to vascular resistance the liver's mean responses to hypoxemia varied. Two showed a small and insignificant rise (HHint and COHabr). The other two challenges did produce reductions in vascular resistance; but they were insignificant. The insignificance among the comparisons of normalized 15 values was also present.

3.2.2.7. SMALL INTESTINE—Blood flow to the small intestine increased significantly during HHint (74%) and during COHabr (36%). But the 18% (COHint) and 24% (HHabr) increases were not significant. With respect to vascular resistance RMANOVA analysis shows in Figure 5A the 15 values did not differ from their control values within the *int* group. However, in the *abr* group there is a significant decrease in vascular resistance during the HH challenge ($P = 0.017$), and during the COH challenge ($P = 0.032$). Figure 5B reports that the 15 values normalized to their controls in both the *int* and the *abr* groups demonstrated no difference. Between groups only HHint differed significantly from COHabr ($P = 0.050$).

3.2.2.8. PANCREAS—Pancreatic blood flow decreased significantly during HHint and COH int to 80% and to 73% of their respective ctl values. Similar to the vascular responses seen in the spleen, Figure 6A shows a second instance of hypoxia provoking an increase in organ vascular resistance. During the HHint challenge the 15 value was significantly larger ($P = 0.008$) than the ctl value. None of the other three 15 values differed from their control

values. Figure 6B showed the COHint 15 value normalized to its own control was significantly smaller ($P = 0.031$) than the normalized 15 value during the HHint challenge. Normalized 15 responses in the *abr* group did not differ significantly. Between groups comparison showed the HHint value to be greater than both the HHabr value ($P = 0.025$) and the COHabr value ($P = <0.001$). COHint did not differ from HHabr, but was significantly greater than COHabr ($P = 0.022$).

3.2.2.9. ADRENALS—Adrenal blood flow increased significantly during HHint and during HHabr to 306% and 154% of their respective ctl values. The increases during COHint and COHabr were not significant. With respect to vascular resistance Figure 7A shows a large and significant ($P = 0.001$) reduction in the vascular resistance in this organ during the HHint challenge, while during the COHint challenge there was no significant reduction. In the *abr* group the HHabr challenge again produced a significant ($P = 0.007$) reduction, but no reduction during the COHabr challenge. In Figure 7B the 15 value normalized to its control during the HHint challenge was significantly less ($P = 0.042$) than the normalized 15 value during the COHint challenge. Further, the value for HHabr was significantly less than that for COHabr ($P = 0.041$). Between groups comparison showed HHint not to differ from HHabr, but to be less than COHabr ($P = 0.009$). The value for COHint was significantly higher than that for HHabr ($P = 0.050$), but did not differ from COHabr.

3.2.2.10. EYES—Ocular blood flow increased significantly during HHint and during HHabr to 267% and 171% of their respective ctl values. With RMANOVA the reduction in vascular resistance seen in Figure 8A during the HHint challenge is significant ($P = <0.001$), whereas that during the COHint challenge is not. In the *abr* group the challenge of HHabr again generates a significant reduction in ocular vascular resistance ($P = <0.001$), while the reduction during the COHabr challenge is not. In Figure 8B with the 15 values normalized to the controls HHint is less ($P = 0.023$) than COHint, and HHabr is less ($P = 0.008$) than COHabr. Between groups comparison HHint does not differ from HHabr, but does from COHabr ($P = 0.006$). COHint is larger ($P = 0.002$) than HHabr, but does not differ from COHabr.

3.2.2.11. DIAPHRAGM—Diaphragmatic blood flow increased during HHint, COHint, HHabr, and COHabr to 979%, 576%, 570%, and 350% of their respective ctl values. Though in this preparation the diaphragm is not operating as it normally would during a hypoxic challenge (at least the HH challenge) and since it is a critically important muscle for delivering oxygen to the organism, we wished to see its response to the two forms of hypoxemia. It showed a significantly reduced vascular resistance in response to all four challenges ($P = < 0.001$ in three of four; $P = 0.004$ in fourth [COHabr]; Figure 9A). There were no significant differences among the 15 values. In the normalized comparisons (Figure 9B) again there were no differences either within each group or between groups.

3.2.2.12. TEMPORALIS—Blood flow in this muscle increased significantly during HHint and COHint to 291% and 218% of their respective ctl values. The significant increase was greater in the HHabr and COHabr cats: to 318% and 465% of their respective ctl values. TABLE 4 (top) presents the significant decreases in vascular resistance.

