ABSTRACT

The regional differentiation of carotid sinus control of arterial pressure-flow relationships was studied in chloralose-anesthetized dogs. Simultaneous pressure-flow measurements were made in the ascending aorta, the celiac artery, the cranial mesenteric artery, the renal artery, and the femoral artery. The carotid sinuses were bilaterally isolated and perfused with pulsatile pressure. The open-loop reflex gain was not symmetrical about and was maximum at pressures below the closed-loop operating point pressure. Changes in both peripheral resistance and cardiac output contributed significantly to the open-loop gain, with the former predominating. Aortic impedance for frequencies above 3 Hz was at a minimum at the closed-loop operating point and increased for both higher and lower values of carotid sinus pressure. For the frequency range from 3 to 9 Hz, regional impedance in all of the beds varied inversely with carotid sinus pressure. The sensitivity of the various beds to changes in carotid sinus pressure around the operating point increased in the order celiac < mesenteric < renal < femoral. Following vagotomy, operating point values of regional resistance and sensitivity were significantly increased. This fact suggests that the aortic arch receptors exert a significant influence on regional vascular impedances at operating point pressures. The fraction of cardiac output in the celiac, mesenteric, and renal beds was nearly independent of carotid sinus pressure before and after vagotomy, but that in the femoral bed increased with carotid sinus pressure. These results demonstrate the nonuniform nature of carotid sinus and aortic arch baroreceptor control of regional blood flow.

It is well recognized that the carotid sinus plays an important role in the short-term control of arterial blood pressure (1). Early work on this reflex was primarily directed toward describing the overall characteristics of the reflex loop, that is, the carotid sinus pressure–systemic arterial blood pressure relationships (2). In more recent years, interest has been focused on the contribution of various components to the overall reflex. For example, the receptor characteristics have been described (3–5), and the relative contributions of changes in peripheral resistance and cardiac output have been measured (6, 7). Although abundant evidence suggests a regional differentiation in the effects of the carotid sinus reflex (8–13), few quantitative studies have been performed on the carotid sinus control of the distribution of cardiac output. To date, most studies involving the influence of the carotid sinus on the distribution of cardiac output have employed the measurement of a limited number of simultaneous blood flows. As a result, it is difficult to obtain a picture of the simultaneous distribution of cardiac output to different vascular beds. Recently, using an open-loop carotid sinus preparation, Kumada et al. (9) have described the variation in regional blood flow and resistance in response to steady-state changes in carotid sinus perfusion pressure, but their regional flow measurements were performed in only a few of the animals that they studied and were not all recorded simultaneously.

Peripheral resistance represents only a portion of the total opposition to pulsatile blood flow. In addition to purely resistive elements, a variety of other factors including inertia and distensibility significantly influences the cardiovascular response to pulsatile blood flow. The concept of vascular impedance was developed to include these factors and represent the total opposition to such flow (14–17). Most studies of carotid sinus baroreceptor control of the peripheral circulation have considered the reflex's effect on vascular resistance only (e.g., 6, 18). However, Bagshaw et al. (19) have shown substantial changes in renal vascular impedance with changes in perfusion pressure in the isolated carotid sinuses of the dog. We know of no study that has described simultaneous changes in regional vascular impedance and aortic input impedance as a function of carotid sinus pressure.

It was the objective of the experiments described in the present paper to determine the carotid sinus reflex control of regional and aortic impedance and
blood flow. Simultaneous measurements of pres-
sures and flows were made in the celiac, cranial mesenteric, renal, and femoral arteries as well as in
the ascending aorta. Studies were performed with the vagi intact and with them transected to eval-
uate the role of aortic arch receptors. An attempt was made to determine if the observed changes in
vascular impedance were active changes resulting from activation of arterial smooth muscle or pas-
sive changes resulting from the pressure-dependent
properties of the vascular wall.

Methods

Experiments were performed on 11 young-adult dogs of either sex (average weight 28.8 ± 1.4 kg). The dogs were medicated with morphine sulfate (0.2 mg/kg), atro-
pine sulfate (0.5 mg), and sodium pentobarbital (3 mg/kg) and subsequently anesthetized with chloralose (100 mg/ kg, iv). The dogs were then intubated with a cuffed
dotracheal tube and ventilated with 100% O2 using a
constant-volume respirator (Ventimeter). Adequate
minute ventilation was achieved with respiratory rates
of about 10/min and tidal volumes sufficient to ensure
satisfactory lung inflation and reduce the incidence
of atelectasis. Minute ventilation volumes were adjusted to
maintain arterial carbon dioxide tension (Pco2) between
37 and 43 torr. Ventilation was assessed by measure-
ments of end-tidal CO2 using infrared capnograph (Go-
dart). Samples of arterial blood were periodically ob-
tained and analyzed for oxygen tension (Po2), Pco2,
and pH (Instrumentation Laboratory, model 213). Meta-
abolic acidosis was corrected with intravenous sodium bicarbonate administration. Replacement fluids during
the course of the experiment consisted of Normosol-R
(Abbott Laboratories, Na+ 140 mEq/liter, K+ 5 mEq/li-
ter, Mg2+ 3 mEq/liter, Cl− 98 mEq/liter, and HCO3− 50
mEq/liter) in half-normal saline given at the rate required
to maintain a central venous pressure of at least 5-5 mm
Hg with a urinary output of at least 1 ml/kg hour−1.

