Observations on the Regulation of Arterial Blood Pressure in Unanesthetized Dogs

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ABSTRACT

Aortic pressure rises as a dog's head is raised and falls as it is lowered. Systemic pressure change was 49% ± 3% of the hydrostatic pressure change at the carotid sinus, chosen as an arbitrary reference, so that pressure at the carotid sinus changed only 51% as much as it would have if systemic pressure had not changed. The responses to head raising and lowering were dynamically asymmetrical, in a way which permits them to be described as being dependent on the rate of head lowering as well as on vertical position. When chloralose-anesthetized dogs maintained with positive-pressure breathing were studied under water, the response was abolished, suggesting its hydrostatic basis. Chronic carotid baroreceptor deafferentation or carotid sinus excision only diminished the response to changes in head position in most animals, and a transient response to head lowering persisted in all. An apparent CNS adaptation to the disruption of baroreceptor afferents makes it impossible to judge the quantitative role of the carotid sinus reflex in the relation of head position to blood pressure in intact dogs. The effects of head motion on blood pressure are predictable in a model of blood pressure control based on the known dynamic relations between carotid sinus and systemic pressures, from which we tentatively conclude that vertical head motion acts on blood pressure through the carotid sinus reflex. If so, the measurement of vascular responses to head motion can serve as a nondestructive, quantitative test of baroreceptor reflex dynamics in intact, unanesthetized animals.

ADDITIONAL KEY WORDS baroreceptor reflexes systems analysis

The circular flow of signals in feedback control systems makes it difficult to obtain the data required for a quantitative description of regulatory action. In the blood pressure control system, such quantitative description is based on experiments in which the circular flow of signals was disrupted. Koch (1) and, more recently, others (2-6) have devised means of controlling pressure at arterial baroreceptor sites independently of systemic arterial pressure. These "open-loop" preparations have provided data on the static and dynamic relations between pressure at the receptor sites and systemic pressure. When these relations are considered together with the fact that systemic pressure obtains at the receptor sites in the intact animal, it is theoretically possible to predict both the mean regulated blood pressure and the extent to which regulatory action will compensate for disturbing influences on pressure. However, the technical difficulties of the open-loop experiments are considerable, and extrapolation of the results to the intact animal is uncertain. It is therefore desirable that other experimen-
tal approaches be made to the quantitative study of blood pressure control.

This paper describes one such method and results obtained with it in the intact, conscious dog. It derives from the fact that arterial pressure is subject to hydrostatic variation in regions of the arterial tree which move vertically with respect to the heart. As the head and neck move in the vertical axis, pressure at the carotid sinus, for example, can be changed by 20 to 30 mm Hg, depending on the size of the dog. In the ensuing moments, mean systemic arterial pressure changes in a direction which tends to minimize the initial change in pressure at the carotid sinus and in pressure elsewhere in the arteries of the head and cephalic portion of the neck.

Even though head motion is easily controlled, our approach still affords only a limited amount of experimental control over pressure in the cervical arteries. Nevertheless, through simple, nondestructive measurements, we can specify how systemic pressure should have changed if pressure at a given reference point in the cervical arterial tree were perfectly regulated, and how in fact it did change. The temporal relations between these two quantities provide a measure of blood pressure control dynamics in the intact animal. These data supplement those from the open-loop experiments referred to above in providing a quantitative description of blood pressure control.

**Methods**

**Surgical Procedures, Postsurgical Care and Training.**—Thirty dogs of either sex, weighing 11 to 33 kg, were studied. Under pentobarbital anesthesia, 30 mg/kg, each dog was subjected to laparotomy and a polyvinyl catheter was placed in the abdominal aorta through an interval iliac artery or one of the lumbar arteries and brought to the exterior through a stab wound in the flank. Beginning 3 days after surgery, each dog was trained to stand quietly while its head and neck were guided to move in the vertical axis according to various temporal patterns. The arterial catheters were flushed with sterile 0.9% saline several times a week throughout the period of study.

After a series of experiments in the intact state, 10 of the dogs were subjected to bilateral denervation of the carotid arterial tree. This procedure was carried out under pentobarbital anesthesia and consisted of adventitial stripping beginning at the common carotid low in the neck, extending cephalad to the bifurcation, and continuing along both the first portion of the external carotid and the internal carotid up to its entrance to the skull. The vessels were then liberally painted with 5% phenol, which caused them to turn a dull white.

