Control of Total Systemic Vascular Capacity by the Carotid Sinus Baroreceptor Reflex

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ABSTRACT
To attain a quantitative understanding of carotid sinus baroreceptor reflex control of cardiac output, we studied the reflex control of total systemic vascular capacity in vagotomized dogs. In experiments measuring blood volume shifts caused by the carotid sinus reflex (series 1), venous return was diverted into a reservoir while cardiac output and central venous pressure were maintained at constant levels. The pressure in the isolated carotid sinuses (ISP) was lowered or raised in 25-mm Hg steps between 75 and 200 mm Hg. This procedure mobilized blood into or out of the reservoir, indicating a decrease or an increase in total vascular capacity, respectively. The mean maximum volume shift, 3.6 ml/kg body weight, occurred in the same ISP region, 135 ± 12.5 mm Hg, where reflex control of total peripheral resistance was strongest. The total volume shift was approximately 7.5 ml/kg for ISP changes from 75 to 200 mm Hg. When mean arterial blood pressure was maintained constant during the ISP step changes, the volume shift almost doubled. In experiments measuring the reflex effect on total systemic vascular compliance (series 2) and in experiments determining the reflex control of arterial compliance (series 3), total systemic vascular and lumped arterial compliances were measured in the same dogs that were used in series 1 experiments. The total systemic vascular and arterial compliances were approximately 2.0 ml/mm Hg kg⁻¹ and 0.0677 ml/mm Hg kg⁻¹, respectively. The reflex did not affect these compliances. We concluded that the reflex controls the total systemic venous capacity to a degree that changes cardiac output potentially by 30-40% per 25-mm Hg change in ISP.

KEY WORDS venous compliance unstressed vascular volume reflex gain total peripheral resistance pressure-volume relationship dog cardiac output arterial compliance reservoir volume

The importance of the capacitive property of the systemic vascular circuit, particularly the systemic veins, has been recognized for some time: this property is involved in the regulation of cardiac output, since it affects the filling pressure of the right heart (1, 2). Evidence for carotid sinus baroreceptor reflex control of venous segments in various tissues and organs has been accumulated from different laboratories (3-6). However, the importance of carotid sinus reflex control of total systemic vascular capacity in the regulation of cardiac output has not been firmly established.

Early studies by Rashkind et al. (7), using a dog preparation in which venous return was diverted into a reservoir while cardiac output was kept constant, have shown that significant shifts of blood between the reservoir and the dog occur when the carotid sinus nerves are stimulated. Guyton (8) has analyzed the role of venous capacity in circulatory mechanics by measuring mean systemic filling pressure and reported that the reflex can alter mean systemic pressure by several millimeters of mercury. More recently Kumada et al. (9) have found that mean systemic pressure increases as much as 2 mm Hg during occlusion of the common carotid arteries. Browse et al. (10) have also indicated definite capacity changes by the reflex; however, they have concluded that the magnitude of these changes is of little quantitative importance in controlling cardiac output. These studies on the total systemic vascular bed are ambiguous as to whether the reflex alters the unstressed vascular volume or the compliance.

In the present study we determined, in the same dogs, both the change in the total systemic vascular compliance and the mobilization of blood volume from or into the systemic vessels caused by the carotid sinus reflex. We also studied the effect of the baroreceptor reflex on arterial compliance and...
CAROTID REFLEX AND CAPACITY VESSELS

the masking effect that reflexly changing arterial blood pressure has on the blood volume which is apparently mobilized. These combined measurements permitted us to define the reflex control of lumped systemic vascular capacity more quantitatively.

Methods

THEORETICAL CONSIDERATIONS

To appreciate the quantitative importance of a reflex change of vascular capacity in regulating cardiac output, one must know the overall pressure-volume relationship of the total systemic vascular bed and the reflex-induced variations in the relationship. In this paper, "capacity" means the amount of blood held by the systemic vascular bed at a specific pressure. This amount of blood depends on both the compliance, which is defined as the slope of the pressure-volume curve (ΔV/ΔF), and the unstressed vascular volume, which is defined as the volume-axis intercept of the pressure-volume curve. Distinction of these two parameters is important for the analysis of overall circulatory mechanics and reflex control of the circulation. When a given change in blood volume or cardiac output passively expands or shrinks the vascular system, the determinant of the resultant pressure change is the compliance. However, when a reflex mechanism actively modifies vascular elastic properties, the resultant change in vascular pressure depends on whether the reflex affects the unstressed vascular volume, the compliance, or both.

Figure 1 depicts a hydraulic analogue of the systemic vascular bed with three lumped elements. Changes in the total compliance, Ca and Cv, are represented by changes in the diameter (and therefore the cross-sectional area) of the arterial and venous chambers, and changes in unstressed vascular volume are represented by the shaded area at the bottom of the arterial and venous chambers. The changes in total peripheral resistance are represented by changes in the diameter of the constriction between the two chambers.