3.2.2.13. LEFT GRACILIS—Blood flow in the left gracilis increased significantly during HHint (185% of its ctl) and insignificantly during HHabr (4% of its ctl). During COHint and COHabr the decreases in flow were not significant. TABLE 4 (bottom) shows significant reductions in vascular resistance during the HH challenges, and non-significant increases during the COH challenges.

3.2.2.14. DISTRIBUTION OF CARDIAC OUTPUT—TABLE 5 presents the % of cardiac output to the various organs whose blood flow and vascular resistances were presented above.

4. DISCUSSION

4.1. MATERIALS/METHODS/PREPARATION

4.1.1. All procedures used in preparing the animal have been used in this laboratory for several decades; there was no reason to suspect the results were due some malfunctioning of these. Using radiolabeled microspheres was a comparatively new procedure for which consultation from the imaging division of the Johns Hopkins Hospital was provided. Basic standard procedures were followed.

4.1.2. However, the preparation underwent anesthesia, paralysis, and somewhat extensive surgical procedures. This limits the interpretation of the data in terms of an awake, normally active preparation. On the other hand the older literature contains many studies comparable to the present study (Browse and Shepherd, 1966; Carmody and Scott, 1974; Daly and Daly, 1957; Daly and Ungar, 1966; Krasney, et al., 1973; Parker, et al., 1975). Regarding the potential effect of anesthesia on the sensitivity of the chemoreceptors, Landgren et al. in the older literature (1954) reported that intracarotid injections of barbiturates (Dial, Nembutal, Pentothal) had no effect on the chemosensory discharge. And more recently Edwards et al. (1980) confirmed the depressant effect of halothane whereas barbiturates (Nembutal 60-120 mg/kg) showed no such effect. Nonetheless, the interpretations below are presented with caution.

4.1.3. Finally, though several studies have been published, in which blood flow and vascular resistance have been measured and calculated in many organs in response to carotid body selective stimulation or a hypoxic challenge, we feel none of those studies is as extensive as this report. Marshall and Metcalfe (1989, 1990) and Marshall in her review article (1994) identify the factors that can influence vascular behavior when arterial chemoreceptors are stimulated.

Since we held $P_a\text{CO}_2$ and pH_a relatively constant and the ventilatory pattern was a constant, and since we presume the tissue hypoxia was the same after 15 of each of the two challenges in both *int* and *abr* groups because the S_aO_2 values were virtually identical as moderate/strong hypoxemic values (cf. TABLE 1), we will focus our efforts to explain our vascular resistance data on the effects of tissue hypoxia plus the sympathetic nervous system's output in response to chemoreceptor and baroreceptor input. As stated in the Introduction, our purpose was to see what effect both cbs + abs, increasing their neural output centrad, had on organ vascular resistance compared to that when just the abs alone increased centrad neural output, to that when just the cbs alone did so, to that when there was no increased chemoreceptor output during a hypoxic challenge. Sometimes both carotid and aortic baroreceptors were operational, sometimes just the carotid baroreceptors.

4.2. RESULTS

4.2.1. POTENTIAL SOURCES—What is noteworthy in the data is the lack of homogeneity in the autonomic control of the organ vascular resistances. When the 15 value is lower than the ctl value, is this because stimulation of the chemoreceptors is (1) insufficient to provoke an adequate output from the sympathetic nervous system (SNS) to attenuate the locally induced vasodilation with an attenuating vasoconstrictive output, or (2) producing a vasodilatory impact via sympathetic vasodilators or (3) the activation of the parasympathetic component? However, parasympathetic innervation of the vasculature

seems least likely since it is thought to occur only in some specific organs such as the salivary glands, some gastrointestinal glands, and genitalia.

4.2.2. ASSUMPTIONS—Certain assumptions are made regarding the Results: (1) According to previous studies in both dog and cat, we (Dehghani and Fitzgerald, 1977; Fitzgerald and Traystman, 1980) and others (Lahiri, et al., 1981) have found the reduction in P_{aO_2} stimulates both cbs and abs whereas reductions in S_{aO_2} due to CO stimulated only the abs. This condition was assumed to exist in the present study. Given the comparable reductions in S_{aO_2} with both forms of hypoxia (cf. TABLE 1), the reduction in P_{aO_2} seems to be a key operative variable in producing the changes seen in several vascular beds. (2) There was no obvious reason to have us doubt the constant operation of the components of the autonomic nervous system (ANS) throughout the multi-phase protocol. However, the level of anesthesia could influence this. We used both the medial canthal reflex, a steady control blood pressure values before each challenge, and the absence of any fighting of the respirator as indices of a constant level of anesthesia. Occasionally, but not systematically, the withdrawal reflex from a toe pinch was used. When used, it matched the canthal reflex results. The lower control blood pressure preceding the COH challenge in the *abrcats* was due, we felt, to it being the last challenge. Conceivably this could have influenced the level of ANS involvement.