In three dogs, the carotid bifurcation, including the carotid sinus, was excised bilaterally. The excision began caudally at the origin of the superior thyroid artery and continued cephalad to near the entrance of the internal carotid to the skull and to near the origin of the lingual artery. A venous autograft connected the common carotid to the external carotid on one side, for we had observed that simple bilateral excision of the carotid bifurcation leads to necrosis of the tongue. The dogs were studied before, and 2 weeks after, the excision procedure.

The dogs were fed Purina dog chow or force-fed with a synthetic diet if they failed to eat their daily ration of chow. Each dog received 400,000 U of penicillin and 500 mg of tetracycline HCl before surgery and daily thereafter for at least 5 days.

**Pressure and Head Motion Measurements.**—Abdominal aortic pressure was measured through the indwelling catheter by a Statham P23 GC strain gauge and Grass polygraph. The strain gauge was held at heart level, as judged by graphic observation of radiopaque markers sewn to the carotid sinus. The other end of the catheter was attached to a Statham strain gauge (referred to as gauge 1) positioned at ground level but biased electrically to read zero when the catheter tip was at heart level. The pressure changes recorded from strain gauge 1 as the head moved vertically were assumed to be equal in magnitude, but opposite in sign, to the difference between the transmural pressures at the carotid sinus and at the aorta. Hence, \( P_c = P_n + (-h) \), where \( P_c \) is transmural pressure at the carotid sinus, \( P_n \) is transmural pressure at the abdominal aorta.
Interstitial fluid is present in a very thin film and thus not freely mobile. The validity of this indirect measure of carotid sinus transmural pressure depends on the following three factors: (1) The densities of blood and 0.9% saline are equal, which is not strictly true, but the difference introduces an error of less than 5% and is in the direction of under-estimating the difference between $P_c$ and $P_n$; (2) The vascular resistances of the carotids as the head moves vertically. This possibility was studied in an acute experiment in which pressures were measured in the abdominal aorta and at the carotid bifurcation (through a catheter in the superior thyroid artery) as the head was moved vertically. Both strain gauges were held at heart level, and the difference in the two mean pressures so recorded did not exceed 2 mm Hg as the head was moved throughout the full vertical range. When the strain gauge attached to the superior thyroid catheter moved with the neck, the expected hydrostatic effects were measured. (3) There is no effect of vertical head motion on cervical interstitial pressure; if there were freely mobile interstitial fluid in the neck, transmural carotid sinus pressure would not change as the head moved. However, interstitial fluid pressure is slightly subatmospheric (8), denoting that interstitial fluid is present in a very thin film and thus not freely mobile.

Intrapleural pressure was measured at the extremity of vertical head position in three dogs by a water manometer attached to a polyethylene catheter passed into the pleural space percutaneously through a 18-gauge thin-wall needle. The catheter was assumed to be patent when the height of the fluid column fluctuated at the dog's respiratory rate.

Data Acquisition and Reduction.—Ensemble averaging was performed on the blood pressure and head position signals by either an average transient computer (CAT-400, Mnemotron Corp.) or general purpose digital computer (PDP-8, Digital Equipment Corp.), programmed to simulate the CAT-400. Both signals were subjected to first-order filtering (—6 db at 0.5 Hz) before analog-to-digital conversion. The filtering removed much of the pressure pulsation at the cardiac frequency and minimized high frequency pressure artifacts due to catheter motion. The pressure changes during 5 to 15 identical sequences of head movement contributed to the final ensemble average, which constituted either 200 (CAT) or 256 (PDP-8) digital points. The array of digital points plot pressure against time over intervals of 16 to 51 seconds, depending on the pattern of head motion under study. The minimum sampling rate was 5/sec.

Either computer was operated so that it commenced accepting data from the two channels when the head was in a given position. The head was then moved at the same relative time during each interval of data acquisition. It is convenient to designate a single sequence of head motion as a "run." Thus, at the end of a series of $N$ runs, a single digital point represented the arithmetic mean of either blood pressure or head position at the same relative temporal point in a timed sequence of head motions. The theoretical value of this averaging process is its diminution of variations in blood pressure unrelated to head motion. If the unrelated influences are regarded as noise and the related ones as signal, the signal-to-noise ratio in the computed average is improved over that in the primary signal by \sqrt{N} (9). Sources of noise in the blood pressure signal were cyclic variations in blood pressure at the cardiac and respiratory frequencies. Sources of noise in the head position signal were small deviations from the desired pattern of head motion.