ANIMAL PREPARATION

The ascending aorta was approached through a left
thoracotomy at the third intercostal space and fitted
with a cuff type of electromagnetic flow probe (Statham type Q). A red rubber chest tube was sewn in place, the
incision was closed in layers, the pneumothorax was
closed, the incision was placed, and the lungs were inflated with a high tidal volume
several times. This procedure of lung inflation
was repeated at intervals of approximately 1 hour during
the course of the experiment to preclude the develop-
ment of partial pneumothorax or atelectasis.

The carotid bifurcations were bilaterally exposed
through a midline incision from the sternum to the level
of the hyoid bone. Carotid sinus isolation was achieved by
cannulation of the external carotid arteries and ligation of all small branches including those supplying the
carotid body. Involvement of nerve fibers in any of
these ligatures was prevented by the use of a dissecting
microscope (Zeiss).

The details of the methods used for perfusing the
carotid sinuses have been described in detail previously
(19). This system consisted of a bilateral flow-through
perfusion system in which the perfusion pressure in the sinuses was controlled. Separate control of mean perfu-
sion pressure and the amplitude and frequency of a
superimposed sine wave was achieved. The perfusion
tubing was inserted into the common carotid arteries
caudal to the carotid bifurcation. The perfusate left the
sinuses through tubing in the external carotid arteries.
Mean carotid sinus pressure was adjusted with a varia-
table-resistance orifice type of valve on the outflow tubing. The perfusate consisted of an oxygenated (95% O2, 5%
CO2) physiological salt solution (19) that was passed
through a heat exchanger before entering the sinuses.

Concurrent with the carotid sinus isolation, the ab-
dominal cavity was entered via a midline incision. The
celiac, cranial mesenteric, and left renal arteries were
identified and serially dissected free of surrounding
tissue. Care was taken to prevent destruction of nerves
surrounding these blood vessels. A cuff type of flow probe
(Statham type Q) of the appropriate size was placed on
each vessel. A pneumatic occlusion device (Rhodes
Medical Instruments) was placed approximately 1 cm
distal to each flow probe and used to produce mechanical
flow zeros. The right femoral artery was exposed at the
level of the femoral triangle, and an electromagnetic flow
probe was similarly placed. Mechanical base lines for the
femoral artery were obtained by snare occlusion distal to
the flow probe. A tight ligature was placed around the
defows to eliminate blood flow to that region. The resulting
blood flow in the femoral artery was assumed to repre-
sent primarily flow to skeletal muscle (9). Blood pres-
sures were recorded at the following vascular sites: carotid sinus pressure via the perfusion inflow tubing,
central venous pressure via the right external jugular
vein, femoral artery pressure via a small side branch,
secting aortic pressure by a catheter inserted through
the wall of the aorta distal to the probe, abdominal aortic
pressure via a catheter in the thoracoabdominal artery,
and mesenteric artery pressure via a catheter in a small
side branch. In the case of the arterial sites, the catheters
were advanced to the origin of a side branch at a site
within 1 cm of each flow transducer. Catheters were
oriented to measure, as nearly as possible, lateral
pressure.

Pressures were measured with Statham P23 series
strain-gauge transducers and the indwelling catheters.
Arterial catheters were standardized using 20-cm long
polyethylene tubes with an internal diameter of 1.15
mm. The dynamic response characteristics of the cath-
eter-manometer systems were determined using a sinusoi-
dal pressure generator (20); the amplitude response was
found to be flat within ±5% up to 20 Hz with a phase
shift of about 2° at this frequency. Static pressure
-calibrations were carried out using a precision mercury
barometer system (Hass Instruments).

Volume blood flow rates were measured using the flow
probes and gated sine wave electromagnetic flowmeters
(Statham models K2000 and M4000). The frequency-
-response characteristics of the flowmeters were deter-
mined electronically. The amplitude ratio was down 5%
at 10 Hz, and the phase lag was approximately 5%/Hz at
low frequencies (21). The flow probes were calibrated in
situ using methods previously described in detail (21).
The spatial separations of pressure and flow measure-
ment sites were recorded at the end of the experimental
procedures.
EXPERIMENTAL PROTOCOL

Following surgical procedures and after the arterial blood acid-base status had normalized, all pressures and flows were simultaneously recorded on analog magnetic tape (Sangamo model 471) prior to complete isolation of the carotid sinuses. Next, the carotid sinus isolation was completed by cannulating the common carotid arteries, ligating the internal carotid arteries, and initiating perfusion. Mean carotid sinus pressure was initially set equal to the value of mean systemic arterial blood pressure. A sine wave component was set at 40 mm Hg peak-to-peak at a frequency of 70/min and maintained constant throughout all of the experimental procedures. After stabilization of perfusion (15-30 minutes), mean carotid sinus pressure was lowered to about 30 mm Hg and held there until systemic variables reached a steady state. These variables were then recorded on analog tape along with pressure base lines and flow mechanical zeros. Subsequently, carotid sinus pressure was raised in steps of about 30 mm Hg up to about 240 mm Hg, and at each step systemic variables were recorded on tape after they had reached a steady state (1-3 minutes). Mean carotid sinus pressure was subsequently reduced in similar steps back to 30 mm Hg. Carotid sinus pressure was then returned to the initial control value, and a bilateral vagotomy was performed. When the subsequent tachycardia and hypertension returned to a steady-state condition (approximately 20 minutes), the variations in carotid sinus pressure were repeated. Examples of data recorded during the variation of carotid sinus pressure from 40 to 250 mm Hg with the vagi intact are shown in Figure 1. Periodic pressure and flow base lines were recorded on the magnetic tape. At the end of the experiment, pressure and flow calibrations were also recorded on the tape.

