Periodicities in efferent discharge of splanchnic nerve of the cat

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Cohen, Morton I., and Phyllis M. Gootman. Periodicities in efferent discharge of splanchnic nerve of the cat. Am. J. Physiol. 218 (4): 1092–1101. 1970.—In decerebrate or urethan-anesthetized cats with pneumothoraex and neuromuscular blockade, efferent splanchnic activity was recorded monophasically and analyzed by computer summing and correlation methods. Three types of periodicity were observed: a) 10/sec waves, which were synchronized to varying degrees with the cardiac cycle (usually in a 3:1 relation), this is thought to be the fundamental periodicity of the vasomotor centers, which may be entrained by afferent input related to the cardiac cycle. b) Oscillation in a 1:1 relation with the cardiac cycle (maximum activity in early diastole, minimum activity in late diastole); this phase relation is interpreted as arising from baroreceptor reflexes. c) Oscillation in phase with the central respiratory cycle (monitored by phrenic discharge), with maximum activity in the middle inspiratory phase and minimum activity in the early expiratory phase; this respiratory modulation was usually considerably greater than the cardiac modulation. These observations show the existence of important synaptic connections between respiratory and vasomotor centers.

IN THE COURSE of an extensive study of brain stem influences on the discharge of a preganglionic sympathetic nerve, the greater splanchnic nerve, the presence of several types of periodicity (e.g., cardiac, respiratory) was noted (24); these have also been found in various sympathetic nerves by other investigators (1, 4, 6, 17, 18, 21, 38, 39, 43, 47, 48, 52, 53, 55). In the present paper we have undertaken a detailed quantitative analysis of such periodicities because we believe that such analysis is an essential prelude to an understanding of central vasomotor regulation and its physiological modifications. Preliminary reports of this work have been presented (12, 25).

METHODS

Experiments were performed on cats (2.7–4.3 kg) which had neuromuscular blockade (gallamine triethiodide or decamethonium chloride) and bilateral pneumothoraex, and were artificially ventilated. After ether induction and initial surgery, the animals were maintained either: a) under ethyl carbamate (urethan) anesthesia (1.0–1.25 g/kg, iv); or b) unanesthetized after midcollicular decerebration. In decerebrate cats, further surgery was performed under a mixture of 50% N2O and 50% O2, to maintain analgesia. Before decerebration, the external rather than the common carotid arteries were tied in order to retain carotid baroreceptor discharge.

The cats were artificially ventilated with 100% O2, and the ventilation was adjusted to give end-tidal CO2 values of 3.8–4.8%, as monitored by a rapid infrared CO2 analyzer. Rectal temperatures were maintained between 36.5 and 38 C. In many cats 5% dextrose in physiologic saline was infused (100 ml/kg per 24 hr).

The left greater splanchnic nerve was located in the costovertebral triangle, cut at its entrance into the celiac ganglion, and desheathed. The left phrenic nerve was immersed in a pool of mineral oil through which a 5% CO2–95% O2 mixture had been bubbled.

All data were recorded on magnetic tape: 1) Efferent splanchnic nerve activity was recorded monophasically (amplifier bandwidth 0.2–1,000 cycles/sec). The adequacy of reproduction of slow potential changes was shown in one experiment with d-c recording, where no difference of waveform was found between the d-c and the RC-coupled signal. In some cases, the potentials were additionally filtered (for subsequent integration) by a high-pass circuit (time constant 5 msec). 2) Efferent phrenic nerve activity was recorded diphasically (bandwidth 80–10,000 cycles/sec). The phrenic potentials were further processed through a leaky integrator circuit (time constant 0.1 sec), to obtain a smoothed waveform (10). 3) The electrocardiogram (ECG) was continuously monitored from a pair of needles placed in the left forepaw and right hindpaw. 4) Arterial blood pressure was measured by a Statham P23DD transducer through a femoral arterial catheter whose tip was located in the thoracic aorta. 5) Tracheal pressure, which indicated the phases of artificial ventilation, was measured by a Statham P23BB transducer attached to a side arm in the closed ventilation system.

