Spinal segments communicating resting sympathetic activity to postganglionic nerves of the stellate ganglion

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Kocsis, Bernat, and Katalin Gyimesi-Pelczer. Spinal segments communicating resting sympathetic activity to postganglionic nerves of the stellate ganglion. Am. J. Physiol. 275 (Regulatory Integrative Comp. Physiol. 44): R400–R409, 1998.—It has been shown earlier using sympathetic reflexes and anatomic techniques that preganglionic neurons controlling different effectors occupy wide and overlapping ranges of adjacent segments in the spinal cord (cardiac: T1–T7, vertebral: T2–T8). Because, however, the majority of preganglionic neurons are silent at resting states, the present study was designed to estimate the segmental map of subsets of these neurons including only those active at rest using simultaneous recordings from the inferior cardiac and vertebral nerves, under chloralose-urethan or urethan anesthesia. In 22 cats, thoracic white rami T1–T8 were cut in a sequential manner. Three-minute-long data segments were recorded between sectionings and analyzed in the frequency domain using the fast Fourier transform. We found that cardiac and vertebral active maps involved segments T3–T5 and T4–T8, respectively. In individual experiments, however, most of the power of rhythmic activity originated from only one or two segments and the dominant segments for the two nerves never overlapped. Moreover, the separation between dominant segments generating cardiac and vertebral nerve discharges was wider and the distribution of tonically active preganglionic neurons projecting to each nerve was narrower under urethan than under chloralose-urethan anesthesia. We conclude that the proportion of active to quiescent preganglionic neurons regulating cardiac and vertebral nerve discharges varies from spinal segment to segment and that active neurons projecting to these nerves are nonoverlapping.

cat; vertebral nerve; inferior cardiac nerve; heart regulation; chloralose-urethan anesthesia; urethan anesthesia

PREVIOUS ANATOMIC and electrophysiological studies aimed at locating organ-specific sympathetic preganglionic neurons (SPNs) agreed on two major characteristics of SPN distribution in the thoracolumbar spinal cord. First, SPNs targeting postganglionic neurons innervating a particular effector are widely distributed in the spinal cord (3, 5, 7, 12, 13, 20, 26, 30, 31, 34, 35), and second, segmental sympathetic representations of different organs greatly overlap (6, 11–13, 20, 27–29, 31, 34). At first sight, such arrangement of functionally different SPNs promotes uniform sympathetic reactions but appears disadvantageous for differential control of various organs and/or their circulation. All these studies, however, used supramaximal methods allowing functional conclusions only for reactions in which the majority of SPNs are coactivated. One prominent example is the flight-or-fight reaction (4, 12), when massive activation of the sympathetic nervous system is indeed manifested by excitation in all (or most) sympathetic effectors. For other situations when a number of SPNs are silent, as, e.g., at rest, the existing data are inadequate to draw legitimate functional conclusions. In fact, previous studies did not examine functional subsets of SPNs activated in any specific reaction; their goal was to describe the distribution of all SPNs available for the control system when adjusting a certain sympathetic effector. Thus there is no guarantee that the “active segments” are also widely distributed and for different effectors overlapping.

An adequate approach to this problem would be to examine the spinal distribution of specific subsets of SPNs activated in different situations, i.e., to build “active segmental maps,” which would not include inactive SPNs. For such analysis in the present study we have chosen two functionally different postganglionic nerves originating from the stellate ganglion and investigated the contribution of segmental outputs to their activities in resting conditions under chloralose-urethan anesthesia. We hypothesized that maps of SPNs involved in maintaining tonic sympathetic outflow may be different from those representing total SPN populations or SPNs activated by different stimulation.

The relationship between subsets of SPNs conveying tonic activity to different effectors in a certain state might be of specific importance because the level of correlation between basal activities of different circuits might influence (i.e., either facilitate or restrain) the chances of their coordinated operation during reactions emerging in that state. Tonic activity in sympathetic nerves appears as a more or less rhythmic (2–6 Hz) sequence of synchronized discharges of a varying number of postganglionic neurons. The characteristics of the sympathetic nerve discharge (SND) are similar in different nerves, and there is a high coherence between regional SNDs, suggesting that common or strongly related circuits are responsible for their generation (15, 18). Although the high nerve-to-nerve coherence is due primarily to shared bulbospinal inputs (2, 18), some synchronization is also possible in the isolated spinal cord (19). For either mechanism, the relative position of the final output neurons might be relevant.