DATA ANALYSIS

Recorded pressures and flows were subsequently replayed from the tape. At each mean carotid sinus pressure, 4-6 cardiac cycles from various parts of the respiratory cycle were chosen for analysis. These curves were subsequently subjected to analog-to-digital conversion and Fourier series analysis as previously described (21). Values of mean carotid sinus pressure were calculated directly from the analog records. The Fourier series coefficients for pressures and flows were all corrected for the frequency-response characteristics of the particular transducer system as described previously (22). Pressures and flows were generally not measured at the same arterial site so that a correction was applied for the spatial separation of these two variables (22). The values of vascular impedance for each cardiac cycle analyzed were corrected for this difference by linear interpolation or extrapolation using pressure transmission data between pressure measurement sites computed for that cardiac cycle. The close placement of pressure and flow transducers minimized such corrections. Impedance amplitude corrections were on the order of 2-5%, and the maximum phase angle correction at 18 Hz never exceeded 20°.

Preliminary analysis of these experiments indicated that large differences in operating characteristics of the carotid sinus control of regional hemodynamics existed in the different dogs. For example, before vagotomy, operating point values of mean arterial blood pressure varied from 105 to 165 mm Hg, cardiac output from 1.5 to 6.8 x 10^3 dynes - sec / cm^2. To develop a more rational basis for averaging data, a normalization procedure was devised. Hemodynamic variables (mean arterial blood pressure, mean blood flows, and regional impedances) were calculated for each cardiac cycle and averaged for each experimental condition. The first step in the normalization procedure was to determine the closed-loop operating point of the reflex. Mean aortic blood pressure was plotted against carotid sinus pressure for each experimental condition, and data points were connected by straight lines. The intersection between

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**Figure 1**

Example of on-line records of hemodynamic variables at different levels of mean carotid sinus perfusion before vagotomy. Variables from top to bottom are carotid sinus pressure (CSP), aortic pressure (P_a), femoral artery pressure (P_f), aortic flow (Q_a), celiac artery flow (Q_c), mesenteric artery flow (Q_m), renal artery flow (Q_r), and femoral artery flow (Q_f). These records are for increasing carotid sinus pressure only.

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this curve and a line of identity approximated the closed-loop operating point. This point is where mean aortic and mean carotid sinus pressure are equal and is the point around which the reflex tends to control blood pressure in closed-loop operation, i.e., the set point (23). The gain of the reflex was determined from this curve as the slope of the graph at various values of carotid sinus pressure. Having identified this operating point pressure, values of all of the other hemodynamic variables at the operating point were determined from the recorded data by linear interpolation. The sensitivities of the other cardiovascular variables to the changes in carotid sinus pressure were also determined from the slopes of their respective curves.

The next step was to divide each hemodynamic variable (carotid sinus pressure, aortic pressure, etc.) by its operating point value. Thus, the value of each normalized cardiovascular variable at the operating point pressure is 1. Values of each normalized variable were then determined from normalized experimental data at values of normalized carotid sinus pressure from 0.2 to 2 in steps of 0.2 by three-point interpolation using a digital computer. Values of normalized cardiovascular variables were then averaged from all of the experiments at specific values of normalized carotid sinus pressure. Statistical significance was determined using methods of paired data analysis (24).

The vascular impedance spectrums at different carotid sinus pressures were normalized in a similar manner. Values of vascular impedance for each experimental condition at frequencies of 0, 3, 6, 9, 12, 15, and 18 Hz were determined from the Fourier analysis results by three-point interpolation. Next, values of vascular impedance at each frequency for each arterial site were plotted as a function of carotid sinus pressure and operating point values were determined. Values of vascular impedance for each site at each frequency were normalized and then determined at values of normalized carotid sinus pressure from 0.2 to 2.0 in steps of 0.2 using three-point interpolation by digital computer. The result of this interpolation procedure was a three-dimensional array at each vascular site of impedance amplitude as a function of frequency and normalized carotid sinus pressure. These three-dimensional arrays were then averaged over the various experiments for each particular condition at specific combinations of frequency and normalized carotid sinus pressure for each arterial site. Only values of impedance for increasing carotid sinus pressure before and after vagotomy are reported in the present paper. In general, hysteresis occurred in the values of vascular impedance. However, the general conclusions that are presented are independent of whether carotid sinus pressure was increasing or decreasing.

Estimates of characteristic impedance (the value of impedance that would exist at a vascular site in the absence of reflected waves and nonuniformities) (25, 26) at each vascular site were determined at each value of normalized carotid sinus pressure by averaging values of impedance for frequencies from 9 to 18 Hz. Such calculations were made for each experimental condition and normalized by dividing by the value of characteristic impedance at a normalized carotid sinus pressure of 1. These curves of normalized characteristic impedance versus normalized carotid sinus pressure for each arterial site were then averaged over all of the experiments. In general, the degree of accuracy of this sort of estimation of characteristic impedance has never been clearly established, but it is considered to be a reasonable approximation (25, 26).