Data Analysis

Analogue-to-digital conversions. By use of digital logic circuits, the recorded variables were used to derive standard timing pulses marking several cycles: 1) cardiac cycle: pulse derived from the R wave of the ECG; 2) central respiratory

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cycle: pulses derived from the integrated phrenic signal and marking the start of the inspiratory (I) and the expiratory (E) phases; 3) artificial ventilation cycle: pulse marking the peak of lung inflation.

**Duration measurements.** Interval distributions of two types were derived by computer (Control Data Corp. 160A or Mnemotron CAT 1000): a) the distribution of intervals between successive pulses of the same signal, such as R-R intervals, which furnished the duration of the cardiac cycle; b) the distribution of the first intervals between pulses of different signals, such as I to E intervals, which furnished the duration of the inspiratory phase.

**Time relations of spontaneous activity.** The time relations of splanchnic activity to the several cycles (respiratory, cardiac, pump) were analyzed by summing the splanchnic potentials in an average-response computer (CAT 1000), using the cycle-related timing pulse to trigger the computer sweep. The timing of the sweep (address duration, number of addresses) was decided after inspection of the appropriate interval distribution. The sweep duration was set to be less than the duration of the shortest cycle in the sample, so that every address contained counts from an equal number of cycles. The computer memory contents were read out in digital form by a printer and in analog form by an inkwriter.

The method of summing tends to make apparent spurious signals (i.e., signals not arising from nerve discharge) which are related to a particular cycle, for example, ECG potentials or motion-induced potentials caused by the arterial pulse. However, these could be specified as artifacts on the basis of the identity of the summed waveform to that of the signal of origin; they could usually be eliminated by repositioning of the splanchnic nerve on the electrode. One type of artifact, caused by lung motion, was identified by its disappearance on stoppage of the ventilation pump and could be similarly eliminated. Further evidence that the recorded activity was not artifactual was its disappearance after procainization of the nerve at the end of each experiment.

**Cardiac and respiratory modulation of splanchnic activity.** To evaluate the relative influences of the cardiac and respiratory cycles on splanchnic activity, an index called the respiratory-to-cardiac modulation ratio (RCMR) was calculated for each sample run. Two variants were type I and type II RCMR.

**Type I RCMR** is the ratio of the peak to peak (maximum to minimum) amplitudes of the respiratory-locked and the cardiac-locked summed waveforms. For each waveform, the normalized peak to peak amplitude (average counts per unit time), obtained from the CAT digital read-out, equals:

\[
\frac{X_{\text{max}} - X_{\text{min}}}{N t}
\]

where \(X_{\text{max}}\) = number of counts in the address with maximum number, \(X_{\text{min}}\) = number of counts in the address with minimum number, \(N\) = number of sweeps, and \(t\) = address duration.

**Type II RCMR** is the ratio of the root mean square deviations (RMSD) of the two waveforms. The normalized RMSD (counts per unit time) equals:

\[
\sqrt{\frac{1}{k} \sum_{i=1}^{k} (X_i - \bar{X})^2}
\]

\(\frac{1}{N t}\)

where \(k\) = number of addresses per sweep, \(X_i\) = number of counts in address \(i\), \(\bar{X}\) = mean number of counts for all addresses, \(N\) = number of sweeps, and \(t\) = address duration.

**Correlation functions.** The records from several experiments were analyzed with a digital correlation computer (Inter-technique Instruments Inc.) to give: a) the autocorrelation function of splanchnic potentials; b) the crosscorrelation function of splanchnic potentials and an ECG-triggered analog voltage pulse. Since the magnitude of the latter function depends on the amplitude and duration of the analog pulse, a calibration factor was determined by using a sine-wave generator to obtain the crosscorrelation between: a) a sine wave of known amplitude and \(b)\) an analog pulse triggered from the synchronizing pulse locked to the sine wave.