The unstressed vascular volume cannot be directly measured under normal physiological conditions because blood flow exists in the systemic bed and transmural pressures in the various compartments of the bed are not zero. However, changes in vascular capacity can be estimated from a shift of blood between the systemic bed and a reservoir in an animal preparation (Fig. 1). Cardiac output is fixed by a pump which perfuses the preparation with blood from a reservoir at a constant-flow rate. Central venous pressure is also fixed at a constant level by adjusting the height of the end of the tube which drains venous return into the reservoir. If the blood volume in the reservoir changes when the reflex system is stimulated, then this change reflects the net volume change of the systemic vessels caused by the reflex.

This shift of blood volume is not a direct measure of the change in unstressed vascular volume per se, since the reflex could change two other vascular parameters which would affect the net shift of blood volume. First, the reflex could change reservoir volume by changing vascular compliance. However, as will be shown in the Results, neither the total systemic vascular compliance nor the arterial compliance are influenced by the reflex within the limits of measurement in this study. Second, the baroreceptor reflex system alters arterial blood pressure by altering total peripheral resistance. With this change in arterial blood pressure, a concomitant blood volume change must occur in the arterial compartment (Fig. 1, shaded area). This passive, indirect volume shift, ΔVpa, is opposed to the shift of blood into or from the reservoir that is caused by a direct reflex change of venous and arterial capacity. If we represent the reflex changes in arterial and venous vascular volume by ΔV a and ΔV v, the net reservoir volume change, ΔV r, will be the algebraic sum of all those factors:

$$\Delta V_r = \Delta V_a + \Delta V_v - \Delta V_{pa} \tag{1}$$

Thus, the net volume shift measured at the reservoir will underestimate the true reflex changes in vascular capacity by ΔVpa. However, it is the net amount of blood mobilized, ΔVv, by the reflex that changes the filling pressure of the heart rather than the true reflex change in vascular capacity. For this reason, we measured this net volume shift in the majority of the dogs. In two dogs, we prevented the reflex change in arterial blood pressure during the measurement of volume change. The result of this procedure is described in the Discussion.

The method used to determine the total systemic compliance parameter has been published previously (11). Briefly, the method is based on the principle that, if the blood volume in a linear resistance-compliance network is changed by an amount, ΔV, and the flow through the circuit is fixed, the resulting pressure change, ΔP, is determined solely by the sum of compliances in the network. Thus the total vascular compliance can be determined as ΔV/ΔP.

The lumped arterial compliance, Ca, can be determined by shifting blood between the arterial system and the reservoir by a second roller pump while cardiac output, venous pressure, and intrasinus pressure
are maintained at constant levels. Since cardiac output, venous pressure, and intrasinus pressure are fixed, there are no reservoir volume changes caused by reflex changes in vascular capacity and total peripheral resistance. Thus, the volume change measured in the reservoir is solely caused by the quantity of blood passively shifted into or out of the arterial compartment by the roller pump. The lumped arterial compliance can be calculated from this change in reservoir volume ($\Delta V_e$) and the resultant change in arterial blood pressure ($\Delta P_a$) as $\Delta V_e/\Delta P_a$.

**EXPERIMENTAL PROCEDURES**

Since three different series of experiments were performed in the same dogs, we will describe only those experimental procedures common to all three experiments. The individual procedures specific to each series are described in Results.

Thirteen mongrel dogs (16.4-31.4 kg) were anesthetized with sodium pentobarbital (30 mg/kg, iv). Cautery and complete ligation of the cut tissue masses were used for every incision to minimize seepage of blood.

The left and right carotid sinuses were isolated (12) from the rest of the circulatory system. The internal and external carotid arteries and any small branches originating from the carotid bifurcation were ligated. A four-way glass junction was connected to the cephalad segments of the common carotid arteries, the caudal portion of the right common carotid artery, and the servocontrolled pressure-generating system (13) used to produce any desired intrasinus pressure. Mean intrasinus pressure was monitored via a catheter placed in the thoracic aorta and vein, respectively, and connected to pressure transducers (Statham P23AC and P23BB). Zero-pressure reference was set at the junction of the inferior vena cava and the inferior vena cava via the right femoral artery and vein, respectively, and connected to pressure transducers (Statham P23AC and P23BB). Zero-pressure reference was set at the junction of the inferior vena cava and the right heart under direct inspection.

A right thoracotomy was performed at the fifth intercostal space under positive-pressure ventilation with 95% O₂-5% CO₂. Figure 2 illustrates the surgical procedure and the perfusion circuit necessary to measure systemic vascular compliance, blood volume shifts, and arterial compliance in the same dog. The right atrial appendage was cannulated first and connected to the outflow side of a perfusion pump (Sarns model 5M6002) primed with whole blood from another dog. The superior vena cava was then cannulated and connected to the inflow side of the perfusion pump. Perfusion was immediately started with an initial flow of about 40 ml/min kg⁻¹. Finally, the inferior vena cava was cannulated, and the pump flow was readjusted so that arterial and venous pressures were approximately equal to the levels that existed before atrial cannulation. Ligature of theazygos vein completed the surgery. Immediately following the right thoracotomy, an injection of succinylcholinechloride (3.5 mg/kg, im) was given to minimize variations of venous pressure and blood volume caused by voluntary ventilatory effort and other skeletal muscle contractions.

