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SUMMARY To quantify the relative contribution of blood flow redistribution and active changes in vascular capacity in the regulation of cardiac output, blood flow and volumes in two parallel vascular beds were measured in response to varying carotid sinus pressures. In nine dogs, carotid sinuses were isolated and intrasinus pressure was controlled. Two external reservoirs were placed between the caval veins and the right heart to measure changes in vascular capacity in splanchnic and extra-splanchnic vascular beds. At intrasinus pressures of 50 and 200 mm Hg, we have simultaneously measured arterial resistances, compliances, changes in flows, and "unstressed vascular volume," and time constants of venous drainage in the splanchnic and extrasplanchnic vascular beds. Compliances and time constants of venous drainage were found to be nearly equal in the two beds. A decrease in intrasinus pressure from 200 to 50 mm Hg resulted in a small redistribution of blood flow (about 5% of cardiac output) from the extrasplanchnic compartment to the splanchnic vascular bed. Changes in reservoir volumes were found to be around 7.0 ml/kg. The splanchnic vascular bed was responsible for a greater change in reservoir volume for a given change in intrasinus pressure. With any change in intrasinus pressure, the change in arterial resistance in the extrasplanchnic vascular bed was greater than that of the splanchnic vascular bed. Blood flow redistribution was not found to be a significant factor contributing to changes in reservoir volume. The changes in reservoir volume seen, must have been due to active changes in vascular capacity in the two channels chosen. Circ Res 48: 274-285, 1981

The importance of changes in the capacitive property of the systemic vascular bed has been recognized for some time. For example, a decrease in capacity can increase the filling pressure of the right heart which, in turn, can increase cardiac output. Evidence that the carotid sinus baroreceptor reflex controls the systemic vascular capacity has been presented from several laboratories (Drees and Rothe, 1974; Rashkind et al., 1953; Salzman, 1957; Shoukas and Sagawa 1973). The amount of blood which can be mobilized from the entire systemic vascular bed by the reflex has also been quantified (Drees and Rothe, 1974; Rashkind et al., 1953; Shoukas and Sagawa, 1973). However, the exact mechanism and source of blood mobilization remains somewhat controversial (Caldini et al., 1974; Coleman et al., 1974; Green, 1975; Mitzner and Goldberg, 1975).

Using a dog preparation in which venous return was diverted into a reservoir while cardiac output was kept constant, Shoukas and Sagawa (1973) showed that significant shifts of blood between the dog and a reservoir occurred when carotid sinus pressure was changed. They hypothesized that the reflex altered the "unstressed" vascular volume of the systemic veins based on the finding that the total systemic vascular compliance did not change significantly. A more recent work by Shoukas and Brunner (1980) indicated that the reflex affects the total compliance to a mild but significant degree.

Caldini et al. (1974) and Coleman et al. (1974) postulated an alternate mechanism to explain the changes in reservoir volume. Caldini et al. (1974) used a preparation very similar to the one used by Shoukas and Sagawa (1973) and found significant shifts of blood volume when epinephrine was infused into the dog. Based on a parallel channel model, Caldini et al. (1974) pointed out that a redistribution of blood flow from regions with large time constants of venous drainage to regions with small time constants would result in passive shifts of volume without any change in "unstressed" vascular volume and/or compliance. This explanation does not involve the active change of venous tone by adrenergic mechanisms.

In the present study, we attempted to test the hypothesis of Caldini et al. by dividing the systemic vascular bed into two parallel channels (splanchnic and extrasplanchnic) which were suspected by these authors to have widely different time constants. We could measure the blood flow redistribution between the two channels, the time constants and compliances of the two channels, and...
blood volume shifts from the two channels associated with the carotid sinus baroreceptor reflex. In the same dogs, we could repeat the previous experiments of Shoukas and Sagawa (1973) to check the reproducibility of the present data.

From these measurements, we conclude that blood flow redistribution between the two parallel channels chosen in our study is not the cause of blood volume mobilization from the systemic vascular bed by the carotid sinus baroreceptor reflex. Therefore, active changes in venous tone by the reflex system remain important determinants of blood volume mobilization.

Methods

Theoretical Considerations

Figure 1 shows a hydraulic analog of the systemic vascular bed with three lumped elements. As shown, the reflex can be assumed to change the arterial and venous compliances by changing the diameter and therefore the cross-sectional area of both chambers. The reflex system can also be assumed to alter the unstressed vascular volume of both of these chambers. Therefore, Figure 1 represents a concept that the reflex system directly affects the capacity of the vascular system, thus altering the pressure-volume relationships of systemic arteries and veins. The net blood volume shifts measured in the volume reservoir at constant venous pressure are not a direct measure of the changes in vascular capacity per se. The volume changes are an algebraic sum of active changes in unstressed vascular volume and compliance and passive changes in arterial and venous blood volume caused by change in arterial pressure consequent to reflex changes in total peripheral resistance. A more detailed consideration of the volume changes in a reservoir has been published previously (Shoukas and Sagawa, 1973).