**RESULTS**

**General Features of Splanchnic Discharge**

Spontaneous efferent splanchnic discharge, monophasically recorded, consisted predominantly of slow waves having amplitudes in the range 10–30 \(\mu V\), with faster activity superimposed. The predominant frequency was about 10 cycles/sec; less commonly, waves with the frequency of the cardiac cycle (3–4/sec) were observed. An example of a 10/sec discharge pattern is shown in Fig. 1A (middle trace). Also shown (bottom trace) are the high-frequency components of the discharge, extracted from the original signal by a high-pass filter (time constant 5 msec).

![Picture of oscilloscope traces](http://example.com/fig1.png)

**FIG. 1.** Oscilloscope traces of splanchnic activity (negativity upward). **A:** Original monophasic recording. **B:** Signal after processing through a high-pass filter (time constant 5 msec). **C:** Monophasic recordings in A, B, and C.
it can be seen that during each slow wave there tends to be an increase of fast activity. The bottom trace of Fig. 1A is similar to recordings of sympathetic activity by other investigators (17, 18, 21, 28, 34) who used high-pass filters.

The existence of slow wave activity was dependent on connections between the spinal cord and lower brain stem, since high-cervical (C1) transection resulted in its disappearance (Fig. 1B), in addition, such sections eliminated nearly all the fast activity. There was, however, some residual activity after spinal cord section as shown by the fact that application of Xylocaine further narrowed the trace (Fig. 1C). The marked reduction in activity occurring following C1 section (performed in 12 cats) persisted for periods of observation up to 3 hr.

The existence of slow wave activity was not dependent on forebrain structures since the waves were seen in decerebrate as well as anesthetized cats.

In addition to the 10/sec activity, splanchnic discharge also showed oscillation in phase with both the cardiac and central respiratory cycles, maximum discharge usually occurring during diastole and during the inspiratory phase. The patterns of discharge in individual cats consisted of different combinations of the several periodic components, as shown in recordings from four vagotomized cats in Fig. 2. In cat A there was a combination of cardiac and respiratory modulation: during cardiac cycles in the late expiratory and the inspiratory phases, splanchnic waves were prominent with peaks in mid diastole; these waves were absent or reduced during the early expiratory phase. In cat B, the 10/sec waves were absent or reduced during the early expiratory phase. In cat C, the 10/sec waves of splanchnic activity, again tending to lock with the cardiac cycle, occurred predominantly during the inspiratory phase and were absent during the expiratory phase. In cat D, the respiratory modulation of splanchnic activity was different in phase from the previous cases; here, the 10/sec waves were most prominent in the late inspiratory and early expiratory phases.

Because of the variability of splanchnic activity, the periodicities were analyzed with an average-response computer by summing the potentials in computer analysis sweeps triggered from appropriate timing pulses.

**Cardiac Modulation of Splanchnic Discharge**

The component of splanchnic discharge time-locked to the cardiac cycle was revealed by computer summing in sweeps triggered by ECG-derived pulses. Two common patterns of cardiac modulation are shown in the summed waveforms of Fig. 3. In cat A the slow waves were locked in a 1:1 relation to the cardiac cycle, with minimum activity near the start of systole and maximum activity in mid diastole. In cat B, the 10/sec waves were locked in a 3:1 relation to the cardiac cycle.

The detection of cardiac modulation by means of time-locked summing is essentially an extraction of a periodic component from splanchnic potentials by crosscorrelation with a periodic pulse sequence derived from the ECG. Since in a given sample run the cardiac cycle duration showed little variation (range 1-5% in different cases), the ECG-derived pulse can be considered a scanning signal of fixed frequency. If a signal being analyzed has no component with the same frequency as the scanning frequency, the crosscorrelation function approaches zero (except for any d-c component) as the sample length becomes very large (36, chapt. 12). However, with a sample of finite length containing frequencies which are near to the scanning frequency, the crosscorrelation function may still exhibit a spurious periodicity due to insufficient averaging.