The data from single runs were excluded from the average for either of the following reasons: obstruction in the arterial catheter or a sighing ventilatory cycle, which was usually identified by the person guiding the dog's head or by its characteristic effects on blood pressure and heart rate. These were a transient increase in both rate and pressure, followed by marked bradycardia and depression in arterial pressure lasting 10 to 15 seconds.

Temporal Patterns of Head Movement.—We sought to approximate the following ideal pattern of head motion: stepwise elevation, stepwise depression, impulsive elevation-depression, impulsive depression-elevation, and sinusoids of various frequency. The step motions required 1 to 2 seconds to execute and were in fact steep ramps; likewise the impulses were approximately triangular, for 1 to 2.5 seconds were required for their execution. The person guiding the dog's head was cued to execute sinusoids by a rotating wheel. Individual cycles were subject to a variety of distortions, although the computed averages were approximately sinusoidal.

Immersion Experiments.—In order to distinguish between reflex effects initiated by pressure changes and those possibly signaled by proprioceptive or vestibular concomitants of vertical head motion or simple traction on cervical vessels, three dogs were studied when totally immersed in water. Each dog was anesthetized with chloralose, 90 mg/kg, iv. In two animals the chloralose was dissolved in polyglycol and in...
Temporal course of abdominal aortic pressure in relation to changes in the vertical position of the dog's head. Initially the head was held low and was raised to its highest seemingly comfortably position and lowered where indicated. The elapsed time between adjacent arrows indicate the time required to execute the motion. The vertical marks on the abscissa occur at 10-second intervals.

The third it was dissolved in 6% sodium borate in water. Each was intubated with a cuffed endotracheal tube and ventilated with positive pressure by a Harvard respiration pump. The effects of vertical head movement were then studied before and during immersion in water at 85° F.

**Results**

**Head Position-Blood Pressure Relations and Their Quantitation.**—The effect of vertical head motion on systemic arterial blood pressure is illustrated in Figure 1, which shows a tracing of unfiltered abdominal aortic pressure. Raising the head increased both heart rate and blood pressure. Lowering the head decreased pressure but not heart rate. Although the qualitative character of the changes is clearly evident, it is apparent that some form of data processing is required to facilitate their quantitation. The upper half of Figure 2 shows the ensemble average of filtered pressure signals from a sequence of five runs conducted over a period of about 10 minutes. The experimental sequence was to hold the dog's head low for 20 seconds, then activate the computer for a 40-second interval of data acquisition, within which the head was raised beginning at the fifth second, was held high for 20 seconds, and then returned to the initial position.

The irregular array of points in the upper half of Figure 2 shows the average temporal course of change in mean arterial pressure in the 40-second interval. The smooth array of points shows the temporal variation of pressure recorded from the strain gauge attached to the fluid-filled catheter taped to the dog's neck. The two pressure signals are calibrated the same, and their superimposition facilitates the interpretation of the ar-

![Figure 2](image_url)
terial pressure change as a regulatory response. The act of raising the dog's head initially lowered transmural carotid sinus pressure by 25 mm Hg. Thereupon, as the averaged blood pressure data in Figure 2 show, arterial pressure began to increase and returned carotid sinus pressure toward its initial value. For this regulatory response to completely offset the initial pressure drop at the carotid sinus, systemic arterial pressure would have had to rise by 25 mm Hg; in fact, however, the aortic pressure increment was only 16 to 18 mm Hg in the quasi-steady state of this brief experiment. Had carotid sinus pressure been perfectly regulated, the blood pressure trace would have overlaid the tracing showing the pressure recorded from the neck catheter. It is convenient to regard the ratio of the steady-state change in aortic pressure to the pressure change recorded from the neck catheter as the static closed-loop gain of the mechanisms regulating carotid sinus pressure. This gain factor is symbolized as W. In the experiment shown in the upper half of Figure 2, W = 17/25 = 0.68. We emphasize that no particular mechanism need be assumed in using this description and mode of data presentation.