Results

OPEN-LOOP REFLEX

The overall characteristics of the open-loop carotid sinus control of aortic blood pressure are shown on the left side of Figure 2. The top left

Summary of open-loop characteristics of the carotid sinus reflex. Top sections from left to right show the variation of normalized aortic pressure, aortic resistance, and aortic flow with normalized carotid sinus pressure. Open circles are data before vagotomy, and solid triangles are data after vagotomy. Bottom sections from left to right show the variation of open-loop gain and aortic resistance and aortic flow sensitivities with normalized carotid sinus pressure. Vertical bars represent ±SE of data points averaged from all of the experiments.
section shows the variation in normalized aortic blood pressure with normalized carotid sinus pressure. The characteristic inverse relationship of these variables was accentuated after vagotomy in the low carotid sinus pressure region. No significant differences existed in the curves before and after vagotomy for normalized carotid sinus pressures greater than 1. This finding supports previous studies which have demonstrated that the aortic arch receptors act primarily as an antihypertensive mechanism (27). Before vagotomy, the aortic arch receptors in part buffered the systemic hypertension associated with low carotid sinus pressure.

Values of open-loop gain are summarized in the bottom left section of Figure 2. The values of open-loop gain at 0.6 and 1.0 were significantly higher after vagotomy. In general, the gain curve appeared to be asymmetrical about the operating point pressure. Values of gain were highest for a normalized carotid sinus pressure of 0.9. Although the closed-loop operating point pressure was slightly elevated following vagotomy, the difference was not statistically significant. The initial control value of mean arterial blood pressure was identical to the prevagotomy closed-loop operating point pressure as shown in Table 1.

The contribution of changes in aortic resistance and aortic flow with changes in carotid sinus pressure to the characteristics of the overall reflex are also shown in Figure 2. The variations in normalized aortic resistance and flow with carotid sinus pressure are shown in the top middle and right sections, and the sensitivities of these quantities to carotid sinus pressure are shown in the bottom sections. Before vagotomy, the overall open-loop gain at the operating point carotid sinus pressure was increased.

### Table 1

<table>
<thead>
<tr>
<th>Hemodynamic Quantities</th>
<th>Initial controls</th>
<th>Vagi intact</th>
<th>Vagi cut</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AP (mm Hg)</strong></td>
<td>135 ± 6</td>
<td>133 ± 5</td>
<td>145 ± 9</td>
</tr>
<tr>
<td><strong>Qa (ml/min)</strong></td>
<td>3,242 ± 351</td>
<td>3,217 ± 358</td>
<td>2,733 ± 364*</td>
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<tr>
<td><strong>HR (beats/min)</strong></td>
<td>145 ± 12</td>
<td>159 ± 13</td>
<td>143 ± 15</td>
</tr>
<tr>
<td><strong>Raa (dynes·sec/cm²)</strong></td>
<td>3,790 ± 476</td>
<td>3,832 ± 501</td>
<td>4,373 ± 536*</td>
</tr>
<tr>
<td><strong>Qca (ml/min)</strong></td>
<td>544 ± 118</td>
<td>537 ± 91</td>
<td>414 ± 54</td>
</tr>
<tr>
<td><strong>Rca (dynes·sec/cm²)</strong></td>
<td>26,833 ± 4,051</td>
<td>23,551 ± 2,805</td>
<td>32,103 ± 5,818*</td>
</tr>
<tr>
<td><strong>Qma (ml/min)</strong></td>
<td>478 ± 46</td>
<td>440 ± 36</td>
<td>278 ± 27</td>
</tr>
<tr>
<td><strong>Rma (dynes·sec/cm²)</strong></td>
<td>24,513 ± 2,814</td>
<td>26,152 ± 2,746</td>
<td>46,010 ± 6,101*</td>
</tr>
<tr>
<td><strong>Qra (ml/min)</strong></td>
<td>338 ± 35</td>
<td>348 ± 28</td>
<td>284 ± 40</td>
</tr>
<tr>
<td><strong>Rra (dynes·sec/cm²)</strong></td>
<td>37,730 ± 6,577</td>
<td>33,153 ± 3,757</td>
<td>41,244 ± 5,480*</td>
</tr>
<tr>
<td><strong>Qra (ml/min)</strong></td>
<td>78 ± 15</td>
<td>79 ± 15</td>
<td>69 ± 14</td>
</tr>
<tr>
<td><strong>Qra (dynes·sec/cm²)</strong></td>
<td>215,353 ± 54,309</td>
<td>188,857 ± 39,515</td>
<td>230,965 ± 81,651</td>
</tr>
</tbody>
</table>

#### Operating Point Sensitivities

| AP | -0.68 ± 0.13 | -0.94 ± 0.10* |
| Qa | -0.19 ± 0.05 | -0.44 ± 0.18 |
| HR | -0.32 ± 0.14 | -0.16 ± 0.23 |
| Raa| -0.50 ± 0.11 | -0.69 ± 0.15 |
| Qca| -0.27 ± 0.03 | -0.28 ± 0.07 |
| Rca| -0.41 ± 0.05 | -0.66 ± 0.14 |
| Rma| -0.20 ± 0.06 | -0.02 ± 0.10 |
| Rra| -0.48 ± 0.11 | -0.92 ± 0.21* |
| Qr | -0.09 ± 0.07 | 0.00 ± 0.06 |
| Rr | -0.59 ± 0.13 | -0.94 ± 0.12* |
| Qr | +0.70 ± 0.17 | +0.62 ± 0.12 |
| Rr | -1.38 ± 0.34 | -1.56 ± 0.25 |

#### Cardiac Output Distribution

| Qa (%) | 16.8 ± 3.2 | 17.4 ± 2.1 |
| Qma (%)| 16.2 ± 3.2 | 15.9 ± 2.5 |
| Qra (%)| 11.0 ± 1.4 | 11.9 ± 1.6 |
| Qfa (%)| 2.5 ± 0.5  | 2.5 ± 0.4  |

AP = mean arterial blood pressure, Qa and Raa = ascending aorta flow and resistance, respectively, HR = heart rate, Qca and Rca = celiac artery flow and resistance, respectively, Qma and Rma = mesenteric artery flow and resistance, respectively, Qra and Rra = renal artery flow and resistance, respectively, and Qfa and Rfa = femoral artery flow and resistance, respectively.

