Servoanalysis of Carotid Sinus Reflex Effects on Peripheral Resistance

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The baroceptors of the carotid sinus (and artery) and the aortic arch are the major sense organs which reflexly control the systemic blood pressure. Since the demonstration of the reflex function of these receptors, there has been much work on the responses of the blood pressure, heart, and peripheral vessels to changes in pressure in the carotid arteries and the aorta, on blood flow in particular organs, and on the responses of the sensory nerve fibers to alterations of blood pressure. Heymans and Neit have summarized present knowledge of the reflex.

In recent years, techniques used to study physical control systems have been applied to the study of biological systems. Two aims of such investigations are to gain insight into the general nature of biological regulation and to see how particular regulations are accomplished. The approach is to state quantitatively the relationship between the stimulus (pressure, temperature, light, etc.) and the response (heart rate, vasmotor activity, pupillary diameter, etc.). A complete description requires analysis of the contributions of each unit: a) the receptor; b) the central nervous system; c) the motor nerves; d) the effector organ. Studies of this kind have been conducted on the pupillary response to light, respiratory-circulatory interrelationships, and the stretch reflex as well as on other systems. The carotid sinus reflex has been studied by techniques involving an electronic analog.

In the medullary blood pressure control system, the important systemic circulatory variables include heart rate, stroke volume, peripheral resistance, systemic blood pressure, and venous pressure, as well as other variables regulated by the pressoreceptor reflexes and by other reflex and non-reflex relationships.

In our study, we subjected the isolated perfused carotid sinus to maintained pressures at different levels, and to square and sine waves of pressure, and measured the resultant systemic pressures and pressure changes. Evidence from this study indicates the relative importance of changes in stroke volume and heart rate as compared to changes in peripheral resistance, but determination of the reflex significance of cardiac factors remains for later work. The role of vagal efferents in reflex responses was not studied.

Methods

Experiments were conducted on 35 cats and 13 dogs. The animals were lightly anesthetized with chloralose (initial dose, 35-45 mg/kg in cats and 50-75 mg/kg in dogs) and heparinized. Blood taken from one or both femoral arteries was led, via a reservoir, into a pump which delivered the blood to both carotid arteries. The output of the pump was depulsated by clamps on the tubing (fig. 1). In addition to the reservoir ahead of the pump, a second reservoir was at times connected to a large cannula threaded through the femoral vein into the vena cava. The use of the reservoirs will be discussed below. The systemic pressure was monitored from the central end of one carotid artery or from a femoral artery. The pressure in both carotid sinuses was monitored either by cannulating the external carotid arteries or by recording pressure in the tubing leading to the carotids. Results from the two monitoring procedures were identical, except that small (5 mm Hg) pressure pulsations seen in the tubing were not seen in the records directly from the sinus.

The output of the amplifier used to record carotid pressure was connected in series with a variable voltage source to the amplifier which controlled the pump, so that pressure at the carotid arteries,
Once set, was held constant despite resistance changes in the vessels fed by the pump. To alter pressure, the voltage in the feedback loop was changed by the variable voltage source; the pump then changed speed to alter the carotid pressure. A sine wave generator in the feedback connection permitted imposition of sine waves of pressure. Since the Sigmamotor pump had a constant stroke output, blood flow was proportional to pump speed and to armature voltage (blood flow measurements are utilized only in splanchnic stimulation experiments; vide infra). The pump system had excellent stability and frequency response (flat to 0.3 cycles/sec). When sine waves of higher frequency were used, a motor-driven (Brewer), valveless, syringe pump, capable of directly delivering sine waves of pressure at 1 to 10 cycles/sec, was connected in parallel with the pressure-controlled pump. The syringe pump was filled with mineral oil, and a long tube was interposed between it and the perfusion system. Care was taken that no oil passed into the perfusion system. All pressures and flows were recorded on a Brush recorder.