In 15 of the dogs studied, the value of W was obtained both from the aortic pressure increment upon head raising and from the aortic pressure decrement upon head lowering. In these experiments the final head position was maintained for 35 seconds. The two measures of W occasionally differed in a single animal, but there was no systematic difference. The mean value of W, pooling the results from the two kinds of experiment, was 0.49 ± 0.03 SEM (n = 20). The lowest value of W was 0.20 and the highest was 0.77. From day to day in a given dog, the measurement of W was closely reproducible and the temporal patterns of the responses were similar.

The mean aortic pressure and heart rate in conscious dogs before a series of experiments with controlled vertical head motion were 109 ± 8 (SD) mm Hg and 116 ± 19 beats/min respectively; after the series of experiments the mean values were 106 ± 9 mm Hg and 109 ± 18 beats/min. These data indicate that some of the dogs had an appreciable tachycardia and were undoubtedly not at ease with the experiment. However, there appears to have been no relation between the measured value of W and the initial or final heart rate.

Dynamic Relations between Head Position and Blood Pressure.—Inspection of the temporal course of these pressure changes shows them to be asymmetrical relative to the direction of head motion. This dynamic asymmetry is evident in Figure 1, for the raw data show that pressure rose much more gradually when the head was raised than it fell when the head was lowered. A similar difference is clear in the upper half of Figure 2, where the averaged pressure increase was oscillatory and did not attain a steady value until about 12 seconds after the head started up, whereas the averaged pressure fell precipitously after
Effect of impulsive changes in head position (smooth traces) on blood pressure (irregular traces) in an intact dog (no. 18). Ensemble average of 15 runs.

Effect of approximately sinusoidal motion of the head in the vertical axis (smooth trace) on blood pressure (irregular trace). The nominal period of the head's motion was 9 seconds. Ensemble average of 5 runs.
REGULATION OF ARTERIAL BLOOD PRESSURE

Comparative changes in blood pressure (irregular traces) when the head of an intact dog (no. 5) was raised through its full vertical range (top, smooth trace) or through only part of its range (bottom, smooth trace). The head was initially positioned at heart level in the experiments shown in the lower half of the figure. The data in the upper half are ensemble average of 5 runs, the others are an average of 10.

Neither frequency multiplication nor "paradoxical" responses to impulsive head raising were invariable findings, but appeared to depend, at least in part, on initial heart rate. Dogs with average heart rates in excess of 120/min usually failed to show heart rate changes as the head moved, whereas dogs with lower average heart rates and concomitant sinus arrhythmias (as in Fig. 1) usually showed transient heart rate changes as the head moved in either direction, with more pronounced dynamic asymmetries in their responses than in those of the animals with the higher heart rates.

The dynamic asymmetry of the response represents a major nonlinearity in the mechanisms by which vertical head position influences blood pressure. Nevertheless, by limiting our attention to head-raising experiments and thus avoiding the transient responses associated with downward head motion, it was possible to demonstrate proportionality to the extent of head raising. Figure 6 shows the pressure changes elicited by raising the head through its full range (Fig. 6, top) and through only part of its range (Fig. 6, bottom), from midposition to a maximally elevated one. There was considerably more scatter in the averaged data when the head was moved through the more limited range, as the magnitude of the residual pulsations in the damped pressure signal had become relatively larger with respect to the mean pressure changes. Nevertheless, it can be seen from Figure 6 that the temporal patterns of both responses and the values of W were similar. Although the experiment of moving the head through the other half of its range was not performed, its result can be predicted from the data in Figure 6. They indicate that systemic pressure increased approximately 8 mm when the head was moved through a 15-mm range (W = 0.53) and 15 mm when it was moved through a 26-mm range (W = 0.58). Presumably, therefore, head movement through the remaining 11-mm range would account for a 7-mm increase in systemic pressure (W = 0.64). Two other dogs were similarly studied, and in both the value of W for partial head movements in the upper half of the range exceeded the value for the full range of head motion, being 0.54 and 0.83 for the partial motions, and 0.44 and 0.70 for the full motions.