Sympathetic neurons in the stellate ganglion of the cat receive input from thoracic segments T1–T9 (5, 25, 26). The highest number of SPNs projecting to the stellate ganglion is in T2 or T3. Other segments contribute less but a second peak was also reported in the distribution histogram at T5 (26). Similar distributions with minor differences were also found in other species, including rats, rabbits, and guinea pigs (7, 27, 28, 31). Some of these SPNs participate in the control of the heart through the inferior cardiac nerve (23, 36), whereas others regulate sympathetic effectors innervated by the vertebral nerve (13, 20). This latter carries postganglionic fibers from the stellate ganglion to the
brachial plexus via the cervical canal of the cervical vertebra.

In a recent study using the transneuronal retrograde viral labeling method, cardiac SPNs were found in segments T1–T7 of the rat (34), indicating that all segments projecting to the stellate ganglion may, in fact, reach the heart. Wide distribution of SPNs controlling the heart was also found in electrophysiological studies (13, 14, 20, 24, 33). Electrical stimulation of SPN axons in white rami (WR) T2–T6 elicited postganglionic activation in the inferior cardiac nerve (13, 33) and cardioacceleration (14, 20). Electrical stimulation of WR T4, T5, and the sympathetic trunk between T5 and T6 evoked large potentials in the vertebral nerve as well. Thus, although vertebral SPNs are located somewhat more caudal, SPNs activated by supramaximal stimuli significantly overlap for the two nerves.

The specific questions we asked were the following: 1) are spontaneously active SPNs proportionally distributed among all segments projecting to cardiac and vertebral postganglionic neurons; 2) do spontaneously active cardiac and vertebral SPN populations overlap; and 3) to what extent is the high coherence between cardiac and vertebral SND determined by intrasegmental connections between the two groups of SPNs?

**METHODS**

Surgical procedure. Experiments were performed on 22 cats of either sex weighing between 2.5 and 3.5 kg and anesthetized with intraperitoneal injection of urethane (1.8 mg/kg; n = 6) or a mixture of α-chloralose and urethan (50 mg/kg and 200 mg/kg, respectively; n = 16). Femoral vein and artery were cannulated on one side for drug injections and for monitoring arterial blood pressure, respectively. Core temperature was measured through a rectal thermometer. Electrocardiogram was recorded between two subcutaneous electrodes, one placed in the right forelimb and the other in the left hindlimb. The concentration of the CO2 in the expired air was measured using a Datex Normocap CO2 monitor. The animals were usually breathing spontaneously through a tracheotomy Y-tube. When necessary, artificial ventilation was introduced at later stages of surgery (during preparation of the WR) or right before the recording period. In these cases, to prevent spontaneous breathing against the cycle imposed by the ventilator, the cats were immobilized with intravenously injected picrocyanurium bromide. The use of muscle relaxants was also necessary in some experiments to avoid movement artifacts associated with sectioning WR.

Baroreceptor denervation and vagotomy were performed in 8 cats (all anesthetized with chloralose-urethan) by sectioning vagal and glossopharyngeal nerves on both sides as they exited the cranium. Sympathetic postganglionic nerves originating from the left stellate ganglion were approached retropleurally after the heads of the first and second ribs were removed. The left renal nerve was prepared retroperitoneally through a left flank incision (see Refs. 15–17 for further details). Central cut ends of the nerves were placed on a pair of platinum electrodes and covered with warm liquid paraffin. In the majority of experiments (n = 20), the activities of both vertebral and inferior cardiac nerves were recorded simultaneously. In the remaining two cats, cardiac SND was not recorded. Renal nerve recording was used as an auxiliary signal in all experiments.

The muscles covering the vertebral end of the ribs were removed on the left side and the thoracic WR (T1 through T8 or T12) were exposed from the surrounding tissue at their whole length, i.e., from the intercostal nerves up to the point where they joined the chain of the paravertebral ganglia. All WR and the sympathetic trunk at the most caudal WR were gently ligated with threads of different colors and covered with gauze soaked with saline.

Experimental protocol. For the recording period, cats were placed in a stereotaxic spinal unit. Nerve recordings and all control parameters were monitored, and the experiment was not started until at least a 30-min stable recording was obtained. Then a 3- to 3.5-min-long control data segment was recorded on tape and the WR were sectioned one after the other. In 19 cats, thoracic WR were dissected sequentially, either starting from the rostral or the caudal end (see Table 1). In three cats, WR were cut in the following order: T4, T6, T5, T3, T7, T1, T2, T8. After each sectioning, when the nerve and blood pressure signals stabilized, 3-min-long segments were recorded on tape. At the end, hexamethonium bromide was injected intravenously and residual signals were recorded from the nerve trunks. To minimize the chance of nonstationarities in the condition of the experimental animal,