Constancy of the perfusion pump's outflow was continuously monitored by an electromagnetic flowmeter system (Medikon K2000 and an extracorporeal flow transducer). In 5 of the 13 dogs, an additional perivascular electromagnetic flow probe was implanted around the ascending aorta to check constancy of aortic blood flow. Both flow signals were smoothed by a filter with a time constant of 1 second. The flow rate of the perfusion pump and aortic blood flow were calibrated at the end of the experiment using a graduated cylinder and a stopwatch. Perfusion flow rate was $96.2 \pm 5.3$ (sd) ml/min kg⁻¹ for the 13 dogs tested.

Central mean arterial and venous pressures were measured through catheters placed in the thoracic aorta and the inferior vena cava via the right femoral artery and vein, respectively, and connected to pressure transducers (Statham P23AC and P23BB). Zero-pressure reference was set at the junction of the inferior vena cava and the right heart under direct inspection. Blood volume in the reservoir was continuously monitored and recorded the hydrostatic pressure of the column of blood with a pressure transducer (Beckman model 607, 215071). The system was calibrated by changing the reservoir blood volume by a known amount and recording the corresponding pressure change.

**Results**

**MEASUREMENT OF BLOOD VOLUME SHIFTS CAUSED BY THE CAROTID SINUS REFLEX**

(SERIES 1)

When clamps a and b in Figure 2 were opened and clamp c was closed, the dog's venous return was diverted into the reservoir, and the main perfusion pump infused a constant volume flow of blood from the reservoir into the right heart. The height of the opening at clamp a in Figure 2 was adjusted so that mean central venous pressure measured in the inferior vena cava would remain at a constant value between 4 and 8 mm Hg. The venous pressure was maintained at one constant value throughout the experiment. Under this
Recording of changes in reservoir blood volume and inferior vena cava (I.V.C.), arterial, and intrasinus pressures during constant perfusion flow. The solid trace in the top channel shows the volume changes occasionally biased by adding or withdrawing blood in the reservoir to obtain maximum recording sensitivity. The dotted trace shows the reconstructed record of volume changes obtained from the solid trace. The dashed trace indicates the mean value of uncontrolled bleeding from start to end of this experimental run, which was 4.2 ml/min.

Experimental condition, the pressure in the isolated sinuses was changed, and the resultant change in the reservoir blood volume was determined as a measure of change in the blood volume in the systemic vascular system. The pressure in the isolated carotid sinuses (ISP) was initially set at 75 mm Hg for several minutes and then elevated in steps of 25 mm Hg to 200 mm Hg. After each step change, ISP was maintained for at least 2 minutes or until reservoir blood volume and arterial blood pressure stabilized at a steady level for 1 minute. After ISP was raised to 200 mm Hg, it was lowered to 75 mm Hg, again in steps of 25 mm Hg to examine reproducibility of the responses. In six dogs, the order of ISP change was reversed, i.e., it was decreased from 200 mm Hg to 75 mm Hg and then returned to 200 mm Hg.

Figure 3 illustrates the recordings made in the series 1 experiments. In this dog, when ISP was lowered from 175 to 150 mm Hg, the blood volume in the reservoir increased about 200 ml in about 2.5 minutes. Mean arterial blood pressure also increased to a new steady level within a shorter period of time. There was a 10-15-second time lag between the onset of the volume shift and the ISP change and a 2-5-second time lag between the onset of the mean arterial blood pressure change and the ISP change. The next step decrease in ISP caused a greater increase in reservoir blood volume and a greater elevation in mean arterial blood pressure with time courses similar to those for the previous changes. Further decreases in ISP resulted in weaker responses in both variables.

In response to step increases in ISP, the reservoir blood volume first increased slightly and then decreased to steady-state levels lower than the previous levels. Mean arterial blood pressure initially fell sharply and then returned gradually to a new steady-state value below the previous level. These biphasic responses of reservoir blood volume and mean arterial blood pressure were only seen during step increases in ISP (Fig. 3).

Mean central venous pressure was maintained constant, and transient changes were no more than 1 mm Hg (Fig. 3). Perfusion flow did not change even temporarily during the entire experimental run.