Shown in Figure 2A is a hydraulic analog of the systemic vascular bed to illustrate the mechanism of passive blood volume mobilization caused by a redistribution of blood flow. Each of the parallel flow channels is composed of arterial and venous resistances, represented by constrictions in the tube and a capacity chamber between the resistances. In this representation, the capacity element in channel 2 is made markedly larger in cross-sectional area than that in channel 1, indicating that the compliance in channel 2 is greater than the compliance in channel 1. For the purposes of this description, the arterial resistance in each channel is assumed to be greater than the venous resistance. We assume the venous resistances to be equal, whereas the arterial resistances need not be equal in each channel. Total net vascular blood mobilization can be estimated from a shift of blood between the systemic vascular bed and the volume reservoir shown in Figure 2B. Cardiac output is fixed by a pump, inserted between the reservoir and right atrium, which perfuses the vascular channels at a constant flow rate. Central venous pressure can be maintained constant, even when venous outflow changes, by adjusting the height of the end of the tube which drains venous return into the reservoir. When carotid sinus baroreceptor pressure is changed, the consequent change in reservoir volume reflects the net balance between the volume changes in both flow channels of the systemic vascular bed. The mechanism depicted in Fig. 2B) proposed by Caldini et al. (1974) and Coleman et al. (1974) assumes that the reflex system increases the arterial resistance in channel
2, \( R_{a2} \), more than the arterial resistance in channel 1, \( R_{a1} \). Since the total flow is maintained constant, this increase in resistance would cause the flow in channel 1 to increase by an amount \( \Delta f \) and the flow in channel 2 to decrease by the same amount. Thus, there would be an increase in the pressure of compliance capacity chamber 1 by an amount \( \Delta P_{C1} \), and the decrease in the pressure of capacity chamber 2 by an amount \( \Delta P_{C2} \). If venous pressure, \( P_v \), is maintained constant and the venous resistances, \( R_{v1} \) and \( R_{v2} \), are equal, then these changes \( \Delta P_{C1} \) and \( \Delta P_{C2} \) will be equal but opposite in direction. Since the compliance of chamber 2 is much greater than that of chamber 1, the decrease in volume in chamber 2, \( \Delta V_2 \), will be much greater than the volume increase in chamber 1, \( \Delta V_1 \). The net difference in blood volumes, \( \Delta V_2 - \Delta V_1 \), will have to come out of the animal and be measured as an increase in reservoir blood volume.

A very similar increase in reservoir blood volume would occur if the compliances of chamber 1 and chamber 2 were equal but the venous resistance in channel 2, \( R_{v2} \), were much greater than that in channel 1, \( R_{v1} \). Under this condition, if there were similarly disproportionate increases in arterial resistances, which would decrease the flow in channel 1, then the pressure decrease in chamber 2, \( \Delta P_{C2} \), would be greater than the pressure increase in chamber 1, \( \Delta P_{C1} \). Since compliances \( C_1 \) and \( C_2 \) are assumed to be equal, the volume decrease in chamber 2, \( \Delta V_2 \), would be much larger than the volume increase in chamber 1, \( \Delta V_1 \). Again, this net difference in chamber volumes, \( \Delta V_2 - \Delta V_1 \), would be measured as an increase in reservoir blood volume. Thus, the magnitude of the net volume shift depends upon the relative magnitudes of the compliances, \( C_1 \) and \( C_2 \), as well as the relative magnitude of the venous resistances, \( R_{v1} \) and \( R_{v2} \).

A convenient way to express the dependence of a passive blood volume shift on the relative magnitude of \( C_1 \) vs. \( C_2 \) and/or \( R_{v1} \) vs. \( R_{v2} \) is the product of venous resistance and compliance. Thus, if the product, \( R_{v2} \cdot C_2 \) in channel 2 is much greater than the product, \( R_{v1} \cdot C_1 \) in channel 1 and there is a redistribution of flow away from the channel with the larger \( R_v \cdot C \) product (channel 2), then the net volume measured in the external volume reservoir will increase. The opposite is also true: that is, if blood flow is redistributed toward the channel with the larger \( R_v \cdot C \) product, then reservoir volume will decrease. The two parallel flow channel model suggests that significant shifts of blood volume may occur through changes in arteriolar tone alone without any neurally mediated changes in venous tone.

Two conditions must be met for this mechanism to be a valid explanation for blood mobilization in the systemic vascular bed. First, there must be a significant difference in the \( R_v \cdot C \) product between the two channels of the vascular bed. Second, the blood flow must be redistributed by the reflex away from the channel with the larger \( R_v \cdot C \) product in response to lowering the carotid sinus pressure.

Figure 3 depicts a hydraulic analog which we conceived as representing the systemic vascular bed. It is identical to the model proposed by Caldini et al (1974). In their experiment, Caldini measured the volume shifts in a single reservoir (see Fig. 2). However, to obtain accurate data on changes in individual blood flows, as well as changes in the capacities of the two channels, it is necessary to use separate reservoirs for individual channels. The following explanation is to clarify the methods used for measuring blood flows, volumes and compliances and determining \( R_v \cdot C \) products. When intrasinus pressure is changed, the steady state changes in blood flow can be measured directly at the outflow of each channel going to the venous volume reservoir. Changes in total vascular capacity also can be determined by measuring the reservoir blood volume shifts in each of the channels. Measurement of these volume changes cannot allow one to distinguish between active changes in vascular compliances and "unstressed" vascular volume changes and the passive volume changes caused by reflex redistribution of blood flow in the channels. It therefore is necessary to determine the vascular compliances and \( R_v \cdot C \) products in both channels.