In most experiments, the vagus nerves were cut to eliminate effects from the aortic arch receptors. Had these receptors been "in the circuit," a given response might have reflected carotid pressure and/or aortic pressure. In a few animals, the vertebral arteries were occluded while the carotids were being perfused. In five additional experiments with dogs, the splanchnic nerves were stimulated at varying frequencies or amplitudes, while the abdominal aorta below the diaphragm was perfused at constant pressure and the flow was recorded. These experiments were done to investigate the characteristics of the splanchnic vasculature and its innervation.

In an effort to check conclusions based on the studies in anesthetized animals, two cats were subjected to high pontine decerebration. The arterial pressure in these animals was recorded during occlusion of the lower abdominal aorta or the opening and closing of a large shunt between the femoral artery and vein.

**RESERVOIRS, ARTIFACTS, BLIND SINUS EXPERIMENTS**

The arterial reservoir consisted of a distensible balloon (1 liter in dogs, 0.25 liter in cats) restricted externally by a plastic mesh. It filled completely at low pressures (40 mm Hg) and did not change volume by more than three per cent at higher pressures. The venous reservoir was an infusion bottle, set so that the meniscus was at the measured level of venous pressure. The connection from the animal to the arterial reservoir was clamped and the venous reservoir opened, while the carotid pressure was varied over part or all of its range. After each run (or when the arterial reservoir was nearly empty), the venous reservoir was emptied and the arterial reservoir was refilled. The reservoirs were used for all studies of response to maintained (DC) pressures. During early studies of phasic pressures, the two reservoirs were used. However, if the changes in input pressure were small (under ± 12.5 mm Hg), the results with and without reservoirs were indistinguishable. The venous reservoir was therefore not used in these experiments, and the arterial reservoir was open to the systemic circulation and to the pump. The arterial reservoir prevented the pumping of blood from the femoral artery into the carotid, which might have produced a mechanical effect with the same appearance as the carotid reflex. The venous reservoir prevented the accumulation of large amounts of blood in the veins, which might have produced mechanical effects opposite to the reflex.

Earlier workers have at times used a "blind sinus" (i.e., have tied off all vessels distal to the carotid sinus) to study carotid reflexes. We did not generally use this preparation for several rea-
sons. However, two experiments were done with the blind sinus. The results were as reported for the open sinus. Where comparable, our results are, as noted below, similar to those obtained by Koch, who used a blind sinus preparation.

**EVIDENCE FOR REFLEX ORIGIN OF RESPONSES**

Eight studies were done (5 cats and 3 dogs, 1 cat and 1 dog also used for blind sinus studies) to check the effects of carotid sinus denervation on the response reported here. Before the sinus nerve was cut, as will be indicated below, a rise in carotid pressure caused a fall in systemic pressure. After the sinus nerves were cut, a rise in carotid pressure caused a small fall in systemic pressure when no reservoir bottle was used. The change of systemic pressure in this case was approximately 25% to 35% of the carotid change. When the reservoir bottle was used, the systemic pressure usually rose slightly as carotid pressure and pumping increased. The maximal magnitude of this pressure change was 10% to 50% of the carotid pressure change. These mechanical effects are very small compared with the reflex changes reported below and were seen only when carotid pressure was widely varied. All response to slow or fast sine waves or to small square waves of pressure was eliminated by denervation.

After completion of the experiments, several animals received large doses of Nembutal. During the administration, a sine wave of pressure was imposed on the carotid sinus. The reflex responses described below were eliminated by the anesthetic. As further evidence for the reflex nature of the changes reported here, we would like to cite: a) the large responses to very small input pressure changes and to changes of frequency (figs. 2, 3, 4, 6); b) the variations in gain as a function of mean pressure and frequency; and c) experiments now being conducted on resistance changes in the isolated perfused limb during changes in carotid pressure give results very similar to those reported here.