Both qualitatively and quantitatively similar results were observed in other dogs in the series 1 experiments. The mean values ± SE of the steady-state changes in reservoir volume, normalized for the individual dog’s body weight, are plotted against ISP in Figure 4 (left). In the figure it appears that almost equal changes in reservoir volume occurred in response to those step changes in ISP within the range from 100 to 175 mm Hg as the P values indicate. However, in individual dogs there was a distinct, single region of ISP where the volume change was maximum, but this region differed from dog to dog. Thus, averaging the
**TABLE 1**

<table>
<thead>
<tr>
<th>Response time</th>
<th>Direction of ISP change</th>
<th>ISP₀ (mm Hg)</th>
<th>ISP₀ - 50 (mm Hg)</th>
<th>P</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 minutes</td>
<td>Increasing</td>
<td>135.07 ± 8.20 (13)</td>
<td>0.28 ± 0.08 (8)</td>
<td>&gt; 0.70</td>
<td>&gt; 0.70</td>
</tr>
<tr>
<td></td>
<td>Decreasing</td>
<td>131.23 ± 6.40 (13)</td>
<td>0.42 ± 0.14 (8)</td>
<td>&gt; 0.70</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td></td>
<td>Increasing and decreasing</td>
<td>133.42 ± 5.20 (26)</td>
<td>0.35 ± 0.08 (16)</td>
<td>&gt; 0.85</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>2.0 minutes</td>
<td>Increasing</td>
<td>133.20 ± 9.30 (13)</td>
<td>0.38 ± 0.05 (7)</td>
<td>&gt; 0.85</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Decreasing</td>
<td>134.37 ± 8.40 (13)</td>
<td>0.62 ± 0.19 (7)</td>
<td>&gt; 0.85</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td></td>
<td>Increasing and decreasing</td>
<td>133.90 ± 5.70 (26)</td>
<td>0.50 ± 0.10 (14)</td>
<td>&gt; 0.85</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3.0 minutes</td>
<td>Increasing</td>
<td>131.40 ± 7.91 (13)</td>
<td>0.61 ± 0.22 (7)</td>
<td>&gt; 0.85</td>
<td>&gt; 0.55</td>
</tr>
<tr>
<td></td>
<td>Decreasing</td>
<td>137.29 ± 8.10 (13)</td>
<td>0.41 ± 0.08 (7)</td>
<td>&gt; 0.85</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td></td>
<td>Increasing and decreasing</td>
<td>134.21 ± 6.40 (26)</td>
<td>0.51 ± 0.11 (14)</td>
<td>&gt; 0.85</td>
<td>&gt; 0.55</td>
</tr>
<tr>
<td>Steady state</td>
<td>Increasing</td>
<td>131.70 ± 7.32 (13)</td>
<td>0.63 ± 0.21 (9)</td>
<td>&gt; 0.85</td>
<td>&gt; 0.55</td>
</tr>
<tr>
<td></td>
<td>Decreasing</td>
<td>139.50 ± 8.10 (13)</td>
<td>0.41 ± 0.07 (8)</td>
<td>&gt; 0.85</td>
<td>&gt; 0.55</td>
</tr>
<tr>
<td></td>
<td>Increasing and decreasing</td>
<td>135.57 ± 5.10 (26)</td>
<td>0.52 ± 0.10 (17)</td>
<td>&gt; 0.85</td>
<td>&gt; 0.55</td>
</tr>
</tbody>
</table>

N is the number of changes in reservoir blood volume at each ISP value.

*P values obtained by t-test of the significance of difference of reservoir blood volume between intrasinus pressure changes.

†P values obtained by t-test of significance of difference of mean ISP values between increasing and decreasing intrasinus pressure.

Volume change data from many dogs at each ISP region tended to flatten the ISP-reservoir volume relationship curve (Fig. 4 left).

To determine what the mean peak volume change is when the flattening caused by averaging is avoided and how the reflex effect is attenuated on either side of the most sensitive region of ISP, the data were replotted after shifting the curves obtained from individual dogs to the left or right so that the ISP at which the peak volume change occurred would superimpose on a single point on the abscissa (ISP₀) (Fig. 4 right). Since ISP was changed in 25-mm Hg steps, ISP values were defined in this graph as ISP₀ - 50, ISP₀ - 25, ISP₀, ISP₀ + 25 and ISP₀ + 50.

The mean values of ISP₀ and the changes in reservoir volume, normalized for the individual dog's body weight, are given in Table 1 for all the dogs in each of the shifted ISP regions and at each time point. The effect of increasing or decreasing ISP on changes in reservoir blood volume was specifically tested. Paired t-test of these data at equal time points and ISPs showed no significant difference between increasing and decreasing ISP (Table 1). For this reason, the data for increasing and decreasing ISP were pooled together. The mean values ± SE of the combined data are also shown in Table 1 for each time point. At each region of ISP the changes in reservoir volume increased with time and reached a steady-state value in approximately 3 minutes.

The mean values ± SE of the steady-state volume changes are plotted on the right side of Figure 4 in contrast to the unadjusted ISP-ΔVᵣ relationship plotted on the left. The statistical test of the difference in volume changes between two successive ISP regions at each time point indicated a highly significant difference (P < 0.005) (Table 1). Compared with the steady-state mean data before shifting the ISP values (Fig. 4 left), the mean volume changes after the shift of ISP (Fig. 4 right) were much greater at the midportion and less at other regions of ISP.