An estimate of the vascular compliances can be obtained by simultaneously changing central venous pressure for both channels by an equal amount and measuring the resultant steady state volume change in each reservoir. For the case of a single flow channel circuit through which flow is constant, the change in reservoir blood volume divided by the change in venous pressure yields the compliances of the channel. However, it should be emphasized that this conclusion is incorrect for the present circuit with two parallel flow channels. Using a two-port analysis technique which takes into account the dynamic and steady state properties (see Appendix I), the steady state changes in volumes de-
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termined by the change in venous pressures are given by

\[ \Delta V_1 = \left( C_1 \frac{R_T - R_{v1}}{R_T} + C_2 \frac{R_{v1}}{R_T} \right) \Delta P_v \]

and

\[ \Delta V_2 = \left( C_2 \frac{R_T - R_{v2}}{R_T} + C_1 \frac{R_{v2}}{R_T} \right) \Delta P_v \]

where \( R_T = R_a + R_{v1} + R_{v2} \). The \( R_v \cdot C \) products of each channel can be obtained by measuring the instantaneous volume changes in both channels after a step elevation of venous pressure, as is shown by Equation 5 in the Appendix. A semilog plot of volume versus time for each channel contains identical information of the \( R_v \cdot C \) products of both channels. Thus, the volume vs. time plot of either channel should be curvilinear if the \( R_v \cdot C \) product of that channel is different from that of the other channel, but if the \( R_v \cdot C \) products of the two channels were to be nearly equal, the plots would look linear (see Appendix). Therefore, the single perturbation of simultaneously raising venous pressure for both channels will yield estimates of the compliance values as well as information on the \( R_v \cdot C \) products.

Experimental Procedures

Nine mongrel dogs of both sexes, weighing between 22.0 and 27.0 kg (mean 24.8 ± 1.6 SD kg) were anesthetized with sodium pentobarbital (30 mg/kg, iv). Heat cauterization and ligation of cut tissue masses were used to minimize blood loss. The left and right carotid bifurcation areas were isolated from the rest of the circulatory system (Shoukas and Brunner, 1980). The pressure within the carotid sinus region was monitored via conjoint catheters placed in the left and right lingual arteries and connected to a pressure transducer (Statham P23AC). The cervical vagosympathetic trunks were exposed and cut to eliminate the buffering effect of the aortic arch baroreceptor reflex and the cardiopulmonary receptor reflexes. Intrasinus pressure was maintained at the desired level by a servo-controlled, non-pulsatile pressure-generating system.

A right thoracotomy was performed at the 5th intercostal space under positive pressure ventilation using room air. Figure 4 illustrates the surgical preparation and perfusion circuit used in these experiments. The right atrial appendage was cannulated first and connected to the outflow side of perfusion pump no. 3 (Sarns, model 5M6002). The inflow side of pump no. 3 was connected to the common reservoir no. 3. The perfusion circuit was primed with heparanized whole blood from another dog. The azygos vein was completely ligated. The superior vena cava was then cannulated and blood drained into reservoir 1. Perfusion pump 1 (Sarns, model 5M6002) pumped blood from reservoir 1 into reservoir 3. Perfusion started with an initial flow of about 35 ml/min per kg. Just prior to cannulating the inferior vena cava, we placed three large-bore cannulae into the femoral veins; one toward the heart, and a pair toward the periphery. These cannulae drained blood into reservoir no. 3 to prevent an extremely low cardiac output and venous congestion in both the splanchnic and leg vascular beds during the cannulation of the inferior vena cava. The inferior vena cava then was cannulated and perfusion flows readjusted so that arterial pressure was approximately equal to the pressure before atrial cannulation. Total perfusion flow rate averaged 75.7 ± 7.5 (SD) ml/min per kg for the nine dogs.

To separate the systemic vascular bed into two parallel flow channels which are thought to have widely differing compliances and \( R_v \cdot C \) products by Caldini et al. (1974) and Coleman et al. (1974), we performed the following procedures: The femoral cannulae which drained blood from the peripheral hind limbs were connected to the superior vena caval cannula. The femoral cannula inserted toward the heart was clamped for the duration of the experiment. Thus the outflow from the inferior vena cava represented venous outflow from intestine, liver, spleen, kidney, and abdominal wall. The superior vena caval outflow contained venous outflow from upper and lower limbs, head and neck skeletal muscles, skin, and brain. The flow from each great vein first passed through a reservoir (reservoir no. 1 or 2) and then through an adjustable speed pump (pumps no. 1 or 2). The flow from the superior vena cava (extraspinalnchic flow) is termed channel 1, and the inferior vena caval flow (splanchnic flow) is termed channel 2. Two pump outflows then passed into a common reservoir (reservoir no. 3). The blood was then returned to the right atrium through a heat exchanger and an air trap by a third constant flow pump (pump no. 3).

Central venous pressures in the two separate
channels were measured within the superior and inferior venae cavae using pressure transducers (Statham, P23BB). Zero pressure reference was set at the junction of the inferior vena cava and the right heart under direct inspection. Venous pressures were controlled by changing the level of the ends of the outflow tubes draining the inferior and superior vena cava.

Arterial pressure was measured in the ascending aorta through a catheter inserted in the left common carotid artery and connected to a pressure transducer (Statham P23AC). Blood volumes in both of the venous outflow reservoirs were monitored continuously by recording the hydrostatic pressures of the columns of blood with pressure transducers (Beckman, model 807, 215071). The system was calibrated by changing the reservoir blood volumes by a known amount and recording the corresponding pressure changes. The resolution of the blood volume changes was 2.0 ml. Pumps nos. 1 and 2 were equipped with tachometers which produced an electrical signal that was proportional to the speed of each pump. The speeds were recorded and calibrated against known flows, using a stopwatch and graduated cylinder. All pressure, flow, and volume signals were smoothed by a low-pass filter with a time constant of 1 second and recorded on an ink recorder (Brush, Mark 200). All data presented were normalized to individual body weights to allow comparison among the dogs.