* P < 0.05 compared with the value for vagi intact.
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pressure was primarily determined by variations in aortic resistance (75%) and to a smaller extent by variations in aortic flow (25%). Following vagotomy, however, the contribution of changes in aortic flow to the overall gain increased (35%) significantly. In the low carotid sinus pressure range, the sensitivity of aortic resistance to changes in carotid sinus pressure increased following vagotomy. This finding suggests that the aortic arch mechanoreceptors participate in the control of peripheral resistance at high values of systemic arterial blood pressure, as previously reported (27-29). Aortic flow sensitivity was only increased following vagotomy in the range of 0.8 < normalized carotid sinus pressure < 1.2. The relative contributions of aortic resistance and aortic flow to the overall characteristics of the carotid sinus reflex were similar to those described by Schmidt et al. (6, 7). In absolute terms, the value of cardiac output at the operating point pressure was reduced following vagotomy (Table 1); this change was statistically significant.

REGIONAL CONTROL

The same inverse relationship shown between aortic resistance and carotid sinus pressure was found in all of the regional beds studied. Normalized curves of regional resistance versus carotid sinus pressure are summarized in Figure 3 before and after vagotomy. Values of regional resistances and sensitivities at the closed-loop operating point as well as initial control values of regional resistance are summarized in Table 1. No significant differences existed between initial control values of regional resistance and operating point values before vagotomy. Following vagotomy, all operating point values of regional resistance except for that for the femoral artery were significantly increased. This finding suggests that the aortic arch receptors exert a significant influence on regional resistance at the normal operating point.

The dependence of regional resistance in the celiac, mesenteric, and renal beds on carotid sinus pressure with the vagi intact was quantitatively similar to that of the total aortic resistance. In contrast, femoral resistance showed a much larger variation with carotid sinus pressure than did the other regional beds. Following vagotomy, the variations in normalized resistance with carotid sinus pressure all increased at both high and low values of carotid sinus pressure. In general, values of normalized regional resistance at high normalized carotid sinus pressures (about 2.0) were significantly reduced following vagotomy. They were likewise increased significantly at low normalized carotid sinus pressures (about 0.2), except for those for the femoral artery bed.

Values of regional resistance sensitivity are summarized in Figure 4 and Table 1. In general, vagotomy increased the sensitivities of all beds to

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changes in carotid sinus pressure with those in the femoral artery being the least affected. Operating point sensitivity (normalized carotid sinus pressure = 1) was significantly increased by vagotomy for the mesenteric and renal resistances. Sensitivities at low values of normalized carotid sinus pressure (e.g., 0.6) were significantly increased in all beds except for the femoral bed. At high values of normalized carotid sinus pressure (about 1.4), the sensitivity of all beds except the renal bed was increased. In general, the curves of regional resistance sensitivity versus carotid sinus pressure were not symmetrical around the closed-loop operating point. Sensitivity was consistently greater at values of normalized carotid sinus pressure less than 1. Following vagotomy, this asymmetry was accentuated in most of the regional beds.

Changes in regional blood flow produced by the carotid sinus were determined by the variations in both cardiac output (Fig. 2) and regional resistance (Fig. 3). The regional distribution of arterial blood flow (flow ÷ aortic flow) is summarized as a function of carotid sinus pressure in Figure 5 and Table 1 before and after vagotomy. The relative flow distributions at the closed-loop operating point pressure before vagotomy were not significantly different from the initial control values. Following vagotomy, the only significant change was a decrease in the flow distribution to the mesenteric bed. The blood flow distribution to the celiac, mesenteric, and renal beds before vagotomy was reasonably well maintained at various values of carotid sinus pressure. The fraction of aortic flow in the femoral artery, however, significantly increased with carotid sinus pressure. These characteristics of regional flow distribution versus carotid sinus pressure were essentially the same following vagotomy, with the variation of the femoral flow fraction being greater.

**AORTIC IMPEDANCE**

Three-dimensional plots of the amplitude of aortic impedance as a function of frequency and carotid sinus pressure are shown in Figure 6 before and after vagotomy. Only mean values are shown without standard errors to prevent confusion. Normalized values of aortic characteristic impedance and aortic resistance before and after vagotomy are summarized in Figure 7. From these two figures, it is apparent that very marked differences exist in the variation of aortic characteristic impedance and aortic resistance with carotid sinus pressure. Values of aortic resistance varied inversely with values of carotid sinus pressure, but values of aortic characteristic impedance were lowest in the vicinity of the normal operating point value of carotid sinus pressure. This generalization holds for essentially all of the frequency components of aortic impedance. The variation of impedance with carotid sinus pressure appeared to be largest at a frequency of 6 Hz.