**Table 1**

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Before denervation</th>
<th>After denervation</th>
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<tbody>
<tr>
<td>4</td>
<td>.67</td>
<td>.16</td>
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<tr>
<td>7</td>
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<td>21</td>
<td>.57</td>
<td>.50</td>
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<table>
<thead>
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<th>Dog no.</th>
<th>Before carotid sinus excision</th>
<th>After carotid sinus excision</th>
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<tr>
<td>22</td>
<td>.70</td>
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<td>24</td>
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There was a delay of 1.5 to 2.4 seconds between the onset of head motion and the onset of a change in averaged arterial pressure. The delay appeared to be independent of the direction of head motion.

Effect of Carotid Arterial Denervation.—The denervation procedure reduced the magnitude of the response to head motion in 8 of 10 dogs studied. Table 1 lists the means and ranges of values of W and their ranges, before and after the procedure. Figures 2, 3, and 7 illustrate the comparative temporal patterns of the response to head motion before (top) and after (bottom) the denervation procedure.

Since the values of W listed are the means of a variable number of time averages of ensemble averages, no altogether satisfactory statistical test is applicable to these data which would permit a blanket probabilistic statement about the effect of the denervation procedure. We did, however, perform the one-tailed sign test; its result indicates that the probability that a decrease in W in 8 of the 9 animals undergoing change was due to chance is less than 0.02.

Figures 2 and 7 show comparative data from the two dogs whose responses to head motion were altered the greatest and the least by carotid denervation. From the data in Figure 2 (bottom) it is evident that the response was almost entirely abolished after denervation, compared to the intact state (Fig. 2, top). At the other extreme, in Figure 7 (bottom) it is apparent that after carotid denervation the response was delayed somewhat, but its steady-state magnitude was no different than in the intact state (Fig. 7, top). In each denervated animal, the pressure increase elicited by head raising was later in onset and more slowly developing than in the intact state.

In contrast, head lowering produced at least a transient pressure decrease in every animal studied, regardless of the steady-state magnitude of the response. Figure 3 shows pressure changes following head lowering before and after denervation. Although the final pressure differed little from the initial one, after the denervation procedure (Fig. 3,
Effect of impulsive changes in head position (smooth traces) on blood pressure (irregular traces) in a de-nervated dog (no. 21). Ensemble averages of 10 runs. Bottom), there remained a transient response which was no less brisk than in the intact state. Thus the dynamic asymmetry of the response is relatively greater after denervation than before, as illustrated also by the persisting paradoxical response to pulselike head motions (Fig. 8).

Effect of Carotid Sinus Excision.—In the three dogs studied, the value of W was reduced after carotid sinus excision (Table 1). Despite the reduction in the magnitudes of the responses, however, their temporal patterns were not altered by carotid sinus excision.

Immersion Experiments; Side-to-Side Head Motion; Effects of Head Motion on Intrapleural Pressure.—The relation between head position and blood pressure was studied before and after immersion. This technique provided a means of cancelling the hydrostatic pressure changes associated with head motion, although vestibular or head-on-neck and neck-on-trunk proprioception would be expected to persist. The necessary anesthesia and positive-pressure respiration alone had little effect on the pressure response to head movement, the values of W being 0.44, 0.56, and 0.63 respectively in the three experimental dogs, but immersion totally abolished the response in each dog ($W = 0$). In two of the dogs, neither the systemic blood pressure nor the heart rate differed in and out of water, in the third dog, the mean blood pressure out of water was 105 mm Hg and increased to 135 under water, although the heart rate did not change. Thus there was no consistent change in the baseline blood pressures which might account for the abolition of the blood pressure response to head movement in the immersed dogs.

Side-to-side movement of the head, with its vertical position fixed at heart level, had no discernible effect on systemic blood pressure.

Intrapleural pressure at the two extremes of head position did not differ by more than 1 cm H2O.