Initially, intrasinus pressure (ISP) was set at 200 mg Hg. By adjusting the heights of the two outflow tubes, we set venous pressures in both channel 1 and 2 at 3 mm Hg. The outflow pumps which drain the two reservoirs into the common reservoir were set to a speed at which the fluid levels in the two reservoirs remained constant. Initially, the sum of two pump flows was exactly equal to the venous outflow. Mean arterial and venous pressures, reservoir volumes, and the two venous outflows were recorded. The total resistance of each channel was calculated as the difference in arterial and venous pressures divided by the corresponding steady state flow.

At an intrasinus pressure of 200 mm Hg, venous pressures in the two channels were raised simultaneously and quickly (approximately 1 second) by an equal amount. This increase amounted to approximately 5 mm Hg. This sudden increase in venous pressures caused concomitant decreases in reservoir blood volumes. The transient changes in blood volumes were used to obtain the \( R_c \cdot C \) products in each channel. The ratios of the steady state changes in reservoir blood volumes to the changes in venous pressures were also determined to obtain a measure of the vascular compliances. Venous pressures were decreased to the control value and the measurements were repeated.

Intrasinus pressure was decreased from 200 to 50 mm Hg while keeping venous pressures constant. Following this change, the blood volume in reservoir 2 usually increased, indicating that the venous outflow (inflow to the reservoir) increased with respect to the constant flow removed from reservoir 2 by pump 2. Conversely, reservoir 1 blood volume usually decreased, indicating that the flow in channel 1 decreased with respect to the constant flow out of reservoir 1 by pump 1. Five minutes after the change in intrasinus pressure, the slopes of the blood volume changes with respect to time gave a measure of the changes in flows in each channel which resulted from changing intrasinus pressure. The shift in flow from one compartment to another following changes in carotid sinus pressure ranged from 50 to 200 ml/min. The speeds of the two outflow pumps 1 and 2 then were readjusted to equal the new venous outflows.

Blood volume shifts into each reservoir also were measured. An increase in reservoir blood volume corrected for changes in blood flow redistribution would indicate a decrease in vascular capacity for each channel.

At an intrasinus pressure of 50 mm Hg, the resistances were calculated and the determinations of transient and steady state volume changes were repeated.

Intrasinus pressure was increased from 50 to 200 mm Hg, keeping venous pressures constant. The outflows changed in directions opposite to those previously described for a decrease in intrasinus pressure. The changes in reservoir volumes were measured again.

To correlate the data obtained in this study using separate channels with previous studies on the entire systemic vascular bed, the two separate venous channels were joined into a single outflow. A clamp was switched from position A to B to divert all blood flow to a single reservoir (see Fig. 4). Thus, all the venous return from channel 1 was diverted into channel 2 and single reservoir 2. This system was analogous to the method used by Shoukas and Sagawa (1973).

At an intrasinus pressure of 200 mm Hg, and with the single reservoir system, the total systemic vascular compliance was measured (Shoukas and Sagawa, 1973). The height of the outflow tube (and thus the venous pressure) was raised causing a steady state reservoir volume change. The ratio of the steady state volume change to the change in venous pressure is the total systemic vascular compliance. The total peripheral resistance of the entire vascular bed was also calculated by the difference in arterial and venous pressures divided by total flow.

Intrasinus pressure then was decreased from 200 to 50 mm Hg while keeping venous pressure constant at 3 mm Hg. The blood volume change in the single reservoir was monitored continuously. This blood volume shift should equal the sum of the blood volume shifts of the previous separate channel reservoirs. At an intrasinus pressure of 50 mm Hg, the total peripheral resistance and total syst-
tomic vascular compliance were again determined. Intrasinus pressure then was increased from 50 to 200 mm Hg, maintaining a constant venous pressure, and the reservoir blood volume change was measured again.

All data are reported as the mean ± SEM. (n = 9). Paired t-tests were performed for data at ISP = 50 and 200 mm Hg. Significance levels were set at P values of ≤0.05.

Results

Flow

In the nine dogs studied, the total perfusion flow ranged from 1675 to 2010 ml/min. The mean values were 75.8 ± 7.5 ml/min per kg. At an intrasinus pressure of 200 mm Hg, the mean flow in channel 1 (extrasplanchnic) was 30.69 ± 5.33 ml/min per kg, while the mean flow in channel 2 (splanchnic) was 47.79 ± 6.84 ml/min per kg. When intrasinus pressure was 50 mm Hg, the mean flow in channel 1 (extrasplanchnic) averaged 31.42 ± 6.34 ml/min per kg and in channel 2 (splanchnic) was 47.01 ± 9.11 ml/min per kg.

The upper panel of Figure 5 shows the changes in flow for each dog resulting from decreasing intrasinus pressure from 200 to 50 mm Hg. In the nine dogs, an average decrease in flow of channel 1 (extrasplanchnic) was 1.11 ± .81 ml/min per kg, whereas the flow in channel 2 (splanchnic) increased by an average of 1.51 ± 2.92 ml/min per kg. The decrease in flow in channel 1 and increase in flow in channel 2 were seen in seven of the nine dogs. Two dogs gave an opposite response. In the seven dogs, the mean decrease in flow in channel 1 was 2.11 ± .59 ml/min per kg and the mean increase in channel 2 flow was 2.71 ± 0.67 ml/min per kg. The lower panel of Figure 5 shows the response to increasing intrasinus pressure from 50 to 200 mm Hg. For the nine dogs, the flow in channel 1 increased by 1.41 ± 0.97 ml/min per kg and the flow in channel 2 decreased by 2.18 ± 1.12 ml/min per kg. In the same seven of nine dogs, channel 1 flow increased an average of 2.55 ± 0.79 ml/min per kg and channel 2 flow decreased 3.43 ± 0.93 ml/min per kg, with the increase in intrasinus pressure. The changes in blood flow distribution were small and were always less than 5% of total perfusion flow in any dog.