**Results**

**STATIC RELATIONSHIP BETWEEN CAROTID SINUS AND SYSTEMIC PRESSURES (FIG. 2)**

The mean systemic pressure, with the carotid arteries connected only to the pump, was usually quite high (120-180 mm Hg). At this time, the back pressure in the carotid artery with the pump off ranged from 80-140 mm Hg. As the pressure in the carotid sinus was raised gradually, systemic blood pressure at first decreased slightly. As the pressure in the sinus was increased farther, the systemic pressure fell more rapidly. The maximal decrease in systemic pressure per unit rise in carotid pressure was usually observed when the carotid pressure was between 160 and 220 mm Hg in the cat and between 100 and 175 mm Hg in the dog. At higher carotid pressures, the fall in systemic pressure in response to an increased carotid pressure was less, and nearly all response disappeared when the carotid pressure was 225-250 mm Hg. The input-output curve was generally sigmoidal, and its shape varied widely (fig. 2). The inordinately high systemic pressures shown in figure 2 probably reflected the lack of normal pulsatile carotid pressure (see below) and the effects of chloralose and vagotomy. When the vertebral arteries were occluded so that lower pressure could be imposed on the carotid sinus, the shape of the input-output curve was not materially changed. No threshold for the response could be found. There was a change in systemic pressure for any change in carotid pressure down to 40 mm Hg; below this level, chemoreceptor reflexes (gasing, raised pressure) were elicited.

**STATIC GAIN**

The open-loop amplification for static pressures (amplification with input pressure controlled by the pump) or gain is considered the ratio of a change in output pressure to a change in input pressure: gain = ΔP systemic/ΔP carotid. This amplification can be measured directly by imposing a small pressure change at each mean input pressure, or can be computed as the derivative of an input-output curve (fig. 2). The results are nearly identical.

In the cats, the maximum amplification ranged from 1 to 15, being between 4.0 and 6.0 in most of them. In the dogs, the maximum amplification was somewhat lower, ranging from 0.8 to 8.0, with the gain in most animals being near 2.0 (fig. 2). Twelve of 35 cats were in a high-gain category (gain...
Relationship between carotid pressure and resultant systemic pressure in a cat. The solid curve shows the actual measurements (scale at the left). The amplification of the reflex is shown by the interrupted peaked curve (scale at the right). Maximum amplification is about 14.

greater than 5.0). Four of 13 dogs showed a gain of 3.0 or greater. As indicated previously, gain varied with mean input pressure, and the shape of the curve of gain versus mean input pressure varied from animal to animal but was constant in each animal. Animals which exhibited a high gain showed a curve which was peaked at some input pressure. Animals with poor reflexes tended to have a constant gain.

Eight cats and five dogs were examined before and after vagotomy. Vagotomy almost always increased the sensitivity of the reflex. The maximal amplification before vagotomy was 3.0 or less in all cat experiments but one, including those in which the maximum amplification after vagotomy was as high as 15. In dogs, the amplification was generally lower before vagotomy, but the difference was less. The amplification was decreased by vagotomy in two dogs and one cat.

**STATIC RELATIONSHIP BETWEEN CAROTID SINUS PRESSURE AND HEART RATE**

The largest changes in heart rate were observed before vagotomy in the dog, and exceeded any seen in the cat. In several dogs, the ratio of percentage change of heart rate to percentage change in output pressure was greater than 1.0 before vagotomy. In the cat, this ratio was always less than 0.25. Inappropriate changes in heart rate occurred after vagotomy in two dogs; the heart rate increased as the carotid pressure was increased. Parasympathetic effects on heart rate cannot be studied with this preparation, since, when the vagus or depressor nerve is intact, the aortic receptors will modify responses; and when the vagus is cut, its motor effects on heart rate are lost. Heart rate changes after vagotomy are undoubtedly produced by corresponding changes in sympathetic discharge.

**RESPONSE TO STEP-PRESSURE CHANGES**

When the pressure in the carotid sinus was changed in steps, 2 to 4.5 seconds elapsed before any response was seen. The systemic pressure then moved opposite to the change in carotid pressure. At times, the systemic pressure tended to overshoot or undershoot from four to seven seconds after the beginning of the response (figs. 3 and 8) and then gradually adjusted to the new level. The time constant of the systemic change, i.e., the time required to reach (1 - 1/e) of the total change, ranged from 10 to 80 seconds and averaged about 20 seconds. The calculated time constant was greatest where the output pressure change was large. The fall of systemic pressure in response to a rise in carotid pressure was usually slower than the opposite response. Heart rate responses (particularly in dogs) were large before and small after vagotomy.
Above: Observed (solid line) and corrected (dotted line) phase angle and gain in a typical cat. Amplification is initially high and falls as frequency increases. Figures in parentheses indicate frequency from 0.01 to 0.07 cycles/sec. Mean pressure and amplitude of input sine wave held constant. 0° indicates that output pressure is highest when input pressure is lowest. Below: Carotid pressure is on the lowest scale, the output pressure in the central carotid on the middle scale. During this experimental run, frequency of the pressure sine wave to the carotid was decreased from 0.04 cycles/sec on the left to 0.02 cycles/sec on the right. Note increase in amplitude of the output sine wave. Note also that mean output pressure rises.