Discussion

Experiments in the horse and giraffe similar to ours in the dog have been reported. Spencer et al. reported that carotid arterial pressure in the horse varied with head motion in keeping with the expected hydrostatic effects and without evidence of self-regulation (11). Data on two unrestrained giraffes reported by Van Citters et al. signified little if any self-regulation of carotid pressure when the animals assumed the upright posture from the supine (12), although there was no simultaneous measurement of the animals' aortic pressures that would permit a statement of whether the carotid pressures fell to the precise extent predicted from simple hydrostatics. However, data presented by Goetz et al. on the systemic pressure changes associated with passive, vertical head movement of a recumbent, anesthetized giraffe indicate a value for $W$ of approximately 0.2 (Fig. 6 in ref. 13). It is apparent that the relative effects of head motion on blood pressure, represented by the value of $W$, are much larger in the dog than in either the horse or...
giraffe. Were the effects relatively as great in either of the larger animals, their aortic blood pressure would undergo quite large changes as the head moved in the vertical axis. For example, if the value of W in the giraffe were one-half, as in the dog, its systemic blood pressure would change by about 200 mm Hg as its head moved through its full range of 16 to 20 feet.

The present results do not indicate whether the effects of vertical head position and motion on blood pressure are brought about by changes in cardiac output or by changes in peripheral resistance. Elsewhere (14), we have reported that changes in vertical head position in other dogs had no sustained effect on ascending aortic blood flow, so that the steady-state changes in blood pressure appear to have been brought about altogether by peripheral resistance changes. It remains for future studies to define the transient effects of head motion on cardiac output and peripheral resistance.

The arterial pressure changes associated with vertical head movement in the intact dog are qualitatively predictable from the known properties of carotid baroreceptor reflexes. Not only the direction of the changes, but also their apparent relation to the rate of head lowering are in keeping with known properties of these reflexes. The experiments carried out under water and with side-to-side head movements show that neither traction on the cervical vessels nor proprioceptive, vestibular, or other nonbaroreceptive reflexes account for the association between vertical head motion and blood pressure. It should be noted that the pressure changes associated with head motion are too small to trigger the cerebral ischemic pressor reflex, which is inoperative when cerebral perfusion pressure is above 60 mm Hg (15). Also, the brain is surrounded by freely mobile cerebrospinal fluid, so that transmural pressure across cerebral vessels ought not to be subject to hydrostatic effects as the head moves. However, these qualitative considerations do not establish whether the blood pressure responses in the intact dog are quantitatively accounted for by the carotid baroreceptor reflexes.

We undertook the experiments with denervation and carotid sinus excision in the hope of answering two questions: Is the head position-blood pressure relation in the intact dog quantitatively attributable to carotid baroreceptor reflexes, and, if so, is the carotid sinus the most appropriate locus in the carotid arterial tree to judge the self-regulation of pressure as head position changes? The only effect of carotid sinus excision was reduction of the value of W. The more radical denervation procedure only occasionally reduced W to near zero (Fig. 2 and 3), and even in animals with the greatest reductions of W, there still persisted a large transient effect of head lowering on blood pressure (Figs. 3 and 8). Three possible mechanisms could account for the post-denervation dependence of blood pressure upon head position.

The first is that innervation was reestablished postoperatively, but it seems unlikely, since observations were made from 1 to 8 weeks after the procedure, with no evident time dependence in the response of a given animal. Incompleteness of denervation was also possible, and to eliminate this possibility carotid sinus excision was performed. The results of experiments after that procedure were similar to those of experiments carried out after denervation. We assume, but cannot prove, that the denervation procedures were uniformly complete.

A second possible mechanism is that pooling and emptying of blood by the venous tree of the neck accounts for part or all of the response in both normal and denervated animals. One can see the external jugular veins collapse and distend as a dog's head moves up and down. We attempted to control this influence by applying external compression to the neck with an elastic bandage, but it had no effect on the responses. We also induced blood pooling in the neck, with the head's position fixed, by manual occlusion of the external jugulars at their entrance to
the thorax. Neither the occlusion nor its subsequent release altered blood pressure, but there is no certainty that jugular occlusion pools as much blood as does lowering the head. In any event, the dynamic asymmetry of the response to head motion, and particularly the paradoxical pressure response to impulsive head raising (Figs. 4 and 8, bottom), cannot be explained by a pooling mechanism, which in fact leads to the expectation of an opposite form of asymmetry. We base this conclusion on our observation that the venous tree fills slowly when the head is lowered (because of valves at the thoracic inlet) but empties promptly as the head is raised.