Resistance

Shown in Figure 6 are the resistances of channel 1 (extrasplanchnic) and channel 2 (splanchnic), as well as the total peripheral resistances of the single reservoir experiments for intrasinus pressures of 50 and 200 mm Hg. At an intrasinus pressure of 50 mm Hg, the mean resistance was 0.0059 ± 0.0022 mm Hg/ml/min per kg for channel 1 and 0.0041 ± 0.0021 mm Hg/ml/min per kg for channel 2 in the nine dogs. Total peripheral resistance was calculated from the average resistances of the parallel flow channels, using the equation for parallel resistances. This calculated value was 0.0023 mm Hg/ (ml/min per kg) which was nearly equal to the value 0.0022 ± 0.0001 mm Hg/(ml/min per kg) obtained in the independent studies with a single reservoir. Paired t-test of the difference between the values calculated from two channel resistance values and the values obtained from the single reservoir experiment showed no statistical significance.

Similar analysis and calculations were done for the resistances at an intrasinus pressure of 200 mm Hg. At this intrasinus pressure, the mean resistance for channel 1 (extrasplanchnic) was 0.039 ± 0.005 mm Hg/(ml/min per kg) and for channel 2 (splanchnic) was 0.0024 ± 0.0008 mm Hg/(ml/min per kg). The calculated total peripheral resistance 0.0015 mm Hg/(ml/min per kg) was again equal to the value of 0.0015 mm Hg/(ml/min per kg) from the independent single reservoir experiment. Paired t-test showed no statistically significant difference.

The resistance values at intrasinus pressures of 50
and 200 mm Hg showed significant differences (P < 0.05) for channel 1, channel 2, and the total peripheral resistance as shown in Figure 6.

Volume-to-Pressure Ratio

Figure 7 shows the ratio of the steady state volume to the step change in venous pressure in the two-channel experiment as well as the ratio in the single reservoir experiment for each dog. The extreme right panel of Figure 7 shows the ratio of the volume change to pressure change which is the total systemic vascular compliance (see theoretical considerations). The mean value for all nine dogs was 1.34 ± 0.15 ml/mm Hg per kg at an intrasinus pressure of 200 mm Hg and was 1.23 ± 0.12 ml/mm Hg per kg at 50 mm Hg. Paired t-test showed a statistically significant difference between values at 200 and 50 mm Hg. For channel 1 (extrasplanchnic), the average ratios of volume change to pressure change at intrasinus pressures of 50 and 200 mm Hg are 0.46 ± 0.04 and 0.45 ± 0.03 ml/mm Hg per kg, respectively. The volume-to-pressure ratios for channel 2 (splanchnic) were significantly larger than those for channel 1, being 0.81 ± 0.11 and 0.69 ± 0.09 ml/mm Hg per kg for intrasinus pressures of 50 and 200, respectively. There was no statistically significant difference by paired t-test between the two ratios values at the two intrasinus pressures for either channel. At an intrasinus pressure of 50 mm Hg, the sum of the average ratio values from the two channels, (namely, 0.46 + 0.81) ml/mm Hg per kg was 1.27 ml/mm Hg per kg, as compared to the total systemic vascular compliance obtained inde-
pendently in the single reservoir experiment, i.e., 1.23 ml/mm Hg per kg. At an intrasinus pressure of 200 mm Hg, the sum from both channels was 1.14 ml/mm Hg per kg as compared to 1.34 ml/mm Hg per kg for the total systemic vascular compliance. Paired t-test of the individual differences in each dog between the sum of ΔV₁/ΔP + ΔV₂/ΔP and the total systemic vascular compliance show significant differences in the values (P < 0.025; n = 9) at both levels of intrasinus pressure (see Appendix).

Volume Time Course

The time courses of the volume changes in both channels were monitored when the venous pressures were simultaneously increased or decreased in a stepwise fashion. For each channel, the log of the volume change was plotted against time in order to obtain the time constant. Figure 8 shows these plots from two different dogs. The left panel shows both channels as straight lines, whereas the right panel shows both channels as curvilinear lines. The plot would be a straight line if the volume change was a simple exponential function of time. However, if the plots were curvilinear, then two or more exponential functions could be fitted. If the plot was found to be linear, a time constant was measured. This straight line behavior occurred in approximately 50% of the cases studied. At the intrasinus pressure of 50 mm Hg, the mean time constants were 11.17 ± 1.69 and 4.75 ± 0.63 seconds for channel 1 (extrasplanchnic) and channel 2 (splanchnic), respectively. At the intrasinus pressure of 200 mm Hg, the mean time constants were 8.53 ± 1.82 and 8.03 ± 1.27 seconds for channels 1 and 2, respectively.