The delay between the input change and the first change in heart rate was short, (0.6-1.2 seconds) as was the time constant to reach a new level (7-25 seconds).

RESPONSE TO SINUSOIDAL PRESSURE VARIATIONS

When slow sinusoidal variations, usually 4-20 mm Hg, were imposed on the carotid sinus, the systemic blood pressure varied approximately sinusoidally. At the lowest frequencies (below 0.01 cycles/sec), the systemic variations were exactly out of phase with the input: when the input pressure was highest, the output pressure was lowest. The amplification was usually between 2.5 and 10 in the cat and between 2.0 and 6 in the dog. As the frequency of the sinusoidal input was increased, the phase difference between input and output increased, and the output response decreased (fig. 4). The observed phase angle increased by 90 degrees (output lagging) at 0.04 cycles/sec and by 180 degrees at 0.10 cycles/sec. In sensitive animals, the observed phase angle at higher frequencies (0.15 cycles/sec) increased by more than 180 degrees (fig. 4). It is possible to consider the phase angle either 0 degrees or 180 degrees at the lowest frequencies. In general, we will follow the former convention, 0 degrees phase difference at low frequencies (figs. 4 and 6).

The observed phase angle has two components, a time delay (when there is no observable response) and a true phase lag (response...
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FIGURE 6
A: Carotid pressure was lowered 15 mm Hg, leading to a 140 mm Hg rise of systemic pressure. B: A sine wave of 12 mm Hg at 10 cycles/sec was imposed on the carotid receptors without changing mean input pressure. Mean systemic pressure fell 100 mm Hg.

FIGURE 7
Mean output pressure and amplification as a function of mean input pressure and frequency in a dog. Mean input pressures are indicated above the line. This experiment was conducted in a dog; as usual, maximal amplification was rather low.

...
negligible. The decrease in mean output pressure continued up to 10 cycles/sec but was less beyond 1 cycle/sec. Only one exception to this fall in mean pressure was noted, in a dog.

**Splanchnic Stimulation Experiments**

In three experiments, the splanchnic nerves were stimulated at a voltage level one-third of that producing maximal vasoconstriction. The frequency of stimulation was sinusoidally modulated between 1 and 10 cycles/sec: $f = f_o + f_m \sin(2\pi f_m t)$; where $f_o = 5.5$, $f_m = 4.5$, and $f_m$ = modulating frequency. This modulating sinusoidal envelope had a frequency ($f_m$) of 0.01 to 0.1 cycles/sec. In two other experiments, the stimulating frequency was held constant at 10 cycles/sec, and the amplitude of the stimulus was varied from zero to one-half the amplitude, causing maximal vasoconstriction. $A = A_o + A_m \sin 2\pi f_m t$; where $A_o$ is the mean stimulus amplitude. Results from the two types of stimulation were indistinguishable. In both types of experiments, the pump controlled flow into the entire abdomen below the diaphragm, the perfusion pressure was held constant at 100 mm Hg, and the changes in flow were monitored as indexes of changes in resistance.

The response to splanchnic stimulation was very slow and was substantially less at 0.02 cycles/sec than at 0.01 cycles/sec (fig. 8). As the stimulus frequency or amplitude was increased during one cycle of the modulating envelope, there was little effect until an apparent threshold was reached. Here vasoconstriction occurred rapidly and increased until the peak of stimulation; resistance then gradually decreased as the stimulus decreased. One splanchnic study was conducted before and after bilateral adrenalectomy. No change in the form of the response was noted, although the amplitude of the response decreased. All responses recorded probably include effects of both vasomotor and adrenal influences.