4.2.3. BRAIN—Vascular resistance during the HHint challenge (Figures 1A, 1B) drops, but is significantly higher than during the other three challenges. This might suggest that the carotid and aortic bodies acting in concert during HHint provoked a modulation of the vasodilatory action of the local hypoxemia. However, it must be appreciated that during HHint aortic blood pressure (P_{ao}) rose from 99.6 ± 6.0 mmHg (Mean $\pm$ SEM) to 119 ± 6.2 mmHg. During two of the other three challenges P_{ao} fell. During HHint blood flow did increase (29.2 ± 3.8 to 86.1 ± 6.3 mL/min/100gm tissue), about 294%. But flow also increased during the other challenges (378%, COHint; 466%, HHabr; 280%, COHabr) It appears the change in vascular resistance is not due to hypotension since P_{ao} rose during HHint, fell during both COHint and COHabr, but did not change during HHabr. With these values and the blood flow values ab/cb involvement seems unnecessary. Presently, then, cerebral vascular changes in response to systemic hypoxemia wait to be explained. The presence and functioning of the ANS in the cerebral circulation has been and remains a controversial issue. These findings are consistent with the flow and conductance data in both anesthetized and unanesthetized rats reported by Marshall and Metcalfe (1990)

4.2.4. HEART—These results suggest that the peripheral chemoreceptors had no direct role in controlling this vascular bed during hypoxemia. Tissue hypoxia of the bed seems to be the dominant factor. However, cb stimulation does increase contractility, and during the HHint challenge the increased afterload on the left ventricle due to increased P_{ao} would suggest a heightened myocardial oxygen demand. These two factors could help reduce vascular resistance and increase coronary blood flow.

4.2.5. KIDNEY—The failure of the kidney vasculature to be influenced by chemoreceptor input was somewhat surprising since cb stimulation does influence kidney performance; e.g., increase in renal sodium and water excretion (Honig, 1989), though these reported functional effects were seen in normoxic animals with stimulation of the cb. Vascular resistance did decrease during all four challenges but the RMANOVA could not find significance in either of the two groups even though the decrease was about 18.7% of the ctl value. Four paired t-Test calculations also could find no significant differences between control and 15 values for each of the two challenges in either of the two groups. Little and Oberg (1975) did report that stimulation of the cb in normoxic cats provoked a renal bed

vasoconstriction. In the present study perhaps during the HHint challenge when P_{ao} increased, the baroreceptors diminished any excitatory action of the chemoreceptors on SNS output. The preparation of Weissman et al. (1976) comes closest to ours in that the cat was ventilated on 10% O₂. This would be the same as our HHint challenge when both abs and cbs were increasing neural output to the NTS, and stimulating SNS output, which was being attenuated by baroreceptor input since their P_{ao} rose from 153 to 169 mmHg. They found a significant increase in renal resistance of 108.6% of the control value with only a 2% rise in blood flow. Our failure to show significant reductions in renal resistance matches the absence of a drop in renal conductance in anesthetized and unanesthetized rats (Marshall and Metcalfe, 1990).

4.2.6. SPLEEN—Figures 3A and 3B could be interpreted as suggesting that the cbs and abs acting in concert generate the largest increase in vascular resistance, whereas the cbs have about the same effect on the splenic vasculature as do the abs. The rise during HHint due to chemoreceptor action was probably being muted by baroreceptor action. Since normalized HHint is greater than normalized COHabr, chemoreceptors are important. But normalized HHint does not differ from either normalized COHint or normalized HHabr. Perhaps the P_{ao} drop of 20 mmHg during COHint was partly responsible for the increase in resistance. The fact that hemoglobin (cf. TABLE 1) increases during both challenges in both groups suggests a squeezing of the spleen, emptying this reservoir and increasing venous return. The large increase in resistance matches the significant reduction in flow and conductance in the unanesthetized rat (Marshall and Metcalfe, 1990).

4.2.7. LIVER—Again this was a somewhat surprising result in that cb stimulation is known to stimulate a change in hepatic function; e.g., provoke a sharp release of glucose (Alvarez and deAlvarez, 1988), elevating both hepatic venous and arterial concentrations of glucose. A decrease in vascular resistance was expected. But hepatic artery blood flow increased insignificantly twice (HHint and HHabr) and decreased insignificantly twice (COHint and COHabr). However, the control blood flows in the *abr* Group preceding each challenge were 75.6% and 69.8% higher than the control flows in the *int* Group suggesting possible aortic mechanisms are involved in liver vascular constriction.