Therefore, to verify the reality of time locking, the procedure (illustrated in Fig. 3) was adopted of comparing histograms constructed from subsamples of different size. In cat A, the average peak to peak amplitude of the summed waveform, as well as its phase relation to the cardiac cycle, remained the same as N increased, while the base-line noise in the trace decreased. These results show that the computation was extracting a truly cardiac-locked component of splanchnic discharge; for according to signal theory (5), the time-locked signal tends to grow proportionately to N.
while the noise tends to grow only proportionately to $\sqrt{N}$. The case of cat B was more complicated. Here the slow wave frequency (10/sec) was almost exactly 3 times the cardiac frequency, and the question was whether the two periodic events were time-locked. The summed waveforms show that as $N$ increased, the phase relation of splanchnic potentials to the cardiac cycle remained the same; and the average peak to peak amplitudes were about the same for the two larger subsamples ($N = 500$ vs. $N = 250$). These results support the conclusion that the two signals were time-locked. The fact that the average peak to peak amplitude for the smallest subsample ($N = 125$) was larger might perhaps be due to insufficient averaging and incomplete elimination of unrelated frequencies, e.g., the periodic component in phase with the central respiratory cycle. The procedure shown in Fig. 3 was used routinely to validate the time relations observed in the summed waveforms.

Similar analyses, done in 21 cats, showed that in 16 cases there was predominantly 3:1 locking (as in Fig. 3B) and in five cases there was predominantly 1:1 locking (as in Fig. 3A). Examination of the summed waveforms showed that in general the time of maximum splanchnic activity was in early diastole (median 85 msec after peak systole), while the time of minimum activity was later in diastole (median 135 msec after peak systole). The observations are summarized in Fig. 4, which shows the incidence of the points of maximum and minimum splanchnic activity in the 21 cats. The nature of these time relations was not obviously related to a variety of factors, such as anesthetic condition, mean blood pressure, carotid sinus nerve section, or vagotomy (Table 1 in ref 24). The lack of obvious effect of vagotomy is apparent in Fig. 4.

The effect of vagotomy on the degree of cardiac modulation, as evaluated by the ratio of the peak to peak amplitudes of the summed waveform before and after vagotomy, was not consistent (increase in seven cases, decrease in six cases). This lack of consistency was probably due to the complication of the simultaneously occurring changes of respiratory modulation produced by vagotomy (cf. below).

**Autocorrelation Analysis of Splanchnic Discharge**

The ubiquitous occurrence of 10/sec periodicity and its temporal relation to the cardiac cycle prompted the application of correlation analysis to the records from four cats.

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**References**

1. This ratio was obtained from the computer analog readouts by the following calculations: the peak to peak amplitude chosen was the voltage swing from the third minimum to the fourth maximum of each correlogram (at a point where the noise component of the autocorrelogram had substantially decayed). The amplitude ratio (cross/auto) was 1:125 after correction for gain of the readout; if perfect locking had occurred, the expected ratio with the analog pulse used was 1:130 (from calibration with a sine-wave generator, see methods); therefore, the corrected amplitude ratio was $30:125 = 0.24$. 

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**Fig. 4.** Histograms of incidence of occurrence of maximum and minimum splanchnic activity during 6 portions of cardiac cycle. Maximum and minimum points were derived from CAT digital readouts.

**Fig. 5.** Comparison, in cats B and C, between autocorrelation function of splanchnic activity (top traces) and crosscorrelation function of splanchnic activity and an ECG-derived analog pulse of 3.2 msec duration (middle traces). Bottom traces: correlogram of arterial blood pressure signal and ECG-derived pulse. Arterial blood pressure (mm Hg): B, 90/40; C, 160/80.
FIG. 6. Original recordings and autocorrelograms of splanchnic activity before and after vagotomy (cat C of Fig. 5). Address duration 6 msec; sweep duration 480 msec. Each correlogram was derived from a sample run containing approximately 500 cardiac cycles. Arterial blood pressure (mm Hg): Pre, 210/130; Post, 160/80.

In the course of the study, it was observed that in some cats vagotomy seemed to increase 10/sec periodicity (see Fig. 9). This impression was confirmed in three cases by comparison of the autocorrelograms before and after vagotomy, as shown in Fig. 6. With intact vagi, the periodicity of discharge was quite irregular, a condition which led to a minimal degree of periodicity in the autocorrelogram. In contrast, after vagotomy the regularity of the waves was much greater, which resulted in a well-defined periodicity in the autocorrelogram.