The total change in aortic characteristic impedance over the total range of normalized carotid sinus pressure was increased following bilateral cervical vagotomy. The value of aortic characteristic impedance at the closed-loop operating point...
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1.8
1.0
0
0 1 2
Vagi intact
Vagi cut
CAROTID SINUS PRESSURE

Variation of ascending aortic resistance (open circles) and characteristic impedance (solid squares) with normalized carotid sinus pressure before and after vagotomy. Points represent means, and vertical bars are ±1 SE.

REGIONAL IMPEDANCE

Three-dimensional plots of regional vascular impedance at the four peripheral arterial sites with the vagi intact are shown in Figure 8. A somewhat different relationship between impedance amplitude, frequency, and carotid sinus pressure was demonstrated at these peripheral sites. In the case of the celiac, renal, and mesenteric arteries, in particular, the variation of impedance at a specific frequency was essentially a monotonic function of carotid sinus pressure. The usual inverse relationship seen with regional resistance was also observed with the frequency components of vascular impedance and carotid sinus pressure for these three sites.

The variation in femoral impedance with frequency at different carotid sinus pressures was somewhat different, however. At low frequencies, i.e., less than 6 Hz, the variation in femoral impedance was an inverse function of carotid sinus pressure. For higher frequencies, however, a minimum began to appear in the variation of femoral...
impedance with carotid sinus pressure. At low carotid sinus pressures, femoral impedance fell from its high d-c values nearly continuously up to 15 Hz. At high carotid sinus pressures, on the other hand, femoral impedance fell from its d-c value to a minimum at 6 Hz and then rose again to higher values.

This pattern of variation of regional impedance amplitude with frequency and carotid sinus pressure was qualitatively similar following cervical bilateral vagotomy. In general, the total change in impedance at all frequencies (including d-c) with normalized carotid sinus pressure was increased following vagotomy. For the renal, mesenteric, and celiac sites, the monotonic inverse relationship of impedance with normalized carotid sinus pressure was maintained following vagotomy. The more complicated variation of femoral impedance with carotid sinus pressure was also maintained following vagotomy. At values of frequency above 6 Hz, a minimum in the impedance variation with carotid sinus pressure occurred.

The frequency variation of regional vascular impedance is shown in Figure 9. Values of aortic, renal, celiac, and femoral impedance spectrums are shown for normalized carotid sinus pressures of 0.2 (solid squares), 1.0 (open circles), and 2.0 (solid triangles). For the case of the aorta, values of the impedance spectrums before and after vagotomy for high and low values of carotid sinus pressure were both higher than impedance spectrums at the operating point (carotid sinus pressure = 1). For the renal and celiac (similar to mesenteric) arteries, a monotonic relationship existed between values of impedance at specific frequencies and carotid sinus pressure both before and after vagotomy. The mesenteric artery impedance demonstrated a similar behavior to that of the celiac artery and was not shown for simplicity. In contrast, the more complicated variation of femoral imped-

![Figure 9](image-url)

**Figure 9**
Regional vascular impedance spectrums before and after vagotomy at three values of normalized carotid sinus pressure: 0.2 (solid squares), 1.0 (open circles), and 2.0 (solid triangles). Points are means, and vertical bars are ± 1 SE.
ance with frequency and carotid sinus pressure is also illustrated in this figure. Following vagotomy, high-frequency values of femoral impedance for high and low values of carotid sinus pressures were both higher than comparable operating point values. In addition, similar results were found prior to vagotomy at the femoral site.

### REGIONAL CHARACTERISTIC IMPEDANCE

The variation of regional resistance and characteristic impedance data with normalized carotid sinus pressure is shown in Figure 10. In general, a similar inverse relationship was found between resistance and characteristic impedance and carotid sinus pressure at all four sites. The changes in regional resistance and characteristic impedance with carotid sinus pressure showed regional variations. For the renal artery, the variations of these two quantities were very nearly the same. However, for the mesenteric and femoral arteries, variations in characteristic impedance were smaller than resistance changes. Nonetheless, the changes that occurred in characteristic impedance with normalized carotid sinus pressure were statistically significant. A summary of operating point values of regional characteristic impedance before and after vagotomy is given in Table 2. In general, there was no significant difference in values of regional characteristic impedance as a result of bilateral vagotomy. On the other hand, the sensitivity of regional characteristic impedance with carotid sinus pressure at the closed-loop operating point was increased at all peripheral sites, as indicated in Table 2.

Values of regional characteristic impedance sensitivity are summarized in Figure 11. The variation of characteristic impedance sensitivity with normalized carotid sinus pressure was generally asymmetrical with maximum values of sensitivity occurring at values of carotid sinus pressure below the operating point.

### Discussion

The results given in this paper describe in quantitative terms the open-loop characteristics of carotid sinus control of regional and systemic arterial hemodynamics in the chloralose-anesthetized dog. The closed-loop operating point values of mean arterial blood pressure, cardiac output, and regional impedance before vagotomy were identical to the initial control values of these variables. This finding adds validity to the concept of the closed-loop operating point as the state about which the cardiovascular system is controlled under closed-loop conditions.
With the vagi intact, the open-loop gain was primarily determined by variations in peripheral resistance with carotid sinus pressure. Following vagotomy, the contribution of changes in cardiac output to the open-loop reflex gain increased. Similar conclusions were reached by Schmidt et al. (6) concerning the relative contribution of these two factors. For cardiac output, they reported much larger changes extending over a wide range of carotid sinus pressure. An explanation for this difference could be the fact that a nonpulsatile perfusion pressure was used in their study. Since the carotid sinus reflex is strongly affected by pulsatile pressures (7, 30), a larger systemic response would be predicted in the study of Schmidt et al. (6), which they reported.