**Occlusion of Shunts in Decerebrate Animal**

In the additional experiments done to compare the amplification of the carotid reflex in anesthetized animals with its amplification in decerebrate cats, the lower abdominal aorta, or a shunt connecting the lower abdominal aorta to the vena cava, was occluded. When the shunt or aorta was occluded or released, there was an initial change in pressure, followed in one or two seconds by a slow correction of the change which we consider to be reflex. The open-loop amplification of the reflex was considered to be equal to the initial change in pressure, divided by the final change after equilibrium had been reached. If the pressure before occlusion was $P_o$, the pressure instantaneously after occlusion was $P_i$, and the final value was $P_f$, then open-loop amplification was considered to be $G_c = (P_f - P_o)/(P_i - P_o)$. If the initial change was 80% corrected, the open-loop amplification of the reflex was calculated to be +4. In these experiments, the response was variable, and it was necessary to average the results. Averaging revealed an amplification of 5 to 10 in the cat. The "gain" in these experiments may be less than the actual reflex gain.
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Discussion

The observed properties of the carotid sinus reflex are:

A. During either maintained pressure changes or pressure sine waves (figs. 2 and 7), the amplification of the reflex has a prominent peak at a certain input pressure, and is less at higher or lower input pressures. This property was also noted by Koch, who used a blind sinus preparation and imposed 20-second changes in input pressure. Amplification ranged from +1 to +15 in the cat and from +0.8 to +8 in the dog.

B. A step change in input pressure induces no response for about two seconds. The output then goes slowly to a new level; moving oppositely to the change in input, there is at times some early overshoot.

C. The sine wave response to imposed sine waves of pressure is maximal and exactly out of phase with the input when the input waves are of low frequency (0.01 cycles/sec and slower). At higher input frequencies, the amplitude of the output decreases, and the output lags the input by a larger phase angle. At 0.08 to 0.10 cycles/sec the calculated phase lag increases by 90 degrees, and the amplitude of the output may be only one-tenth of the input (calculated phase lag is the measured lag corrected for delay). Beyond 0.08 to 0.15 cycles/sec there is no sine wave response.

D. As the frequency of the sine wave input to the carotid sinus is increased, the mean output pressure falls. This effect (rectification) continues after the output sine wave response disappears. Neil has remarked on this property: "The reflexogenic effects of a pulsatile pressure are much greater than that of a steady sinus pressure at the same mean."

Most of the foregoing properties are shown in figures 2-8.

PROPERTIES OF THE COMPONENTS OF THE REFLEX

Pressoreceptors have a threshold, respond to both the mean pressure and the rate of change of pressure, and show a time constant to reach a new firing level. Receptor firing may be linearly approximated by the equation: $F_0 + K_1 \frac{dP_1}{dt} = K_2 (P_t - P_t)$ where $F_0$ is the receptor frequency, $P_t$ is the input pressure, $P_t$ is the threshold, and the two other terms are derivatives of firing rate and input pressure respectively. The $dF_0/dt$ term is necessitated by the adaptation time required to reach the final firing level. The $dP_1/dt$ term is required by the initial overshoot and is also seen when linearly rising or falling pressures are applied to the input.

If the provision is added that $F_0$ cannot be negative, the receptor has rectifying properties. If a sine wave is imposed on a receptor at a mean pressure which is just below receptor threshold for static pressures, the receptor will respond to the segment of the imposed wave which is above threshold and/or to the (positive) rate of change of pressure, and the receptor will generate impulses. If the frequency of the sine waves is increased, more impulses will be generated. This shows that the phenomenon is not solely a reflection of threshold (without the $dP_1/dt$ term). It is possible that the frequency-dependent rectification depends in part on some other nonlinear property of the receptors, or that synaptic phenomena or characteristics of other portions of the reflex are involved. That rectification is not negligible can be seen in figures 4-7.