Circulation Research, Vol. XXXIII, July 1973

FIGURE 4

Steady-state changes in reservoir volume vs. intrasinus pressure. Left: Volume changes averaged over absolute intrasinus pressure. Right: Volume changes corrected for peak response at ISP₀. The vertical bars indicate ± SE. P values indicate statistical significance of the difference of volume changes between consecutive intrasinus pressures. See text for explanation.
MEASUREMENT OF REFLEX EFFECT ON TOTAL SYSTEMIC VASCULAR COMPLIANCE (SERIES 2)

Using the method previously published (11) and briefly described in Theoretical Considerations, we determined whether the carotid sinus baroreceptor reflex controlled total systemic vascular compliance in the same 13 dogs in which the blood volume shift was measured. Venous return from the caval veins was diverted directly into the inflow side of the perfusion pump by having clamps a and b closed and clamp c open. With ISP controlled at 75 mm Hg and cardiac output and venous return maintained at a constant value, 50 ml of blood was infused into the dog within 30-45 seconds through a catheter placed in the left femoral vein. Figure 5 illustrates the records of the series 2 experiments.

The arrows in channel 3 indicate the small amounts of infusion repeated at various ISPs. This small infusion (∆V) caused central venous pressure to rise by ∆P without any measurable transient change in perfusion pump flow or aortic flow. After the venous pressure response to each infusion reached a steady state, ISP was elevated in 25-mm Hg steps. Since each step elevation in ISP caused a fall in central venous pressure, there was no need to restore venous pressure by withdrawing the infused blood from the dog. The decrease in central venous pressure was partly caused by the reflex increase in systemic vascular capacity (Fig. 3). In five dogs, ISP was initially set at 200 mm Hg and then lowered to 75 mm Hg in steps of 25 mm Hg. In this case, 50 ml of blood was withdrawn from the dog to measure the total compliance.

### Table

<table>
<thead>
<tr>
<th>ISP change</th>
<th>ISP - 25</th>
<th>ISP</th>
<th>ISP + 25</th>
<th>ISP + 50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean ± SE(N)</td>
<td>P</td>
<td>P*</td>
<td>Mean ± SE(N)</td>
<td>P</td>
</tr>
<tr>
<td>0.87 ± 0.16 (13)</td>
<td>&gt; 0.80</td>
<td>&gt; 0.80</td>
<td>0.96 ± 0.14 (11)</td>
<td>&gt; 0.65</td>
</tr>
<tr>
<td>0.57 ± 0.17 (13)</td>
<td>&lt; 0.005</td>
<td>&lt; 0.005</td>
<td>1.01 ± 0.12 (13)</td>
<td>&gt; 0.001</td>
</tr>
<tr>
<td>0.72 ± 0.12 (26)</td>
<td>&gt; 0.65</td>
<td>&gt; 0.65</td>
<td>0.80 ± 0.06 (10)</td>
<td>&gt; 0.65</td>
</tr>
<tr>
<td>1.35 ± 0.19 (13)</td>
<td>&lt; 0.01</td>
<td>&lt; 0.01</td>
<td>1.44 ± 0.05 (10)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>1.28 ± 0.33 (13)</td>
<td>&gt; 0.70</td>
<td>&gt; 0.70</td>
<td>0.58 ± 0.58 (9)</td>
<td>&gt; 0.70</td>
</tr>
<tr>
<td>1.47 ± 0.33 (13)</td>
<td>&gt; 0.70</td>
<td>&gt; 0.70</td>
<td>0.58 ± 0.58 (9)</td>
<td>&gt; 0.70</td>
</tr>
<tr>
<td>1.41 ± 0.22 (26)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.62 ± 0.58 (9)</td>
<td>&lt; 0.005</td>
</tr>
<tr>
<td>1.40 ± 0.21 (13)</td>
<td>&gt; 0.80</td>
<td>&gt; 0.80</td>
<td>1.31 ± 0.25 (10)</td>
<td>&gt; 0.65</td>
</tr>
<tr>
<td>1.54 ± 0.32 (13)</td>
<td>&lt; 0.001</td>
<td>&lt; 0.001</td>
<td>0.62 ± 0.58 (9)</td>
<td>&lt; 0.005</td>
</tr>
</tbody>
</table>

### Figure 5

Recording of inferior vena cava (I.V.C.), arterial, and intrasinus pressures during small infusions of blood for compliance measurements at constant perfusion flow. Arrows indicate the start of infusion. Toward the end of each section, intrasinus pressure was elevated and the compliance measurement was repeated.
Effect of Intrasinus Pressure on Compliance (ml/mm Hg kg^{-1} body weight)