The sensitivity of aortic resistance to carotid sinus pressure is increased following vagotomy at both high and low values of carotid sinus pressure. The increased sensitivity of aortic resistance at low carotid sinus pressure following vagotomy (Fig. 6) is consistent with a significant role for the aortic arch receptors in reflex control at high values of systemic arterial blood pressure (27). The increase in normalized aortic resistance at high values of carotid sinus pressure is only apparent. The increase in the operating point value of the aortic resistance is responsible for the difference in the curves at high carotid sinus pressures. If nonnormalized values of aortic resistance are plotted versus carotid sinus pressure, the difference in pre- and postvagotomy aortic resistance data at high carotid sinus pressures disappears.

Following vagotomy, the sensitivity of aortic flow is increased for values of normalized carotid sinus pressure in the range of 0.8 to 1.2. A much larger decrease in cardiac output is seen through this range of carotid sinus pressures. Because of the complexity of the mechanisms controlling cardiac output, this result is not easily explained. Generally, we have observed a reduction in central venous pressure with increasing carotid sinus pressure (unpublished observation). This change should reduce stroke volume and cardiac output, since only small changes in heart rate are observed between these values of carotid sinus pressure. The increased sensitivity of the peripheral vasculature following vagotomy may also extend to the venous circulation (8) and could contribute to the increased sensitivity of cardiac output around the operating point following vagotomy.

**REGIONAL CONTROL**

Significant differences were observed in the sensitivity of the various regional beds to carotid sinus pressure changes. The values of sensitivity at the operating point for the various beds increased in the order celiac < mesenteric < renal < femoral. In general, after vagotomy, all regional resistance sensitivities were increased, and a similar ranking of sensitivity was found in the various beds. This increment in sensitivity of the beds following vagotomy was femoral < celiac < renal < mesenteric. This order is nearly opposite to that of absolute sensitivities of the various beds before vagotomy and suggests that the effects of the two reflex receptor areas on individual beds may not be algebraic.

The graphs of normalized regional resistance versus carotid sinus pressure (Fig. 3) indicate significant decreases in the former at high values of carotid sinus pressure following vagotomy. This finding also represents only an apparent increase in sensitivity at high carotid sinus pressures because of the significant increases in the operating point values of regional resistance (Table 1) following vagotomy. Thus, no significant difference exists in nonnormalized regional resistances at high carotid sinus pressures following vagotomy, as was the case with aortic resistance.

Regional variations in the distribution of cardiac output were observed under steady-state open-loop conditions. The fraction of cardiac output in the celiac, mesenteric, and renal beds was essentially independent of carotid sinus pressure (Fig. 5), but that in the femoral bed increased with carotid sinus pressure. A similar pattern was observed before and after vagotomy. Because of the general decrease in the cardiac output with carotid sinus pressure, the three former flows decreased with carotid sinus pressure on an absolute basis, although femoral flow still increased. Thus, increases in carotid sinus pressure would be expected to be associated with a decrease in mesenteric, celiac, and renal blood flows and an increase in limb blood flow. This pattern is similar to that reported by Vatner et al. (12) in response to carotid sinus nerve stimulation in the unanesthetized dog. Similar components of regional blood flow responses have been reported in intact animals in which pressor responses occur secondary to hypothalamic stimulation (31), acute emotional stress (32), and central sciatic nerve stimulation (33). Also, a similar pattern of blood flow distribution occurs in response to moderate exercise in the dog (34), which is also associated with an increase in mean arterial blood pressure. The opposite response has been observed in experimental hemorrhagic shock in the dog (35). In the acute, compensated stage, the percents of cardiac
output to the renal and hepatosplanchnic areas were unchanged from control values, but the percent to the extremity was significantly reduced. This distribution of cardiac output is what one would expect based on the results given in this study (Fig. 5).

Thus, changes in the distribution of cardiac output are strongly influenced by the neural reflex mechanisms. These mechanisms can be viewed as representing the first line of control. Obviously, the effects of other factors (e.g., hormonal, metabolic, etc.) are superimposed on the action of the neural reflexes. The carotid sinus mechanoreceptors are not simply arterial blood pressure controllers; rather, they significantly influence the distribution of cardiac output.

**VASCULAR IMPEDANCE**

Vascular impedance at any particular site is a function of the mechanical and geometrical properties of the entire vascular system distal to that site (25). The contribution of the various distal blood vessels to vascular impedance, however, is extremely complex. The high-frequency values of vascular impedance (above 5 Hz) depend primarily on the mechanical and geometrical properties of relatively large blood vessels in the immediate vicinity of the site of interest (19, 26). The value of vascular impedance at zero frequency (resistance) represents the mechanical and geometrical properties of relatively small vessels, i.e., arterioles, etc. Thus, values of vascular impedance spectrums provide information about both large and small vessels in a vascular bed. Although linearity does not apply for a wide range of pressures, a piecewise linear approximation at a particular vascular state is reasonable (25).

Values of aortic impedance at frequencies of 3 Hz and above show an entirely different variation with carotid sinus pressure than do values of regional vascular resistance. At all values of frequency before and after vagotomy, values of aortic impedance are minimum near the closed-loop operating point pressure (carotid sinus pressure = 1).