The exact stimulus of the receptor is not known. Peterson believes that the diameter of the vessel is the best correlate of impulse frequency in the nerve, and that there may be some error in the use of pressure as the input. Others feel that the sensitivity of the receptor is reflexly set by the sympathetics. Since the sympathetics in the neck were cut, our animals may have lacked this hypothetical control of the receptor. If not, we have described a more complicated feedback system than was our intent, and the term "open loop" may be inappropriate.

Several other comments must be made about the receptors. In published records, receptor response to static pressures is not linear. Also, receptor response to phasic pressures has not been determined exactly. It is possible that
the response to rate of change of input pressure varies with the sign of the rate of change of pressure, i.e., the constant $K_2$ in the last equation for the receptor may be different for positive $\frac{dP_i}{dt}$ and for negative $\frac{dP_i}{dt}$. Also, the overall reflex sensitivity is probably a function of a population of receptors.

No information exists to justify an exact equation describing the influence of the medullary regions that send out the motor commands for blood pressure control. The sympathetic motor fibers fire most when the least information arrives from the pressoreceptors, i.e., when carotid pressure is low, whereas the vagal motor fibers fire least at this time. The medullary connections appear to be influenced by higher centers. A linear approximation would be: $F_s = F_{so} - K_4 F_c (t - t_o)$; where $F_s$ is sympathetic firing rate, $F_{so}$ is sympathetic firing rate when the nerves from the carotid receptors are silent, $F_c$ is the carotid firing rate, and $(t - t_o)$ indicates a time delay.

A most important aspect of the reflex response is the time constant between activity in the sympathetic nerves and the resultant change of the vascular resistance: the amplification of the response was substantially less at 0.02 cycles/sec than at 0.01 cycles/sec (fig. 8): The splanchnic innervation and vasculature thus constitute a low-frequency filter on the output side of the system. Another characteristic, which will not be included in our equation, is that the splanchnic vessels constrict more rapidly than they dilate. Recently, Warner has described the sympathetic and vagal control of heart rate. Sympathetic effects on heart rate as described in detail in his study are similar to the effects we have described on peripheral resistance. An approximate expression for splanchnic resistance is: $R_s + (dR_s/dt) = K_5 F_s (t - t_o)$; where $R_s$ is the resistance of the splanchnic bed, $F_s$ is the frequency of sympathetic firing, and $(t - t_o)$ denotes the time lag in the system. Further, if $P_o$ (output pressure) is proportional to $R_s$, then: $P_o + (dP_o/dt) = K_5 F_s (t - t_o)$.

The major properties of the reflex appear to be explained by the known properties of the biological units. The variable amplification of the reflex shows the non-uniform characteristics of individual receptors or the distribution of receptor thresholds with pressure. The lag in response to phasic changes in input and the long time constant seem to be reflections of the slow response of the splanchnic vasculature, as does the lack of phasic response at high frequencies. Overshoot in response to square wave input reflects receptor overshoot (ratio of $K_2/K_3$ in receptor equation). The rectification and its frequency dependence must in major part result from receptor threshold and response to rate of change of input. Our descriptive equation for the receptor, combined with a slowly responding splanchnic bed, seems to account qualitatively for all responses noted.

**CARDIAC RESPONSE**

It would appear that, before vagotomy, the dog utilizes changes in heart rate to a greater extent than the cat does. Both animals utilize heart rate changes in adapting to rapid pressure changes at the pressoreceptors.

**IMPORTANCE OF CAROTID REFLEX**

The effectiveness of this reflex depends, in major part, on its sensitivity or "gain." The ratio of the change in output (systemic pressure) to change in input (carotid pressure gain) in a normally functioning system (closed loop) can be related by the following equation to the gain in the system in which the input is isolated (open loop): $G_c (1 - G_c) = G_o$; or $G_c = G_o/(1 - G_c)$. If the open-loop gain is 1, closed-loop gain is 1/2, and any perturbation of blood pressure will be only one-half corrected. With our highest open-loop gains, around 15, any outside influence on blood pressure will be over 90% corrected, and the carotid reflex appears very effective.