The third possible mechanism, which we regard as most likely, is that there exist extracarotid baroreceptors in the arteries of the head and neck which continue to function after carotid denervation. It would be erroneous to conclude, however, that such baroreceptors normally dominate in animals in which the denervation procedure had the least effect, or to conclude from the approximate halving of W after carotid sinus excision that the carotid sinus reflex normally accounts for about half of the normal response. These two conclusions assume no change in the central nervous processing of information from baroreceptor afferents that remain after either procedure, but since there is no chronic hypertension after either procedure, it would seem that such a change has in fact occurred. One can extend this line of reasoning to imagine the situation in which a progressively more complete cervical arterial denervation might be accompanied by a progressively greater weighting of afferent information from ever fewer remaining cervical baroreceptors.

An analogous conclusion has been drawn from the failure to produce more than a brief period of hypertension unless all baroreceptor afferents in the ninth and tenth nerves are disrupted (Chap. 9 in ref. 16). We conclude that denervation experiments cannot answer the two questions we had hoped they would, leaving us without an objective measure of the quantitative role which the carotid sinus reflex plays in the head position-blood pressure relation of the intact dog.

A different approach is required to resolve this uncertainty, which would be a trivial concern were it not for the potential utility of the head position-blood pressure relation as a nondestructive, quantitative test of carotid sinus reflex activity. One approach is to measure signal traffic within the reflex path during head motion, but, aside from the formidable technical difficulties, such measurements would only be interpretable if we knew transfer relations for the various elements of the reflex pathway. Knowledge about these transfer relations is very incomplete, but there is a sizable body of data on the overall, open-loop transfer relation (1-6). With some assumptions, which are discussed in following paragraphs, the open-loop transfer relation can be used to formulate a dynamic model of baroreceptor reflex control of blood pressure. If the effects of head motion are altogether due to carotid sinus reflex action, then the simulation of our experiments with the model ought to evoke responses from it which correspond to those we have evoked in the dog.

A block diagram of the model is shown in Figure 9. It represents the baroreceptors of the blood pressure control system as being located in the carotid sinus and in the arteries of the trunk, notably the aortic arch and origin of the right subclavian arteries (16). As shown in Figure 9, head motion has a direct effect on only one afferent path. In the model,
afferent signals from the two groups of baro-
receptors are simply additive, and equally
and invariantly weighted. Sagawa and Wata-
nabe (4) have presented evidence on the
interaction of baroreceptor afferents. They
showed that the two carotid sinus reflexes
interact additively in affecting systemic pres-
sure. The data of Stegemann and Muller-
Butow (3) can be interpreted the same way.
We assume that this result applies as well
to the interaction between carotid sinus and
trunk baroreceptor afferents. On that assump-
tion, the following equation describes the
relation between changes in vertical head
position ($\Delta l$) and changes in blood pressure
($\Delta p$):

$$\frac{\Delta p}{\Delta l} = W = \frac{G}{1 + G + GH}$$

(1)

where $G$ is the open-loop gain of the ca-
rotid sinus reflex, the product $GH$ is the
open-loop gain of the aortic arch-right sub-
clavian baroreceptor reflex, and $\Delta l$ is meas-
ured as a hydrostatic pressure change in the
same units as $\Delta p$. The equation can describe
the dynamic relations between $\Delta l$ and $\Delta p$ if
its variables can be expressed as functions
of the Laplace complex variable. Even though
$G$ is manifestly nonlinear even for small
perturbations (2, 5), it can still be described
in the Laplace domain using the mathe-
matical formulation of unidirectional rate sen-
sitivity, described by Clynes (10). Until
more information is available about the trunk
baroreceptor reflexes, we must assume that
their open-loop dynamic characteristics are
the same as those of the carotid sinus reflex,
but that they may differ in magnitude, as
represented by the scalar, H. Allison and
Sagawa's preliminary report indicates that $H$
is less than unity (6). For $G$, we have used
a static magnitude of 2.8; it is the value which
the nonlinear model of Levison et al. (5)
yields when forced by pulsatile pressures.
With the static value of $G$ equal to 2.8, the
value of $H$ can range from 0 to 1 and yield
values of $W$ which fall within the range of
our data; the mean value of $W$ is accounted
for by setting $H$ equal to 0.64. Other details
of the model, and their relation to experi-
mental data on the open-loop carotid sinus
reflex, are discussed in the appendix. Figure
10 shows the model's response to simulated
head motion. There is satisfactory corre-
spondence between the model's behavior and
our experimental data.