This minimum of aortic impedance at the closed-loop operating point pressure is similar to results obtained by Peterson (36) using an entirely different approach. He introduced a constant-amplitude flow step into the ascending aorta of anesthetized dogs during diastole at different values of initial arterial blood pressure. The rapid transient value of the pressure response to the constant-amplitude flow step was a minimum at the normal blood pressure level of the dog. Since the flow increment was of constant amplitude, the pressure response was equivalent to a high-frequency impedance, i.e., characteristic impedance. Thus, the results observed in the present study are similar to those presented by Peterson (36).

In a recent series of publications from our laboratory, we have demonstrated that in unanesthetized and anesthetized (chloralose) dogs regional vascular impedance spectrums above 3 Hz are essentially independent of changes in mean arterial blood pressure produced secondary to cardiac autonomic nerve stimulation and vasoactive drug injection (22, 37). However, when systemic arterial blood pressure is increased subsequent to carotid sinus hypotension, values of aortic impedance spectrums are significantly increased over control values (38). These studies taken together suggest that the carotid sinus exerts an active influence on the impedance properties of the arterial tree in such a manner as to produce a minimum impedance at normal values of arterial blood pressure. It is tempting to speculate that this minimum in vascular impedance at normal values of arterial blood pressure is of some hemodynamic benefit to the animal, perhaps because it minimizes the external work of the left ventricle. However, such speculations cannot be supported by any objective criterion at this point.

In general, the variations in regional impedance spectrums with carotid sinus pressure are qualitatively similar to the changes in regional resistance with carotid sinus pressure, that is, as carotid sinus pressure increases, impedance decreases. Therefore, the total opposition to pulsatile blood flow (the sum of these impedance components) is inversely related to carotid sinus pressure before and after vagotomy. A difference exists in the femoral artery in which variations are observed especially at high values of carotid sinus pressure. The degree to which variations in peripheral wave reflection affect the impedance spectrums cannot be assessed from these data. In an attempt to eliminate the potential effects of altered wave reflection from peripheral terminations, characteristic impedance was estimated by averaging values of impedance between 9 and 18 Hz. Characteristic impedance has been estimated in a similar, though quantitatively different, manner by a number of different investigators (19, 25, 37, 39-41). Estimated values of regional characteristic impedance generally show an inverse relationship with normalized carotid sinus pressure.

An inevitable question must be asked. Do these...
changes in characteristic impedance with carotid sinus pressure represent direct active responses or indirect passive responses? A direct effect would suggest that the carotid sinus directly controls the mechanical and geometrical properties of relatively large arteries. An indirect effect would be the result of changes in mechanical and geometrical properties of arteries secondary to changes in mean arterial blood pressure per se. There is considerable information in the literature which suggests that vascular smooth muscle in large to small arteries participates in neural reflex mechanisms. For example, it has been shown that stimulation of efferent sympathetic nerves produces significant responses on the main pulmonary artery (42), femoral artery (43), mesenteric artery (44), carotid sinus (4), abdominal aorta (45), and anterior tibial artery (46), among others. It has been shown that aortic smooth muscle can be reflexly activated in response to hemorrhage (47). Abboud (48) has demonstrated that in the forelimb of the dog small arteries are most sensitive to sympathetic stimulation and arterioles are most sensitive to circulating catecholamines. Efferent sympathetic nerve stimulation produces significant effects on vascular impedance spectrums in the main pulmonary artery (41), and the carotid sinus exerts a significant effect on renal artery impedance in the anesthetized dog (19). These results suggest that the impedance spectrum at a given vascular site may be reflexly modified by virtue of the action of sympathetic nerves on vascular smooth muscle in small to large arteries, in addition to their effect on so-called microvessels.

It has also been demonstrated that the mechanical and geometrical properties of the blood vessels are pressure dependent (actually strain dependent). In general, as pressure increases, the elastic modulus as well as the internal radius and the radius-wall thickness ratio increase (49–51). One question still remains. Are these changes in impedance spectrums direct reflex effects or indirect effects mediated through changes in arterial blood pressure? To provide indirect answers to this question, values of characteristic impedance at the various arterial sites studied were plotted as a function of transmural pressure (unpublished observation). However, following activation of vascular smooth muscle (e.g., by norepinephrine) values of characteristic impedance possess a minimum value at pressures on the order of 100–140 mm Hg similar to the curves shown in Figure 12 for the aorta and the femoral artery. In general, values of characteristic impedance for the mesenteric and the renal arteries, especially at low values of transmural pressure, are nearly constant and do not increase monotonically with pressure. This effect at these two sites, however, is small.

Additional evidence for a direct reflex effect on impedance spectrums can be inferred from the effects of vagotomy. If the effects of variation in impedance spectrums were only the indirect result of the variation in mean arterial blood pressure, it would be anticipated that values of characteristic impedance would fall along the same curve for conditions before and after vagotomy. Although this may be the case for the renal, mesenteric, and celiac sites (the latter not shown in Fig. 12), it is certainly not true in the aorta and in the femoral artery. However, affairs are not that simple, as usual. As far as the ascending aorta is concerned, values of characteristic impedance appear to be higher following vagotomy at all levels of systemic blood pressure, especially below 150 mm Hg. In contrast, this relationship appears to be reversed in the femoral artery for which values of characteristic
impedance are higher before vagotomy, especially below 150 mm Hg. The differences in the responses of the two arteries may simply represent the way in which they are affected following smooth muscle activation. Although these results are not the same, they do suggest that some difference exists in the state of vascular smooth muscle before and after vagotomy at these two arterial sites. This indirect evidence suggests that the changes in vascular impedance are higher before vagotomy, especially where they are affected following smooth muscle.

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