4.2.8. STOMACH—The plots in Figures 4A and 4B suggest that the cbs and abs acting in concert can offset the vasodilation in spite of the attenuating influence of baroreceptor input due to the higher P_{ao} . But each, acting singly, was unable to do so. P_{ao} fell ~20mmHg during COHint which would have added to ab input for SNS output; but during HHabr there should have been no baroreceptor influence. Since in Figure 4B HHint (cbs + abs) did not differ from COHint (abs only), but did differ from HHabr (cbs only; $P = 0.017$), perhaps during HHint the abs exert a more dominant effect on this vascular bed than the cbs. If so, to our knowledge this appears to be the first time a functional role for the abs has been suggested.

4.2.9. SMALL INTESTINE—Figure 5A suggests that at the 15 mark of hypoxemia in the *int* animals the SNS was sufficiently stimulated by the chemoreceptor configurations involved (cb+ab and ab alone) so as to offset the extensive local vasodilatory action of systemic hypoxia, while the impact of the cb acting alone on the SNS apparently was not sufficient to prevent the vasodilation. However, whereas baroreceptor activity would have added some amount to the SNS output due to the ~20mmHg drop in P_{ao} during COHint, there was no baroreceptor action during HHabr. If this interpretation is valid, then this vascular bed appears to be the second locus in which the abs seem to exert a greater effect during hypoxemia than do the cbs. Little & Oberg (1975), using an anesthetized paralyzed artificially ventilated normoxic cat in which they selectively stimulated the cbs, found a reflex vasoconstriction in the intestine. Weissman et al. (1976) report a significant rise in

intestinal blood flow in cats ventilated on 10% O₂ to 107% of control, but no significant change in resistance. This is consonant with our HHint data. The changes in intestinal conductance in the rat (Marshall and Metcalfe, 1990) are matched in general by the changes in resistance in the cat.

4.2.10. PANCREAS—Figure 6A shows the second instance of a hypoxic challenge producing a vasoconstriction in this preparation. Acting in concert the cbs and abs increased the vascular resistance, while baroreceptor action was probably attenuating SNS output. But the cbs acting alone (HHabr) and the abs acting alone (COHint) did offset the vasodilatory effect of local tissue hypoxia. But since HHabr did not differ from COHint, the effect of cbs on this organ's vascular resistance was the same as that of the abs. But ab stimulation had some additional input from the baroreceptors. Kaneto, et al.(1967). report cb stimulation produces an increase in insulin secretion. One of the vascular actions of insulin is vasodilatory, clearly not the case in this preparation's pancreas. To our knowledge other studies of vascular responses to hypoxemic challenges in the cat do not single out the effect of hypoxemia on the pancreas.

4.2.11. ADRENALS—Figures 7A and 7B show the cbs stimulate a vasodilation of adrenal vasculature (HHint, HHabr), while the abs did not have that effect. The facts that (1) HHint does not differ from HHabr, and (2) COHint has no effect suggests that this phenomenon is due entirely to the action of the cbs. And whereas there was no change from control baroreceptor involvement during HHabr, the blocking of SNS during HHint could have facilitated the dilatory action of the cbs. Unfortunately the mechanism behind this phenomenon is not available. This resistance data corresponds to the conductance data from the rat (Marshall and Metcalfe, 1990).

4.2.12. EYES—Again the data suggest an active vasodilatory influence stemming from stimulation of the cbs. This possibility is reinforced again in Figure 8B by the facts that (1) HHint does not differ from HHabr and (2) COHint is larger than HHint and HHabr, but does not differ from COHabr. The apparent vasodilatory action of the cbs on the vasculature of the adrenals and eyes is consistent with the action of the cbs on the pulmonary vasculature during hypoxic pulmonary vasoconstriction (Fitzgerald, et al., 2012; Fitzgerald, et al., 1992; Levitzky, 1979; Levitzky, et al., 1977; Wilson, and Levitzky, 1989). To our knowledge no other study of the effects of hypoxemia on feline vasculature report the effects of hypoxemia on the ocular bed.

4.2.13. DIAPHRAGM—Since the 15 COHabr value did not differ from the other 15 values, it appears the SNS input remains relatively constant. Since blood pressure rises significantly (HHint), remains relatively constant (HHabr), falls significantly (COHint, COHabr), the vasodilatory effect appears totally under the control of local tissue hypoxia. We are unaware of any other study of the behavior of the diaphragmatic vasculature during four such hypoxemic challenges to the cat. But again, this resistance data corresponds to the flow and conductance data from the anesthetized rat (Marshall and Metcalfe, 1990). The fact that the control values in the *abr* group are significantly less than those in the *int* group suggests that aortic mechanisms may control this bed.