In one cat (original recordings in Fig. 11), the autocorrelation function was computed for splanchnic activity at several end-tidal CO$_2$ levels. At the highest CO$_2$ level (8.2 %), the autocorrelogram showed a mixture of 10/sec periodicity and 4/sec periodicity (the period of the cardiac cycle); and when the end-tidal CO$_2$ was lowered, the 10/sec periodicity disappeared.

**Respiratory Modulation of Splanchnic Discharge**

The time relations of splanchnic discharge to the central respiratory cycle (indicated by efferent phrenic discharge) were revealed by computer summation in analysis sweeps triggered by the start of either the inspiratory or expiratory phase. As shown in the waveforms of Fig. 7, splanchnic activity increased during the I phase towards a maximum in the middle of the I phase; it then decreased, reaching a minimum during the early E phase; and it then increased towards a plateau level during the middle and late E phases. This was the most common pattern; it occurred over a wide range of respiratory cycle durations and in both decerebrate and urethane-anesthetized cats (Table 2 in ref 24). The incidence of the times of maximum and minimum splanchnic activity in 21 vagotomized cats is shown in Fig. 8, where it can be seen that maximum activity usually occurred in the middle of the I phase and minimum activity usually occurred in the early part of the E phase.

Several experimental procedures were used which changed the state of the respiratory centers and thereby also changed respiratory modulation of splanchnic discharge: a) vagotomy; b) change of CO$_2$ tension; c) change of anesthetic level. The general finding was that procedures which increased or decreased phrenic activity also increased or decreased, respectively, splanchnic respiratory modulation.

A typical example of the increase of splanchnic respiratory modulation produced by vagotomy is shown in Fig. 9, where it can be seen that after vagotomy there was a marked increase in the peak to peak amplitude of the summed splanchnic waveform. It can also be seen that a major portion of the increased activity during the inspiratory
SPLANCHNIC NERVE PERIODICITIES

TABLE 1. Effect of vagotomy on peak to peak amplitude of respiratory-locked component of splanchnic discharge

<table>
<thead>
<tr>
<th>Cat</th>
<th>Amplitude Ratio, Postvagotomy</th>
<th>Anesthetic State</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.1</td>
<td>D</td>
</tr>
<tr>
<td>2</td>
<td>3.3</td>
<td>D</td>
</tr>
<tr>
<td>3</td>
<td>3.0</td>
<td>U</td>
</tr>
<tr>
<td>4</td>
<td>1.9</td>
<td>U</td>
</tr>
<tr>
<td>5</td>
<td>1.6</td>
<td>D</td>
</tr>
<tr>
<td>6</td>
<td>1.4</td>
<td>U</td>
</tr>
<tr>
<td>7</td>
<td>1.3</td>
<td>D</td>
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<tr>
<td>8</td>
<td>1.2</td>
<td>U</td>
</tr>
<tr>
<td>9</td>
<td>1.2</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>0.8</td>
<td>D</td>
</tr>
<tr>
<td>11</td>
<td>0.8</td>
<td>U</td>
</tr>
<tr>
<td>12</td>
<td>0.7</td>
<td>U</td>
</tr>
</tbody>
</table>

Number of cats = 12. D = decerebrate. U = urethan. *Arranged in order of decreasing amplitude ratio, as calculated from summed waveforms. †Comparison between bilateral and unilateral vagotomy.

Phase was in the form of 10/sec waves. The effect of vagotomy was expressed quantitatively by the ratio of the peak to peak amplitudes of the respiratory-locked summed waveforms before and after vagotomy (Table 1). This ratio (postvagotomy-to-prevagotomy) was greater than 1.0 in 9 of 12 cases (range 5.1-0.7, median 1.4), indicating that vagotomy usually increased splanchnic respiratory modulation.

In the experimental preparation with intact vagi, the central respiratory cycle tends to synchronize with the pump cycle; but after vagotomy, the relation between the two cycles is random (as was shown by χ² analysis of the incidence of the I and E pulses in the pump cycle).