<table>
<thead>
<tr>
<th>Intrasinus pressure (mm Hg)</th>
<th>No. of dogs</th>
<th>Mean ± se</th>
<th>P†</th>
<th>Mean ± se</th>
<th>P</th>
<th>Mean ± se</th>
</tr>
</thead>
<tbody>
<tr>
<td>75</td>
<td>9</td>
<td>1.17 ± 0.07</td>
<td></td>
<td>1.52 ± 0.11</td>
<td>&gt; 0.90</td>
<td>1.85 ± 0.16</td>
</tr>
<tr>
<td>100</td>
<td>8</td>
<td>1.12 ± 0.07</td>
<td>&gt; 0.72</td>
<td>1.44 ± 0.10</td>
<td>&gt; 0.50</td>
<td>1.75 ± 0.15</td>
</tr>
<tr>
<td>125</td>
<td>9</td>
<td>1.09 ± 0.08</td>
<td>&gt; 0.65</td>
<td>1.45 ± 0.13</td>
<td>&gt; 0.84</td>
<td>1.75 ± 0.15</td>
</tr>
<tr>
<td>150</td>
<td>8</td>
<td>1.18 ± 0.07</td>
<td>&gt; 0.99</td>
<td>1.60 ± 0.12</td>
<td>&gt; 0.70</td>
<td>1.77 ± 0.15</td>
</tr>
<tr>
<td>175</td>
<td>8</td>
<td>1.18 ± 0.11</td>
<td>&lt; 0.002†</td>
<td>1.60 ± 0.10</td>
<td>&gt; 0.80</td>
<td>1.81 ± 0.15</td>
</tr>
<tr>
<td>Mean value</td>
<td>13</td>
<td>1.15 ± 0.03</td>
<td>&lt; 0.002†</td>
<td>1.52 ± 0.05</td>
<td>&lt; 0.001†</td>
<td>1.78 ± 0.07</td>
</tr>
</tbody>
</table>

*Compliance values at t = 3 minutes are equal to steady-state values.
†P values obtained by t-test of significance of difference of mean compliance at each intrasinus pressure.
‡P values obtained by paired t-test of significance of difference of compliance between each time.

At each ISP the total compliance was determined at 10 seconds and 0.5, 1, 2, and 3 minutes after the infusion; these values were normalized with respect to the body weight of the individual dogs. The normalization was necessary to allow comparison of the compliance values among dogs of different weights. Since deterioration of the dog’s condition became apparent after 3 hours because of poor oxygenation of arterial blood and continual decrease in reservoir blood volume, the order of the compliance and blood volume shift experiments was alternated in successive dogs.

Table 2 summarizes the effect of ISP on total systemic vascular compliance. The compliance values at equal time points tended to increase slightly as ISP was elevated from 75 to 175 mm Hg. However, paired t-test of the significance of the difference in mean compliance values between successive regions of ISP showed no significant difference. This observation was in sharp contrast to the marked reflex effect on the reservoir blood volume in the dogs described previously. Since there was no statistically significant difference, the compliance values at equal time points were pooled irrespective of ISP and are shown in Table 2 (bottom).

These combined data were used to analyze the effect of time on the compliance value after completion of the infusion or bleeding. Shown in the bottom row of Table 2 are the P values, obtained by paired t-test between each consecutive time point value. The statistical test indicated a highly significant difference between the 10-second and 0.5 minute responses, the 0.5- and 1.0-minute responses, and the 1.0-minute and 2.0-minute responses. There was no statistically significant difference between the 2- and 3-minute responses, and the compliance value at 3 minutes was considered to be the steady-state value. The exponential time course is similar to that found in our previous study (11). The plateau value, 2.0 ml/mm Hg kg^{-1} body weight is slightly (by about 17%) less than the previous value, 2.4 ml/mm Hg kg^{-1}. However, we could not find any statistically significant difference between these two values (P < 0.65).

DETERMINATION OF REFLEX CONTROL OF ARTERIAL COMPLIANCE (SERIES 3)

In 5 of the 13 dogs we studied whether the reflex significantly changed arterial compliance, using the same experimental preparation as that in series 1. The method for this measurement is described in Theoretical Considerations. Figure 6 (left) shows experimental runs from which the arterial compliance value was obtained at an ISP of 50 mm Hg. After ISP was fixed at 50 mm Hg and reservoir volume, mean arterial blood pressure, and venous pressure had settled at steady levels, mean arterial blood pressure was decreased approximately 50 mm Hg by transferring blood from the artery to the reservoir through the auxiliary roller pump (Fig. 2). This decrease in mean arterial blood pressure caused a steady-state increase in reservoir blood volume (ΔV_a) (100 ml in this example). The ratio of the change in reservoir blood volume to the change in mean arterial blood pressure was calculated as a measure of lumped arterial compliance. Mean arterial blood pressure was then raised approximately 25 mm Hg by reducing the pump.
speed; a 50-ml change in reservoir volume resulted. This change gave another value of arterial compliance at a higher range of mean arterial blood pressure.

ISP was randomly changed to other levels, and the measurement of arterial compliance was repeated in the same manner. Figure 6 (right) shows similar measurements after ISP was elevated to 200 mm Hg. The values of arterial compliance thus measured were also normalized with respect to the individual dog's body weight.