Volume Shifts

The changes in reservoir volume for the parallel channel and single reservoir experiments when intrasinus pressure was decreased from 200 to 50 mm Hg, are shown in Figure 9. In all the dogs, reservoir blood volume increased in the single reservoir experiments. The mean increase in reservoir volume was 4.83 ± 1.03 ml/kg. In channel 2 (splanchnic), reservoir volume increased by 6.60 ± 1.41 ml/kg for all the dogs. For channel 1 (extrasplanchnic), the mean value of the reservoir volume showed an increase of 1.02 ± 0.051 ml/kg despite the fact that three of the nine dogs showed a decrease in volume. In each of the dogs, the change in reservoir volume was always greater in channel 2 than in channel 1. For each individual dog, the algebraic sum of the volume shifts from the two channels was nearly equal to the change observed in the single reservoir experiment.

The reservoir volume changes in response to increasing intrasinus pressure are shown in Figure 10. The right panel shows the changes in volume for the single reservoir experiments. Reservoir volume always decreased in response to increasing intrasinus pressure from 50 to 200 mm Hg in all dogs. The average decrease was 6.43 ± 0.85 ml/kg. The center and left panel of Figure 10 shows the volume changes in channel 2 (splanchnic) and channel 1 (extrasplanchnic). In response to the increase in intrasinus pressure, channel 2 volume decreased in all dogs by an average of 8.42 ± 1.32 ml/kg. The average volume change in channel 1 for all the dogs was an increase of 2.28 ± 1.32 ml/kg. In the seven cases where the reservoir volume in channel 1 increased, there was always a large decrease in channel 2 reservoir volume. Therefore, the algebraic sum
of the two channels, 6.14 ml/kg, showed a decrease and was nearly equal to the volume decrease of 6.43 ml/kg in the single reservoir experiment.

Discussion

This experimental preparation demonstrates that the carotid sinus baroreceptor reflex exerts control of both resistive and capacitive properties of the systemic vascular bed. The magnitude of reflex change in arterial resistance is indeed different between the two parallel flow channels studied. The direction of the blood flow redistribution is of special interest. When intrasinus pressure was decreased from 200 to 50 mm Hg, the extrasplanchnic channel flow decreased while the splanchnic channel flow increased. This direction of flow redistribution is opposite to that hypothesized by Caldini et al. (1974) and Coleman et al. (1974). As was discussed previously, for a net increase in blood volume to occur in the reservoir, it would be necessary that blood flow decreases in an area of large R·C product. We found no significant differences in the time constant of either channel with changes in intrasinus pressure, and the ratio of the change in volume to the change in venous pressure of the splanchnic channel was nearly twice that of the extrasplanchnic channel. When intrasinus pressure was decreased, the blood flow in the splanchnic channel increased. Since the time constants of the two channels were nearly equal, no change in the reservoir volume can be attributed to the flow redistribution mechanism. In fact, we always measured an increase in reservoir volume in response to decreases in intrasinus pressure. Therefore, we would conclude that the increase in reservoir volume following a decrease in intrasinus pressure is likely to be caused by active changes in vascular capacity. Caldini et al. (1974) have also suggested that there must be active changes in venous tone which alter the unstressed vascular volume during epinephrine infusion.

To examine whether the systemic vascular bed responds differently to epinephrine and the baroreceptor reflex, we performed an additional experiment in three of the dogs tested. In these dogs, epinephrine was infused at constant rates of approximately 2 μg/min per kg while either keeping intrasinus pressure fixed or allowing it to follow the increase in arterial pressure. Regardless of the intrasinus pressure conditions, infusion of epinephrine always produced a decrease in flow in the extrasplanchnic channel and an increase in flow in the splanchnic channel. The reservoir blood volumes in both channels increased; however, the volume increase in the extrasplanchnic channel was larger. Although the number of observations is small, we probably can consider that the overall responses to epinephrine are similar to those of decreasing intrasinus pressure.

Our experiments show no significant differences in time constants in the two channels and that the

blood flow redistribution was opposite to the direction hypothesized by Caldini et al. (1974) and Coleman et al. (1974). However, this need not completely negate the significance of the proposed mechanism. It may simply be that the particular division of the systemic vascular bed we chose did not demonstrate the mechanism, but some other division(s) can have appropriately different time constants and exhibit appropriate redistribution by the baroreceptor reflex. Mitzner et al. (1975) divided the systemic vascular bed into three parallel flow channels: the superior vena caval channel, the hepatic venous channel (splanchnic flow), and the channel draining below the hepatic vein. They found that epinephrine infusion caused no changes in superior vena caval flow, an increase in splanchnic flow of 8%, and a decrease in flow below the liver of 8%. The combination of splanchnic flow and flow below the liver minus the femoral flow would be comparable to channel 2 flow in the present experiments. Mitzner’s data indicate no change in flow in that combination of vascular beds. However, a small blood flow redistribution was seen in the present study. The differences could very well be due to the reflex control of skeletal muscle vascular beds drained through the femoral veins.

The results of our study are consistent with those of Mitzner and Goldberg (1975) and Green (1975), who found nearly equal compliances in experiments using parallel channels. Mitzner and Goldberg (1975) found nearly identical compliance values for flow channels similar to those chosen in our experiments. In addition, the value of the total systemic vascular compliance decreased by approximately 10% when intrasinus pressure was decreased from 200 to 50 mm Hg. The finding is consistent with, but slightly smaller than, the results of a recent study by Shoukas and Brunner (1980) in which vascular compliance decreased approximately 22% for the same magnitude of change in intrasinus pressure.