To avoid the possible complications due to vagal afferent input, which might act independently of central respiratory modulation, most of the experiments were done on vagotomized cats. The simplifying effect of vagotomy is shown in Fig. 10. It can be seen that with intact vagi splanchnic activity was modulated in phase with both the central respiratory and the artificial ventilation cycles; but after vagotomy splanchnic discharge, though still phase locked to the central respiratory cycle, was not related to the pump cycle, as shown by the flatness of the summed waveform time-locked to that cycle. Thus, in the experiments on vagotomized animals there was no significant influence of lung inflation on splanchnic periodicity; and, therefore, the observed respiratory modulation was due purely to central interactions.

Changes of CO₂ tension altered both the magnitude of phrenic discharge and of respiratory modulation of splanchnic activity. It can be seen in Fig. 11 that as end-tidal CO₂ was lowered there was a reduction of the peak to peak amplitude of the respiratory-locked summed waveform of splanchnic activity, together with a reduction of phrenic discharge. A similar change could be produced by a deepening of anesthetic level, which reduced splanchnic respiratory modulation concomitantly with phrenic discharge.

**Fig. 10.** Modulation of splanchnic discharge in phase with artificial ventilation and central respiratory cycles. *Left:* inkwriter traces. *Right:* CAT readouts of summed splanchnic potentials, each waveform derived from 60 analysis sweeps triggered by start of I phase.

**Fig. 11.** Effect of end-tidal CO₂ level on respiratory modulation of splanchnic discharge. *Left:* inkwriter traces. *Right:* CAT readouts of summed splanchnic potentials, each waveform derived from 60 analysis sweeps triggered by start of I phase.
Table 2. Respiratory-to-cardiac modulation ratio

<table>
<thead>
<tr>
<th>Cat*</th>
<th>Respiratory-Cardiac Modulation Ratio†</th>
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<tr>
<td></td>
<td>Vagi intact</td>
<td>Vagi sectioned</td>
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<td></td>
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<td>II</td>
</tr>
<tr>
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<tr>
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<td>0.3</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Number of cats = 19. D = decerebrate. U = urethan. *Arranged in order of decreasing ratio (largest ratio for each cat used). †Calculated from: type I: peak to peak amplitudes, and type II: root mean square deviations, of respiratory-locked waveforms triggered from start of I phase.

![Figure 12](image-url) Summed splanchnic waveforms illustrating the interaction of cardiac and respiratory modulation (N = 60 for each trace). Top: analysis sweeps triggered from start of I phase (left) and E phase (right). Five gates, each of duration 500 msec (time relations to respiratory cycle indicated by horizontal bars), were used to pass ECG-derived pulses. Each ECG-locked summed waveform (1–5) was derived from CAT analysis sweeps (address duration 1 msec) triggered by pulses falling during the appropriate gate. Bottom left: summed waveform of arterial blood pressure during ECG-triggered sweeps.

Interaction of Cardiac and Respiratory Modulation of Splanchnic Discharge

The relative strength of respiratory and cardiac modulation of splanchnic activity was evaluated numerically by the respiratory-to-cardiac modulation ratio. The values of this ratio in 19 cats are shown in Table 2; in 15 of these 19 cats the RCMR was greater than 1.0. Thus the average voltage oscillation in phase with the central respiratory cycle was greater, and often considerably so, than that in phase with the cardiac cycle. Furthermore, this relation held in both decerebrate and urethan-anesthetized cats.

The existence of interaction between cardiac- and respiratory-related periodicity was apparent in original recordings (Fig. 9), which showed that cardiac-related periodicity tended to be greater in some portions of the respiratory cycle than in others. This interaction was analyzed with the average-response computer by the method shown in Fig. 12. The splanchnic potentials were summed in analysis sweeps triggered from ECG-derived pulses which were sorted according to position in the central respiratory cycle. Thus, each waveform in Fig. 12 shows the activity in cardiac cycles which started in a particular portion of the respiratory cycle. It can be seen that the cardiac-locked component was considerably larger during cardiac cycles starting in the inspiratory phase (traces 1 and 2) than during those starting in the expiratory phase (traces 3, 4, and 5); and it was greater in the late than in the early expiratory phase (compare traces 3 and 5). This interaction between the two types of periodicity is a factor determining the value of the respiratory-to-cardiac modulation ratio.