4.2.14. TEMPORAL—The Temporal muscle's reduction in resistance during HHint (to 41% of control; cb+ab), with baroreceptors attenuating, was a slightly less reduction than that during COHint (to 37.7%;ab with baroreceptors facilitating) and HHabr (to 29.0%;cb with little/no baroreceptor influence). But all three were significantly higher than the reduction during the COHabr challenge (to 16.4% of control). This suggests that the chemoreceptors had an influence on the SNS output. However, this challenge in the

Diaphragm reduced the resistance only to 35% of the control. With no chemoreceptor influence acting it appears that the carotid baroreceptors may have had a more marked impact on the diaphragmatic vasculature than on that of the temporal's.

4.2.15. *LEFT GRACILIS*—Gracilis during HHint reduced its resistance to 64% of the control, a higher level than the Diaphragm. SNS output was governed by abs and cbs and attenuated by baroreceptors. During HHabr with very little or no baroreceptor influence and only the cbs stimulating SNS output resistance fell only to 88% of the control. And in both the COHint and COHabr vascular resistance actually increased to 126% and 106% of their controls respectively. Presently we do not find a reasonable explanation of the reflex mechanisms involved in these responses.

In our preparation diaphragmatic, temporal, and gracilis muscle blood flow increased significantly during 5/6 HH challenges (not significant during HHabr in the gracilis; cf TABLE 4). This was matched to a decrease in resistance during HH challenges in both groups of cats. Weissman et al. (1976) report a decrease in femoral blood flow in cats ventilated on 10% O₂, as well as a significant increase in resistance. The reason for this conflict in data presently escapes us since it seems intuitively reasonable that ventilation on 10% O₂ should provoke an organism wide vasodilation. Further, the P_{ao} in their preparation rose to 110% of the control value during the 10% O₂ exposure. If this had any effect at all, it would seem that it would have diminished a baroreceptor-mediated SNS increased output to vasoconstrict. Our temporal and gracilis resistance data are generally consistent with gastrocnemius conductance data of the anesthetized rat (Marshall and Metcalfe, 1990). As seen above, our results coincide very frequently with their report of other rat data (Marshall and Metcalfe, 1990).

Sometimes our results coincide with the cat study of Marshall and Metcalfe (1989), and sometimes not. In their anesthetized cats they challenged with various grades of inspired oxygen (15 to 6%) for 3 minutes. We focus on their results from the artificially ventilated cats (1989; their Figure 6). Our 15 minute exposures to lowering the S_aO₂ to the mid-30% level with 10% oxygen or CO was, perhaps, a key difference. The longer exposure might have provided a greater opportunity for cardiovascular changes to occur.

But we compare their results with ours since the same species is used, both are artificially ventilated, the changes in P_aCO₂ are minimal in both studies, though our values (low 30 s mmHg) are significantly higher than theirs (low 20 s mmHg). The P_aO₂ values at the end of the challenge are comparable (low 20 s mmHg) even though their duration is 3 min and ours is 15min.

Marshall and Metcalfe (1989) report a non-significant increase in P_{ao} of 10%, whereas our increase of 20 mmHg during the HHint challenge was significant. Further, they observed a 15% decrease in heart rate during 6% O₂ in the ventilated cat, we observed no change in heart rate, just as in a previous study (Fitzgerald, et al.) where the range was 175-190/min.

Whereas Marshall and Metcalfe (1989) report a significant decrease in renal blood flow and conductance; we found a non-significant increase in blood flow plus a non-significant decrease in resistance. Conceivably the difference is traceable to the duration of the exposure. We have no 3 min values.

Marshall and Metcalfe (1989), perfusing the cranial mesenteric artery (which in humans perfuses the lower duodenum, 2/3 of the transverse colon, and the pancreas), report a significant decrease in blood flow and vascular conductance. We observed a significant increase in blood flow to the small intestine with either no change in vascular resistance

(HHint) or a significant decrease (HHabr). We observed a significant decrease in pancreatic blood flow (HHint) as well as a significant increase in resistance. These results at least partially coincide with those of Marshall and Metcalfe (1989).

Marshall and Metcalfe (1989) report a non-significant increase in femoral blood flow and vascular conductance. We observed a significant increase in gracilis blood flow (HHint) and a significant reduction in vascular resistance.