Arterial compliance values determined at mean arterial blood pressures of 75, 100, and 125 mm Hg and at a given ISP of 125 mm Hg showed no statistically significant difference ($P > 0.4$). Furthermore, the compliance values obtained at various ISPs in the range from 50 to 200 mm Hg also showed no statistically significant difference ($P > 0.4$). Figure 7 presents these compliance values plotted against ISP. The compliance values over all the ISP regions and mean arterial blood pressure range were pooled; the mean value ± sd was 0.0677 ± 0.025 ml/mm Hg kg$^{-1}$. The ratio of this value to the total systemic compliance (2.06 ml/mm Hg kg$^{-1}$) was approximately 1 to 30, which is very close to the ratio that Guyton et al. (14) obtained.

REFLEX CONTROL OF TOTAL PERIPHERAL RESISTANCE

To compare the reflex control of capacity vessels to that of resistance vessels, the gain of the carotid sinus reflex control of total peripheral resistance was determined for the different levels of ISP from series 1 experimental data. The gain was calculated by dividing the steady-state changes of mean arterial blood pressure by the step changes in ISP.
Lumped arterial compliance vs. intrasinus pressure. The vertical bars indicate ± sd.

(Fig. 3). These pressure ratio values reflect the reflex control solely on total peripheral resistance, since cardiac output and venous pressure were kept constant in the series 1 experiments. The mean values ± se of steady-state gain are plotted against ISP in Figure 8 (left). Significant difference in the gain appeared only between the ISP region of 75-100 and 100-125 mm Hg and between 125-150 and 150-175 mm Hg.

We examined whether a peaking in the ISP-gain relationship resulted from shifting ISP values as it did in the reservoir volume change data. The shift resulted in a clear peaking of the curve at ISP₀ and a sharp drop on both sides of it. After this shift, the effect on gain of increasing or decreasing ISP was tested. The result again showed no statistically significant difference (P > 0.75). Therefore, the data were pooled and are shown in Figure 8 (right). Between each consecutive pair of ISPs there was a highly significant difference (P < 0.002). The mean value of ISP₀ for the reflex control of resistance was 135.3 ± 7.7 mm Hg. Paired t-test of the difference between this ISP₀ value and the ISP₀ value for the reflex change in reservoir volume (135.6 ± 5.7 mm Hg) showed no statistically significant difference (P > 0.95).

Discussion

There has been little quantitative information published on overall carotid sinus reflex control of venous capacity. Using closed-chest anesthetized dogs, Schmidt et al. (13) found a peak overall gain of about 2.0 for the carotid sinus reflex occurring between an ISP of 125 and 150 mm Hg after vagotomy. Within this range of ISP the relative contributions of the percentile changes in cardiac output and total peripheral resistance to the changes in arterial blood pressure were approximately equal. This finding is consistent with the gain in the present study of approximately 1.0 in the reflex control of total peripheral resistance. The peak gain occurred at an ISP of approximately 135 mm Hg, which is also consistent with findings by other investigators (13, 15). These findings probably indicate that the carotid sinus reflex in our dogs was as active as that in other experiments, despite the open-chest surgery and the manipulation of the caval veins and the perfusion circuit.

Rashkind et al. (7) were the first to quantify changes in systemic vascular capacity; they used a preparation similar to that of series 1 and electrically stimulated a carotid sinus nerve. They found that maximal stimulation of the nerve caused 75-mI decreases in reservoir volume in dogs weighing 20 kg. If we assume that their electrical stimulation was equivalent to changes in ISP from 75 to 200 mm Hg, the volume change (75 ml) that they obtained would be only half of that obtained in our series 1 experiments. Apparently, Rashkind et al. did not control central venous pressure as rigorously as we did; they allowed it to decrease by approximately 1.5 mm Hg as seen in Figures 2 and 3 in their paper. This procedure would underestimate volume changes by 60 ml for dogs weighing
20 kg, assuming a total compliance of 2.0 ml/mm Hg kg⁻¹. After this correction the volume changes observed by Rashkind et al. would increase to 135 ml, which is nearly equal to the present observed value.

Ross et al. (16) obtained a mean cumulative vascular volume change of 12.9 ml/kg when ISP was maximally changed from very low to very high values. However, as illustrated in Figure 4 of their paper, central venous pressure increased approximately 5 mm Hg during baroreceptor hypertension. Using the same compliance value of 2.0 ml/mm Hg kg⁻¹, this 3-mm Hg increase in venous pressure would account for a 6-ml/kg overestimation of reflex changes in vascular volume. Correction of their data would decrease their value to 6.9 ml/kg, which again is consistent with the results obtained in series 1.

Browse et al. (10), using a preparation similar to the one in our series 1 experiments, showed that when ISP was changed from maximal hypotension to maximal hypertension the volume shift was 7.7 ml/kg. This result agrees with the present cumulative volume change, i.e., 7.5 ml/kg for ISP changes from ISP₀−50 to ISP₀+50. Browse et al. (10) concluded that the volume changes were ineffectual with respect to total blood volume or cardiac output.