Discussion

The importance of the splanchnic region and of splanchnic discharge in blood pressure regulation has long been known (3, 37). The effects of splanchnic nerve section and stimulation on several circulatory variables have been extensively investigated, and it has been concluded that a major portion of the activity in the nerve is vasoconstrictor in function (8, 33, 40, 50, 51). Further evidence for this vasoconstrictor function was provided by studies from this laboratory (24, 26), which showed a close relation between changes of blood pressure and of splanchnic activity. Therefore, study of patterns of splanchnic discharge should furnish important information on central vasomotor organization.

Three major types of periodicity were observed in splanchnic discharge: a) slow waves (frequency about 10/sec) synchronized to a greater or lesser extent with the cardiac cycle; b) discharge synchronized in a 1:1 ratio with the cardiac cycle; c) discharge phase-related to the central respiratory cycle. These periodic changes of activity did not usually produce fluctuations of systemic blood pressure, presumably because of the delays in transmission to, and excitation of, vascular smooth muscle (7, 23, 41, 49-51).

The first major type of periodic activity consisted of slow waves at about 10/sec. These waves arise from synchronized activity of individual fibers, as suggested by the facts that: a) higher frequency activity is superimposed on the waves (Fig. 1); b) individual sympathetic fibers fire in the frequency range 1–10/sec (6, 20, 29, 31, 35, 44, 54). In interpreting monophasic recordings from whole nerve, it should be borne in mind that the fluctuations of potential reflect summated activity of individual fibers. In particular, the difference between inhibition and desynchronized excitation was clearly shown in experiments involving brain stem repetitive stimulation (24, 34).

The ubiquity of the 10/sec waves in splanchnic recordings suggests that they reflect the fundamental organization of
the vasomotor centers. This suggestion is supported by the following considerations:

1) Similar periodicity has been found in other sympathetic nerves, such as cervical sympathetic (17) and inferior cardiac (27, 28, Fig. 7 in ref 44). The presence of this periodicity at different segmental levels suggests that it is of supraspinal origin; this idea is supported by the observation that the 10/sec waves disappear after cervical cord section (Fig. 1).

2) This type of activity is affected by afferent discharge related to the cardiac cycle, since in most cases the waves were at least partially locked in a 3:1 relation to the cycle (Figs. 3, 5). Furthermore, the degree of periodicity was increased after vagotomy (Fig. 6), an effect which could be partially due to elimination of vagal baroreceptor input.

3) Changes in this type of activity are associated with changes of blood pressure. For example, cervical cord section, which eliminates the waves (Fig. 1), also produces a drastic fall in blood pressure; and spontaneous rises or falls of blood pressure are often preceded by increases or decreases, respectively, of 10/sec wave activity (24).

4) An electric shock delivered to the medullary pressor region results in damped oscillation (at 10/sec) of splanchnic discharge following the initial evoked potential wave, and a similar oscillation follows an electric shock to the medullary depressor region (13); in each cat, the evoked oscillation had the same period as the spontaneous oscillation.

The presence of oscillation in neural systems suggests the existence of inhibitory feedback networks. The 10/sec oscillations in sympathetic discharge may be driven by oscillatory outflow from the brain stem vasomotor centers, possibly originating through interactions between the specialized pressor and depressor regions of the medulla (2, 9, 46), where electrical stimulation gives facilitation and depression, respectively, of sympathetic discharge, as well as poststimulus oscillation of splanchnic discharge (13). Alternatively, the medullary outflow may be nonoscillatory, producing oscillation by action on spinal cord feedback networks; in this case, the similarity of oscillations in different sympathetic nerves would be due to similar characteristics of the different spinal cord networks.

We may also suggest an analogy with the 70–100/sec oscillations in phrenic discharge (56), which can be influenced by electrical stimulation in a manner similar to splanchnic discharge (13).