5. CONCLUSIONS

Though the results from a study such as this must respect the potential influences of other factors able to control the vasculature during challenges invoking the action of the ANS (e.g., circulating catecholamines, AT₂), the data do suggest that the ANS played a dominant role...sometimes vasoconstricting even in the face of a system-wide vasodilation due to the local effects of tissue hypoxia, sometimes attenuating such local effects, and sometimes vasodilating. The spleen and pancreas are examples of the first effect; several organs could serve as examples of the second; and the adrenals and eyes are examples of the third effect. Yet in some organs the SNS seemed unable to overcome the systemic vasodilation; for example, the heart and diaphragm, the two “pumps” responsible for delivering oxygen to the tissues, seemed to have a muted, if any, SNS vasoconstrictive input to their vasculatures. Or perhaps the distribution/density of α_1 adrenergic receptors in these beds is less than in other beds. And two organs (stomach and small intestine) seemed to suggest a dominant role for the abs in their vascular responses to hypoxemia. The fact that the diaphragmatic *ctl* resistance values were lower in the *abr* group than those in the *int* group suggests the possibility that aortic mechanisms may promote a diaphragmatic vasoconstriction.

To explore more closely organ vascular resistances in a more normal condition while still using the anesthetized animal it would be interesting to see the effect of lowering the P_aCO_2 during the hypoxic challenge. A hypoxic challenge increases ventilation. With constant metabolism such an increase lowers P_aCO_2 . Since increased P_aCO_2 dilates the vasculature, certainly the cerebral vasculature, and probably other beds as well, it would be interesting to explore the effect of decreased P_aCO_2 during the hypoxic challenge. A final thought relevant to the effect of a lowered P_aCO_2 is that the cbs do not respond as vigorously to hypoxia if the background is alkalotic.

Hopefully the above report will stimulate further studies of the role of the arterial chemoreceptors and the other components of the ANS in controlling the cardiovascular system during a challenge to the very *raison d'être* of its function, oxygen delivery to the tissues.

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BRAIN VASCULAR RESISTANCE

Figure 1.

BRAIN. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). OPEN BARS = ctl values; SHADED BARS = 15' values (Applies also to Figures 2-9) *: 15' value is less than control (ctl) value ($P = <0.001$). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15'/ctl). *: HHint > COHint ($P = 0.003$). Parentheses at bottom of columns indicates what chemoreceptors are being stimulated, if any.

CORONARY VASCULAR RESISTANCE

Figure 2.

HEART. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). * : 15 value is less than control (ctl) value ($P = <0.001$). B. Mean $\pm$ SEM of the five 15 values normalized to their controls (15 /ctl).

SPLENIC VASCULAR RESISTANCE

Figure 3.

SPLEEN. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). *: 15 value is greater than control (ctl) value ($P = <0.001$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). *: 15 value is greater than control (ctl) value ($P = 0.002$). B. Mean $\pm$ SEM of the five 15 values normalized to their controls (15 /ctl). *: HHint > COHint ($P = 0.041$).

STOMACH VASCULAR RESISTANCE

Figure 4. STOMACH. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). * : 15' value is less than control (ctl) value ($P = 0.033$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). . * : 15' values are less than 2 control (ctl) value ($P = 0.001$, $P = <0.001$). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15'/ctl).

SMALL INTESTINE VASCULAR RESISTANCE

Figure 5. SMALL INTESTINE. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; n = 5). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; n = 5). * : 15' values are less than control (ctl) value (P = 0.017, P = 0.032). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15' /ctl).

PANCREATIC VASCULAR RESISTANCE

Figure 6.

PANCREAS. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). *: 15' value is greater than control (ctl) value ($P = 0.008$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15'/ctl). *: COHint is less than HHint ($P = 0.031$).

ADRENAL VASCULAR RESISTANCE

Figure 7.

ADRENALS. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). *: 15' value is less than control (ctl) value ($P = 0.006$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). *: 15' value is less than control (ctl) value ($P = 0.001$). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15'/ctl). *: HHint is less than COHint ($P = 0.042$); HHabr is less than COHabr ($P = 0.041$).

EYES VASCULAR RESISTANCE

Figure 8.

EYES. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; n = 5). *: 15' value is less than control (ctl) value ($P < 0.001$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; n = 5). *: 15' value is less than control (ctl) value ($P < 0.001$). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15'/ctl). *: HHint is less than COHint ($P = 0.023$); HHabr is less than COHabr ($P = 0.008$).

DIAPHRAGMATIC VASCULAR RESISTANCE

Figure 9.