There is evidence in the literature to support the observation that blood flow in the splanchnic channel increases when intrasinus pressure is decreased. In particular, Bagshaw and Cox (1977), Polosa and Rossi (1961), and Vatner et al. (1970) all found that muscle vascular resistance can change much more than can visceral vascular resistance. Thus, for a given decrease in intrasinus pressure, there is an unequal vasoconstriction in the two vascular beds. Therefore, with a constant cardiac output, splanchnic blood flow would increase and extrasplanchnic flow would decrease in equal amount. In a more intact animal, with varying cardiac output, it is also possible that similar changes in vascular resistance may or may not occur.

The nearly 7 ml/kg increase in single reservoir volume following a decrease in intrasinus pressure is in agreement with previously reported studies of Shoukas and Sagawa (1973). This volume change represents the net amount of volume that the reflex
can mobilize. However, as Shoukas and Sagawa (1973) have shown, if arterial pressure is controlled, a much larger increase in reservoir volume is seen. This volume change can be twice as large as that seen under the uncontrolled arterial pressure in this study. As was mentioned previously, capacity can change by an alteration in compliance, an alteration in "unstressed" vascular volume, or passive volume shifts caused by changes in intravascular pressure. The 10% change in compliance seen can only account for changes in volume of approximately 1.5 ml/kg. Since there were no large changes in flow distribution and the time constants of both channels were nearly equal, volume changes by this mechanism would be small. Therefore, the decrease in capacity of the vascular bed must have been caused by decreases in "unstressed" vascular volume when intrasinus pressure was decreased. In this study, the splanchnic channel was found to exhibit greater changes in vascular capacity than the extrasplanchnic channel. We thought that one source of this difference in volume responses is likely to be the active participation of the spleen. In two dogs, we performed splenectomies after all data had been taken. This attenuated the volume response in the splanchnic channel. Our calculation indicated that the spleen was responsible for approximately 30% of the change in splanchnic reservoir volume. Thus, other organs or vascular beds were responsible for the major change in vascular capacity in the splanchnic channel.

One very interesting result is that changes in vascular capacity seem to be highly dependent upon the direction of the intrasinus pressure changes. Decreasing intrasinus pressure caused each channel to decrease its capacity and increase reservoir blood volume. Increasing intrasinus pressure caused the splanchnic channel to increase capacity and decrease reservoir volume, whereas the extrasplanchnic channel decreased capacity and increased reservoir blood volume. The changes in total vascular capacity in single reservoir experiments showed an increase in reservoir volume when intrasinus pressure was decreased and a similar magnitude of decrease when intrasinus pressure was increased. However, the relative contributions of the two channels are very different, depending on the direction of the intrasinus pressure change. Two possibilities do exist that need further investigation. First, Shoukas and Brunner (1980) have shown recently that the static overall open loop gain of the baroreceptor reflex is smaller for increasing intrasinus pressure than for decreasing mean intrasinus pressure. Second, there is evidence by Mitzner and Goldberg (1975) that venous resistances can increase with infusion of epinephrine. Since changes in venous resistances could not be reliably obtained in the physiological experiments, the sensitivity of the system to changes in venous resistances was tested in a computer simulation. We found that disproportionate changes in venous resistance could change not only the magnitude of blood flows and volume in the two channels but also the direction of flow shift. Taken together with the notion that there are differences in static open loop gain of the reflex between increasing and decreasing directions, it is not unlikely to see the reversal of direction in the change in reservoir volume of the extrasplanchnic channel. Therefore, changes in venous resistances are potentially important in determining reservoir volume changes and need further investigation.

Although passive blood volume changes caused by flow redistribution by the reflex could not account for the changes in reservoir blood volume seen in the two channels chosen here or in single reservoir experiments, we must emphasize that this finding does not totally negate the potential value of the Caldini-Coleman hypothesis for other physiological stimuli. We conclude, however, that the carotid sinus baroreceptor reflex is likely to exhibit control over changes in vascular capacity primarily through concomitant reflex changes in venous tone.

Appendix

Steady State Compliance Analysis

For the model shown in Figure 3, the corresponding two-port transfer equations for the two channels are:

\[
\begin{bmatrix}
F_a(S) \\
F_v(S)
\end{bmatrix} = \frac{1}{A} \begin{bmatrix}
R_v + \frac{1}{C_v S} & -\frac{1}{C_v S} \\
-\frac{1}{C_v S} & -1 + \frac{1}{C_v S}
\end{bmatrix} \begin{bmatrix}
P_a(S) \\
P_v(S)
\end{bmatrix}
\]

and

\[
\begin{bmatrix}
F_a(S) \\
F_v(S)
\end{bmatrix} = \frac{1}{B} \begin{bmatrix}
R_v + \frac{1}{C_v S} & -\frac{1}{C_v S} \\
-\frac{1}{C_v S} & -1 + \frac{1}{C_v S}
\end{bmatrix} \begin{bmatrix}
P_a(S) \\
P_v(S)
\end{bmatrix},
\]

where

\[
A = \text{det} \left[ \begin{array}{cc}
R_v + \frac{1}{C_v S} & -\frac{1}{C_v S} \\
-\frac{1}{C_v S} & -1 + \frac{1}{C_v S}
\end{array} \right],
\]

\[
B = \text{det} \left[ \begin{array}{cc}
R_v + \frac{1}{C_v S} & -\frac{1}{C_v S} \\
-\frac{1}{C_v S} & -1 + \frac{1}{C_v S}
\end{array} \right],
\]