The observations that the degree of locking of 10/sec waves to the cardiac cycle varied from case to case and that such locking was absent in a few cases (Fig. 5, cat C) mean that this periodicity arises independently, but can be entrained by afferent input related to the cardiac cycle. Among the factors which may influence the ease of entrainment is the relation between cardiac cycle duration and the intrinsic period of sympathetic oscillation (Figs. 3, 5).

In cases with a 1:1 relation of splanchnic waves to the cardiac cycle, the observed phase relations (maximum activity in early diastolic, minimum activity in late diastole) can be explained as a simple consequence of known baroreceptor reflexes (30): the increased baroreceptor discharge during systole causes a delayed inhibition of splanchnic discharge, while the fall of pressure from peak systole causes reduction of baroreceptor discharge, resulting in a delayed removal of inhibition. The relatively long delay between afferent and efferent activity changes may be explained by several factors: a) temporal dispersion of discharge from different baroreceptor fibers at the same vascular site (19, 22); b) differences in timing of baroreceptor discharge from different vascular sites (32); c) transmission delays within the complex networks of the vasomotor centers; d) travel time from medullary centers to splanchnic nerve (the minimum latency from an electric shock in the medullary pressor region to an evoked potential in the splanchnic nerve is about 40 msec (15, 24)).

The modulation of splanchnic discharge by the central respiratory cycle had a characteristic pattern: increasing activity throughout the late expiratory and early inspiratory phases, maximum activity in the middle of the inspiratory phase, and minimum activity in the early expiratory phase. Thus, the timing of maximum splanchnic activity is shifted relative to that of phrenic discharge, which is greatest at the end of the inspiratory phase. However, the splanchnic discharge pattern resembles very closely that of expiratory-inspiratory neurons (EI neurons) (14). Furthermore, the change of splanchnic discharge due to hypocapnia (Fig. 11) is similar to that of EI neurons: reduction of discharge during the inspiratory phase and increased discharge during the early expiratory phase (11). These similarities suggest that the respiratory modulation of splanchnic discharge is probably driven mainly from systems with phase-spanning discharge patterns (14).

The respiratory modulation of splanchnic discharge is a result primarily of outflow from the respiratory centers to the vasomotor centers, since it occurs when there is minimal sensory input related to ventilation, i.e., after neuromuscular blockade and vagotomy. However, when the vagi are intact, there is an important vagal afferent influence, since lung inflation, acting via pulmonary stretch receptors, produces a fall of blood pressure (16). In spontaneous breathing there is presumably a summation of a) central respiratory modulation, which tends to increase sympathetic discharge during the inspiratory phase, and b) vagal afferent modulation caused by inspiratory lung expansion, which tends to inhibit sympathetic discharge (16). The latter effect might explain the observation in some studies that there is an increase of sympathetic discharge during the expiratory phase of spontaneous breathing (42). If the central and reflex effects were of comparable strength, the final result could be absence of respiratory modulation of sympathetic discharge.

An interesting observation in the present study was the usually greater importance of respiratory than of cardiac modulation, as shown by the values of the respiratory-to-cardiac modulation ratio. A major contributing factor to this phenomenon seems to be the variation of cardiac modulation with time in the central respiratory cycle (lesser cardiac modulation in the early expiratory phase and greater modulation in the inspiratory phase, see Fig. 12).

It seems paradoxical that respiratory activity has a greater influence on sympathetic discharge than afferent input related to a specific cardiovascular variable (arterial pressure pulse). However, it should be kept in mind that in addition to the phasic baroreceptor input, there is tonic input produced by steady or slowly changing pressures (19,
The close temporal relationship between vasomotor and respiratory discharge indicates the existence of connections between the two systems. Compared to other factors, such as the inertia of the effector system and the mechanical changes due to ventilation, these relations are probably of relatively minor importance for vascular changes occurring within one respiratory cycle. However, the existence of important synaptic connections between the vasomotor and respiratory centers may play a major role in coordinating their activity during changing physiological conditions.

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