DIAPHRAGM. A. Left four bar graphs are data for intact (*int*) cats (mean $\pm$ SEM; $n = 5$). * : 15' value is less than control (ctl) value ($P = < 0.001$). Right four bar graphs are data for aortic body resected (*abr*) cats (mean $\pm$ SEM; $n = 5$). * : 15' value is less than control (ctl) value ($P = < 0.001$). B. Mean $\pm$ SEM of the five 15' values normalized to their controls (15' / ctl). No significant differences within group(s) or between groups.

Table 1

Blood Gas Values for the five animals in each group, *int* and *abr* (Mean $\pm$ SEM). Note the relative constancy of pH and P_aCO₂ values and the comparable reductions in S_aO₂ between the two groups.

	pH _a	P _a CO ₂ (mmHg)	P _a O ₂ (mmHg)	S _a O ₂ (%)	Hb (gm%)
A. INTACT (n = 5)					
CONTROL:	7.43 $\pm$ 0.02	32.5 $\pm$ 1.7	129 $\pm$ 13	100	10.2 $\pm$ 0.9
HH (15 min)	7.35 $\pm$ 0.04	34.0 $\pm$ 1.7	24 * $\pm$ 2	36.2 * $\pm$ 1.6	12.6 $\pm$ 0.7
CONTROL:	7.40 $\pm$ 0.09	34.0 $\pm$ 0.7	133 $\pm$ 12	100	11.6 $\pm$ 0.6
COH (15 min)	7.40 $\pm$ 0.03	34.2 $\pm$ 1.9	147 $\pm$ 13	39.7 * $\pm$ 2.6	11.7 $\pm$ 0.6
B. ABR (n = 5)					
CONTROL:	7.42 $\pm$ 0.01	33.7 $\pm$ 0.7	136 $\pm$ 6	99.8 $\pm$ 0.2	10.6 $\pm$ 0.9
HH (15 min)	7.37 $\pm$ 0.03	32.8 $\pm$ 1.7	19 * $\pm$ 1	32.3 * $\pm$ 3.4	12.0 $\pm$ 0.6
CONTROL:	7.39 $\pm$ 0.02	32.9 $\pm$ 2.2	142 $\pm$ 6	100	10.8 $\pm$ 0.7
COH (15 min)	7.39 $\pm$ 0.01	31.9 $\pm$ 1.8	141 $\pm$ 10	35.8 * $\pm$ 1.4	11.3 $\pm$ 0.5

* Different from control value (P = 0.001)

Table 2

Mean $\pm$ SEM. (*top*) presents the changes in cardiac output (C.O.) during the control (ctl) and 15 challenge phases (HH, COH) of the five experiments in the two groups of cats. * : P<0.05
 (*middle*) presents the changes in aortic blood pressure (P_{ao}) during the control (ctl) and 15 challenge phases (HH, COH) of the five experiments in the two groups of cats. * : P<0.05
 (*bottom*) presents the changes in total peripheral resistance (TPR) during the control (ctl) and 15 challenge phases (HH, COH) of the five experiments in the two groups of cats. * : P<0.05

	<u>INTACT</u>		<u>ABR</u>	
	ctl→HH	ctl→COH	ctl→HH	ctl→COH
	*	*	*	*
C. O. (mL/min)	312→499	316→462	379→630	425→523
	$\pm 24 \pm 46$	$\pm 33 \pm 37$	$\pm 28 \pm 56$	$\pm 40 \pm 43$
	(Mean $\pm$ SEM) * : P = <0.05 in the five cats in each group.			
	<u>INTACT</u>		<u>ABR</u>	
	ctl→HH	ctl→COH	ctl→HH	ctl→COH
	*	*	*	*
P _{ao} (mmHg)	99.6→119	98.0→80.6	109.8→100.2	87.8→67.6
	$\pm 6.0 \pm 6.2$	$\pm 8.7 \pm 7.4$	$\pm 3.0 \pm 11.9$	$\pm 6.9 \pm 3.8$
	(Mean $\pm$ SEM) * : P = <0.05 in the five cats in each group.			
	<u>INTACT</u>		<u>ABR</u>	
	ctl→HH	ctl→COH	ctl→HH	ctl→COH
	*	*	*	*
TPR	0.319 0.238	0.310 0.174	0.290 0.159	0.207 0.129
Reduced by	25.4%	43.9%	45.2%	37.7%
	(Mean $\pm$ SEM) * : P = <0.05 in the five cats in each group.			

Table 3

Increases (as % of control values) in blood flow to various areas of the Brain during the HH and COH challenges in both *int* and *abr* groups.