Guyton (8) showed that elevation of mean systemic filling pressure provided the force to propel blood toward the heart from the periphery. Quantification of mean systemic filling pressure requires the knowledge of both total systemic vascular capacity and blood volume in the compartment. Using a total vascular compliance of 2.06 ml/mm Hg kg⁻¹ body weight and a peak blood volume change of 3.39 ml/kg per 25 mm Hg, the change in ISP is equivalent to a change in mean systemic filling pressure of 1.6 mm Hg. The total volume change of 7.5 ml/kg for an ISP change from 75 to 200 mm Hg will increase the filling pressure as much as 3.6 mm Hg. In fact, Kumada et al. (9) measured a peak increase in mean circulatory filling pressure of 2 mm Hg when ISP was lowered by occluding the common carotid arteries in dogs. This result is consonant with the results obtained from our experiments. Using Guyton’s diagram on the equilibrium between venous return and cardiac output curves and assuming that there is no reflex change in cardiac contractility and that resistance for venous return remains unchanged, the 1.6-mm Hg increase in mean systemic filling pressure increases cardiac output by as much as 30%, and the 3.6-mm Hg increase can cause a 60% increase. This potential change in cardiac output seems rather significant.

There was no detectable difference in total systemic and lumped arterial compliance at various ISPs within the limits of accuracy of our method. In the lumped parameter model in Figure 1, the observed shift in blood volume is probably caused by a reflex change in unstressed vascular volume. However, we emphasize that these observed volume shifts do not directly indicate changes in unstressed vascular volume. The systemic vascular bed includes many series and parallel resistance and capacitance vessels. We cannot eliminate the possibility that the reflex altered the pressures in some of the smaller veins and thus passively changed reservoir volume. However, in isolated venous segments there is direct evidence for a reflex change in unstressed vascular volume. For example, in a segment of the mesenteric vein, Alexander (17) showed that the pressure-volume curve did shift left and right from the control when ISP was either lowered or raised. In contrast, the reflex effect on the slope of the pressure-volume curves was insignificant within the operating range of venous pressure. Whether this situation existed in our experiment is not the purpose of this study.

As Eq. 1 in Theoretical Considerations indicates, the measured reservoir volume shift is the difference between the reflex change in the total systemic vascular capacity and the passive volume shift associated with the reflex change in mean arterial blood pressure. Since arterial blood pressure and therefore arterial blood volume were changing, the reservoir volume shifts underestimated the maximum changes in venous capacity. Using the measured arterial compliance of 0.0677 ml/mm Hg kg⁻¹, a 25-mm Hg reflex increase in arterial pressure would cause a 1.68-ml/kg increase in arterial blood volume. However, if a reflex change in arterial blood pressure were prevented, the reservoir blood volume shift would be greater by that amount, namely, 5.3 ml/kg instead of 3.6 ml/kg.

To examine this point, we fixed arterial blood pressure in two of the dogs. We found that the volume shift was greatly increased, as expected. Figure 9 shows the recordings made in one of these dogs when mean arterial blood pressure was allowed to change (left) and when mean arterial blood pressure was fixed (right). Arterial blood pressure was fixed by using a secondary roller pump that transferred blood between the reservoir and
the arterial compartment via a large-bore catheter placed in the left femoral artery (Fig. 2). The direction and the rate of flow through this pump were manually adjusted so as to keep mean arterial blood pressure at a constant control level.

Figure 9 (left) shows that the reservoir volume decreased by approximately 175 ml over the entire ISP change of 100 mm Hg. In contrast, when arterial blood pressure was controlled at 75 mm Hg as shown in Figure 9 (right), the total volume shift was approximately 260 ml for the same ISP change. The change in reservoir volume in the ISP region from 150 to 175 mm Hg with controlled arterial blood pressure was twice as large as that without controlled arterial blood pressure. In either very high or low ISP regions where the reflex changes in mean arterial blood pressure were small, the difference in volume shift was not significant. Similar results were observed in the other dog.

This greater change in reservoir volume with fixed mean arterial blood pressure reflects what the carotid sinus reflex system really does to the total capacity of the systemic vascular bed. However, the volume change with uncontrolled mean arterial blood pressure indicates the net volume of blood that the overall reflex system can actually mobilize as it changes vascular resistance and vascular capacity.

Finally, our finding that the ISP₀ for the reflex volume shift was almost the same as the ISP₀ for the reflex change in total peripheral resistance is important if the reflex system is to control arterial blood pressure effectively. If there were no decrease in total vascular capacity accompanying the reflex increase in total peripheral resistance when ISP was decreased, the passive shift of blood into the arterial compartment would result in a poorer filling of the heart and a lower cardiac output. Consequently, the reflex increase in arterial blood pressure would be attenuated.

Therefore, the carotid sinus baroreceptor reflex controls systemic resistance vessels and capacitance vessels in concert. If it were not for this simultaneous control of vascular capacity and total peripheral resistance, the carotid sinus reflex would be less effective in regulating arterial blood pressure.

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References


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