Note that the model describes events which
occur in the intact dog within a time span of
1 minute or less, corresponding to the dura-
tion of individual runs in our experiments.

![Figure 10](http://circres.ahajournals.org)
As with any model, it is a mixture of experimental observation and untested assumption and is thus tentative. It is obvious that mechanisms other than those included in the model operated in the animals that had been subjected to the carotid denervation procedure. The question, which denervation experiments cannot settle, is whether those mechanisms also operate in the intact animal. The model is formulated on the basis that they do not. It serves to indicate the respective strengths of carotid and trunk baroreceptor reflexes which would have to obtain if that point of view is to be sustained.

The present results show that blood pressure depends on vertical head position, although they leave the mechanisms of this relation in doubt. Whatever the mechanism, its consequences are clear enough, although they depend on one's point of reference in the arterial tree. If the reference point is the carotid sinus, the head position-blood pressure relation appears as a regulatory response, because it reduces the variations in carotid sinus pressure to about half as much as one would expect from the unregulated hydrostatic effects of changes in the vertical position of the head. However, this regulation of carotid sinus pressure against hydrostatic effects is not very precise, since they are only half compensated. Approximately the same is true if the reference point is the inlet to the cerebral arterial system, since the vertical level of the carotid sinus is close to that of the circle of Willis. If the point of reference is approximately the midpoint of the common carotid or vertebral arteries, the head position-blood pressure relation also appears as a regulatory response, but as a very precise one, since at this level steady-state arterial pressure is altogether independent of the hydrostatic effects of vertical changes in head position. However, if the point of reference is an artery outside the head or neck, then the relation appears only as one of the sources of variation or noise in blood pressure. Each view is limited but not incorrect, and none need imply any assumption about mechanism. We chose the carotid sinus as a reference point because the carotid sinus reflex provided a qualitatively plausible mechanism for the head position-blood pressure relation, and we have carried over that view in our tentative quantitative model. Subsequent experiments may change our view of the mechanisms involved, but will not alter the fact that systemic blood pressure in the intact dog changes as the head moves vertically, one consequence of which is a rather imprecise regulation of carotid sinus pressure against the hydrostatic variations.

Appendix

This appendix sets forth the details of the dynamic model which gives rise to Figure 10. The problem is to determine a dynamic expression for $G$ in equation 1. Levison et al. (5) present a model for $G$ which requires a special-purpose circuit, much of which is involved with simulating the different responses of the open-loop reflex to pulsatile or nonpulsatile carotid sinus pressures. Since the transition from pulsatile to nonpulsatile pressures is not relevant to our studies, we have chosen to model the reflex using Clynes's mathematical formulation (10), adjusting its parameters so as to approximate the data presented in Levison's thesis (17) upon which reference 5 is based. The data on the open-loop system are quite diverse and so we have been guided in part by the responses of their model, which presumably reflects their judgment about "typical" responses. Our model of $G$ is

$$G(s) = \frac{2.8}{(5s+1)^2} + \frac{\Omega}{(3s+1)(4s+1)(3.3s+1)}$$

The operator, $\Omega$, designates that the second term of the expression operates only when the first time derivative of mean sinus pressure is positive. The coefficients of $s$ have the dimensions of seconds. The function, $G(s)$, is intended to describe mean pressure changes.
only, and to be forced only by mean pressures. However, its parameters are set to be representative of the function of the reflex when normally pulsatile pressures obtain at the carotid sinus. In that sense, the model describes the view of the biological system that one would have in an experiment in which the relations between pulsatile sinus and systemic pressures were seen only after the pressure signals had been put through low pass filters. Our model of G does not include a sign reversal, which is acquired elsewhere in the intact system model.

Note that the responses of the intact model to simulated ramp-like changes in head position show relatively little dynamic asymmetry (Fig. 10, left). In those simulations, the positional change was accomplished in 2 seconds, corresponding to most of our experiments. In Figure 10, right, the dynamic asymmetry is prominent because the positional changes were executed more rapidly, as in the experiment shown in Figure 4. The model predicts that systemic pressure would undergo increasingly marked transient decreases below the final value as the velocity of head lowering is increased, but the velocities which are realizable in the conscious dog provide only a small fraction of the possible stimulation of the reflex model through its sensitivity to the simulated rate of pressure increase.

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