Regional Brain Blood Flows during the HH or COH Challenges.
as a % Increase of the Control Value

TISSUE	INTACT		ABR	
	HH	COH	HH	COH
cerv.spinal cord	389%	477%	504%	371%
cerebellum	310	358	408	269
medulla	464	444	457	315
pons	442	404	490	331
midbrain	349	424	474	325
diencephalon	292	431	452	364
hippocampus	325	467	564	296
caudate	256	340	319	223
occip.lobe	264	362	370	289
pariet.lobe	286	374	420	253
front.lobe	278	376	436	247
temp.lobe	269	370	418	262

Table 4

Mean values for several cardiovascular variables in the five cats in each group for the Temporal muscle and the Left Gracilis muscle.

<u>TEMPORAL</u>				
INTACT	CTL	15 HH	CTL	15 COH
Real Flow(mL/min)	0.37	0.98	0.45	0.98
P _{ao} (mmHg)	99.6	119.0	98.0	80.6
C.O. (mL/min)	312	499	316	462
% C.O.	0.1	0.2	0.1	0.2
Flow/100gmtissue	2.3	6.7	2.8	6.1
Vasc.Res.(P _{ao} /F100gm)	43.3	17.8	35.0	13.2
Reduction as % of ctl		41.1		37.7
ABR	CTL	15 HH	CTL	15 COH
Real Flow(mL/min)	0.65	2.06	0.71	3.28
P _{ao} (mmHg)	109.8	100.2	87.8	67.6
C.O. (mL/min)	379	630	425	523
% C.O.	0.2	0.3	0.2	0.6
Flow/100gmtissue	3.4	10.8	3.7	17.2
Vasc.Res.(P _{ao} /F100gm)	32.1	9.3	23.7	3.9
Reduction as % of ctl		29.0		16.4
<u>LEFT GRACILIS</u>				
INTACT	CTL	15 HH	CTL	15 COH
Real Flow(mL/min)	0.62	1.14	0.71	0.46
P _{ao} (mmHg)	99.6	119.0	98.0	80.6
C.O. (mL/min)	312	499	316	462
% C.O.	0.2	0.2	0.2	0.1
Flow/100gmtissue	2.0	3.7	2.3	1.5
Vasc.Res. (P _{ao} /F100gm)	49.8	32.2	42.6	53.7
Reduction as % of ctl		64.7	inc. by 26.0	
ABR	CTL	15 HH	CTL	15 COH
Real Flow(mL/min)	0.88	0.92	0.95	0.67
Pao(mmHg) 1	109.8	100.2	87.8	67.6
C.O. (mL/min)	379	630	425	523
% C.O.	0.2	0.2	0.2	0.1
Flow/100gmtissue	2.7	2.8	2.9	2.1
Vasc.Res.(P _{ao} /F100gm)	40.7	35.8	30.3	32.2
Reduction as % of ctl		88.0	inc. by 6.3	

Table 5

Mean % of cardiac output delivered to the various organs studied during the HH and COH challenges in the *int* and *abr* groups.

DISTRIBUTION OF CARDIAC OUTPUT

<u>ORGAN</u>	HHint		COHint		HHabr		COHabr	
	CTL	HH	CTL	COH	CTL	HH	CTL	COH
	% C.O.	% C.O.	% C.O.	% C.O.	% C.O.	% C.O.	% C.O.	% C.O.
BRAIN	2.8	5.1	3.0	7.7	2.3	6.5	2.7	6.2
HEART	3.6	19.1	5.0	17.8	5.4	18.4	4.4	19.6
KIDNEY	24.0	20.9	27.8	18.6	21.2	14.8	17.9	13.6
SPLEEN	4.5	1.0	4.0	1.1	5.4	1.4	5.4	1.4
LIVER	14.8	12.5	16.8	10.0	21.4	13.1	21.0	13.3
STOMACH	1.2	1.2	1.6	1.4	0.8	1.0	0.9	1.4
SMALL INT.	10.9	11.8	15.8	17.7	14.0	9.0	11.7	12.9
PANCREAS	0.7	0.3	0.7	0.4	0.9	0.5	0.9	0.8
ADRENALS	0.2	0.5	0.5	0.4	0.4	0.4	0.5	0.3
EYES	0.5	0.9	0.7	0.4	0.8	0.7	0.5	0.4
DIAPH.	0.4	2.3	0.5	1.9	0.8	2.2	0.7	1.9
TEMPORAL	0.1	0.2	0.1	0.2	0.2	0.3	0.2	0.6
LFT.GRAC.	0.2	0.2	0.2	0.1	0.2	0.2	0.2	0.1