P_a and P_v are arterial and venous pressures and F_a and F_v are the arterial and venous flows.
Since the total inflow is the sum of \( F_a \) and \( F_{a2} \) and is held constant, these sets of equations can be solved for venous flows \( F_v \) and \( F_{v2} \) in terms of their respective venous pressures \( P_v \) and \( P_{v2} \). This solution yields:

\[
-F_v(S) = \frac{C_1 C_2 S^2 R_{v2} (R_a + R_{a2}) + C_2 S R_{v2}}{S^2 \tau_1 \tau_2 (R_a + R_{a2}) + S (\tau_1 R_a + \tau_2 (R_a + R_{a2} + R_{v2}))} \cdot P_v(S)
\]

\[
-F_{v2}(S) = \frac{C_1^2 S^2 R_v (R_a + R_{a2})}{S^2 \tau_1 \tau_2 (R_a + R_{a2}) + S (\tau_1 R_a + \tau_2 (R_a + R_{a2} + R_{v2})))} + R_{a1} + R_{a2} + R_{v1} + R_{v2}
\]

where \( \tau_1 = R_v C_1 \) and \( \tau_2 = R_{v2} C_2 \).

In our experimental preparation, the changes in reservoir volumes \( \Delta V_1 \) and \( \Delta V_2 \) are the time integrals of the changes in venous flows after equal magnitude step changes in venous pressure \( P_v(S) = P_v \) \( P_v(S) = P_v \). Therefore, we can integrate the above two venous flow equations to obtain the volume changes caused by the venous pressure change. Thus:

\[
\Delta V_1(S) = \frac{C_1 C_2 S^2 R_{v2} (R_a + R_{a2}) + C_2 S R_{v2}}{S^2 \tau_1 \tau_2 (R_a + R_{a2}) + S (\tau_1 R_a + \tau_2 (R_a + R_{a2} + R_{v2})))} \cdot P_v(S)
\]

and

\[
\Delta V_2(S) = \frac{C_1 C_2 S^2 R_v (R_a + R_{a2}) + C_2 S R_v}{S^2 \tau_1 \tau_2 (R_a + R_{a2}) + S (\tau_1 R_a + \tau_2 (R_a + R_{a2} + R_{v2})))} + R_{a1} + R_{a2} + R_{v1} + R_{v2}
\]

We can apply the final value theorem to the above two equations to yield the steady state solutions to the ratios \( \Delta V_1/\Delta P_v \) and \( \Delta V_2/\Delta P_v \). This results in the respective solutions:

\[
\frac{\Delta V_1}{\Delta P_v} = C_1 \frac{R_a + R_{a2} + R_{v2}}{R_a + R_{a2} + R_{v1} + R_{v2}}
\]

\[
+ C_2 \frac{R_{v2}}{R_a + R_{a2} + R_{v1} + R_{v2}}
\]

\[
\frac{\Delta V_2}{\Delta P_v} = C_2 \frac{R_a + R_{a2} + R_{v1}}{R_a + R_{a2} + R_{v1} + R_{v2}}
\]

As can be seen from Equations 3 and 4, the ratios of \( \Delta V_1/\Delta P_v \) and \( \Delta V_2/\Delta P_v \) are not the compliances \( C_1 \) and \( C_2 \) of the individual channels, but a combination of \( C_1 \) and \( C_2 \), each of which is weighted by the ratio of arterial and venous resistances. For this reason we are reluctant to call \( \Delta V_1/\Delta P_v \) and \( \Delta V_2/\Delta P_v \) the compliances, \( C_1 \) and \( C_2 \), of the individual channels. Furthermore, since we know that arterial resistance and possibly venous resistance would change during changes in intrasinus pressure, the ratios of the resistances are not constant in Equations 3 and 4. Therefore, using the ratios of \( \Delta V_1/\Delta P_v \) and \( \Delta V_2/\Delta P_v \) as \( C_1 \) and \( C_2 \) could lead to the erroneous conclusion that \( C_1 \) and \( C_2 \) are changing when indeed only the ratios of the resistances are changing.

Although the ratios of \( \Delta V_1/\Delta P_v \) and \( \Delta V_2/\Delta P_v \) are not individual compliances \( C_1 \) and \( C_2 \), the ratio of total volume change divided by \( \Delta P_v \) is the total systemic vascular compliance, \( C = \frac{\Delta V}{\Delta P_v} \).

**Transient Analysis of Volume Change**

From Equations 1 or 2, the volume transient to a step change in venous pressure is of the form

\[
V(t) = \frac{K \alpha}{r_1 - r_2} + \frac{K (r_2 - \alpha)}{r_2 - r_1} \cdot e^{-r_2 t}
\]

where \( r_1 \) and \( r_2 \) are the roots of the polynomial pole and \( K \) and \( \alpha \) contain the compliances and resistances of the model. As can be seen from Equations 1 and 2, the polynomial pole equations for both channels (i.e., the denominators) are equal. However, the zeros (the numerators) of both equations are markedly different. The coefficients of both exponentials in Equation 5 depend upon the roots and primarily the zeros. These coefficients would be markedly different for a given channel. In channel 1, the coefficient \([K(\alpha - r_1)]/[r_1(r_1 - r_2)]\) is much greater than the coefficient \([K(r_2 - \alpha)]/[r_2(r_1 - r_2)]\), whereas, in channel 2, the coefficient \([K(r_2 - \alpha)]/[r_2(r_1 - r_2)]\) is much greater than the coefficient \([K(\alpha - r_1)]/[r_1(r_1 - r_2)]\) for an arterial-to-venous resistance ratio of approximately 4 to 1. The larger this arterial-to-venous resistance ratio, the greater the differences in the coefficients. Therefore, although the volume transients from each channel contain two exponentials, only one of the exponential terms will predominate.
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