Previous publications reveal little information about the amplification of the pressoreceptor reflexes. When carotid arteries are clamped, it is difficult to calculate the amplification since the pressure change is large, there is an unknown back pressure, and the
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pulsations are often not measured before or after the changes. The maximal amplification of the reflex calculated from earlier publications appears to be very low, usually about 1.0. This finding may reflect the facts that no search for highest amplification was made and that in some experiments pressure changes were imposed on the sinus for only a short period of time.

Appendix

Generalized Equation for the Carotid Sinus Reflex

Qualitative physiological descriptions may not be sufficient for two reasons: a) Studies have often been conducted under conditions where the interaction of variables was examined over a limited range, and the results do not justify generalization. Statements which indicate that "A" can affect "B" can be especially misleading when the relationship is weak and unimportant. b) Several regulating systems may produce a response, and an experiment in which only two variables are examined may be misleading. A physiological response may not be predictable unless each contribution can be quantitated.

An exact description of a reflex requires that we know both the form of the input-output equation and the magnitude of the constants. We may, however, be able to tell which reflex control system is operating from the form of its actions without exact knowledge of the magnitudes of the constants, gain, etc. The form of our equation is more reproducible than the values of the constants. In future experiments, we will use high-speed computers, since only in this way can we make our data fully quantitative.

As an approximation to the static response, the curve of gain versus input pressure can be considered to have the form of a power function, symmetrical about the point of maximal gain. The resulting equation is:

\[
\Delta P_o = -[G_m + K_7 (P_1 - P_m)^n] (\Delta P_t) \quad (1)
\]

where \(\Delta P_o\) and \(\Delta P_t\) are changes in output and input pressure respectively, \(G_m\) is maximal gain, \(P_m\) is the input pressure at which gain is maximal, and \(n\) is an even number. Heart rate responses are described by a similar equation.

Transient Responses

Equation 1 must be supplemented when \(dP_t/dt\) is not zero.

Square and Sine Waves

When the input was a square wave, 2-4.5 seconds elapsed before any response occurred. In approximately half of the experiments, the output pressure then rose slowly, taking up to 100 seconds to reach a new level. In the remainder of the experiments, the time constant was as long, but the output pressure showed an early overshoot and then went slowly to the new level.

The fact that the output pressure slowly reaches a new level requires that the output side of the equation contain a term one derivative higher than any term on the input side. If there are no derivative terms on the input side (no overshoot), the output is a function of the input and the derivative of the output. With overshoot the output is further responding to the rate of change of input. The terminal period is again a slow movement to the final pressure. A linear approximation is:

\[
K_2 - (dP_o/dt) + K_3 (d^2P_o/dt^2) = K_4 (dP_t/dt) (t - t_o) \quad (2)
\]

where \(dP_o/dt\) is rate of change of output pressure, \(d^2P_o/dt^2\) is second derivative of output pressure, \(dP_t/dt\) is rate of change of input pressure, and \((t - t_o)\) shows a time delay. The sine wave data are consistent with equation 2.

The vagal heart rate responses to square or sine waves imposed on the carotid sinus when the vagus is intact can be described if the corresponding rate terms are substituted for the output pressure terms in equation 2, with the exception that the constants and time constants will differ. Equation 2 considers only the transient or phasic responses to transient or phasic inputs and must be used with equations 1 and 3 (below); 1 and 3 must make equation 2 inaccurate to some small degree.

Effects of Phasic Input on Mean Pressure

As phasic inputs were imposed on the input with the mean input pressure held constant, the mean pressure fell. As the frequency of these inputs increased, the pressure fell farther. This frequency-dependent rectification requires one additional equation:

\[
\Delta \bar{P}_0 = G_8 (P_1 + dP_t/dt - K) - \frac{[Sgn (P_1 + dP_t/dt - K) + 1]}{2} \quad (3)
\]

where \(\Delta \bar{P}_0\) is the change in mean output pressure due to phasic inputs, \(G_8\) is an amplification factor for rectification, and \(Sgn\) (signum) is a function having a value of +1 when positive and -1 when negative. This form of equation also appears to describe mean heart rate changes with phasic in-
puts. The reflex appears to be satisfactorily described by the three equations.

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doi: 10.1161/01.RES.12.2.152

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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