| Table 1. Dominant segments of the spinal cord maintaining tonic SND in the postganglionic (vertebral and inferior cardiac) nerves of the left stellate ganglion in individual experiments |
|-----------------------------------------------|--|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Expt Baroreceptor denervation | Cut | T3 | T4 | T5 | T6 | T7 | T8 | Separation | Coherence |
| Chloralose-urethan anesthesia | | | | | | | | | |
| 712 | Int | C | V | - | - | 1 | 0.35 |
| 718 | Den | C | V | - | - | 1.25 | 0.95 |
| 704 | Int | -C | -V | - | - | 1.5 | 0.45 |
| 502 | Den | -C | -V | - | - | 1.5 | 0.5 |
| 710 | Den | -C | -V | - | - | 1.5 | 0.67 |
| 1,016 | Den | -C | -V | - | - | 2 | 0.15 |
| 918 | Den | C | -V | - | - | 2 | 0.7 |
| 418 | Int | -C | -V | - | - | 2 | 0.7 |
| 507 | Den | -C | -V | - | - | 2 | 0.77 |
| 11,186 | Int | -C | -V | - | - | 2.5 | 0.86 |
| 514 | Den | C | V | - | - | 2.5 | 0.3 |
| 1,099 | Den | -C | -V | - | - | 2.5 | 0.74 |
| 711 | Int | -C | -V | - | - | 2.5 | 0.7 |
| 1,111 | Int | -C | -V | - | - | 3 | 0.7 |
| 1,028 | Int | C | -V | - | - | 3.25 | 0.35 |
| Average | C | V | - | - | 3.5 | 0.35 |
| Urethan anesthesia | | | | | | | | | |
| 1,211 | Int | -C | -V | - | - | 2.25 | 0.83 |
| 715 | Int | -C | -V | - | - | 2.5 | 0.79 |
| 616 | Int | -C | -V | - | - | 2.75 | 0.75 |
| 421 | Int | -C | -V | - | - | 2.75 | 0.75 |
| 625 | Int | -C | -V | - | - | 3.5 | 0.92 |
| Average | C | -V | - | - | 3.75 |

WR, white rami; Int, intact; Den, denervated. Extent of disparity between neighboring segments contributing > 20% to vertebral and cardiac sympathetic nerve discharge (SND) is shown by placement of "V" or "C," respectively, proportionally closer to their dominant segment. Sectioning was started from rostral (1) or caudal WR (1) or WR originating from the expected dominant segments (3). Average separation is different if P < 0.05 (Student's 2-sample t-test). Urethan vs. chloralose-urethan: P = 0.016542. Denervated vs. intact: P = 0.141027 (chloralose-urethan); P = 0.008779 (all combined). * In these experiments, there was a second peak in coherence function at 10 Hz.
all efforts were made to perform this protocol as quickly as possible. The length of the recording samples was chosen to ensure reliable spectral estimates (18). The total recording period usually lasted 1.5 h.

Nerve recording and signal analysis. Postganglionic SND in different nerves were recorded monophasically, amplified with differential amplifiers, filtered between 1.5 Hz and 1.5 kHz, and, together with the arterial blood pressure signal, stored on magnetic tape. Off-line analysis of the recorded signals was performed after analog-to-digital conversion at a sampling rate of 250 Hz. This sampling rate exceeds the maximum expected frequency contained in the resting SND by 20 times and the highest possible frequency that can be found in SND during severe cerebral ischemia (17) by at least 5 times. After removal of any possible direct current shift and slow trends, the neurograms in 45–50 windows each containing 1,024 samples were subjected to Fourier analysis using the fast Fourier transform method, as described in detail earlier (18). Autospectra were computed for each SND and the coherence functions for different pairs of simultaneously recorded nerve signals using 3- to 3.5-min segments of continuous recordings. The power of the nerve signals was evaluated on the basis of the root mean square (RMS) value. Because most of the SND power in the autospectra occurred below 6 Hz, changes in the RMS mostly represented the changes in the basic rhythmic component of the SND. Experiments in which 10-Hz rhythm appeared in any of the SND autospectra (i.e., in a few urethan-anesthetized cats) were excluded from this study. The contribution of each segment to the total resting SND was calculated as the difference between the RMS before and after the WR was cut. Data obtained from different experiments were combined after normalization of the segmental contributions as the percentage of the difference between the control recordings taken in the intact cat and after ganglionic blockade.

RESULTS

In control recordings, all sympathetic nerves exhibited synchronized discharges appearing rhythmically with a characteristic frequency between 2 and 6 Hz (Fig. 1). In baroreceptor-intact cats (under both urethan and chloralose-urethan anesthesia; see METHODS), rhythmic sympathetic bursts were tightly locked to the cardiac cycle (Fig. 1A). In barodenervated cats, although working in the same range of frequencies, the cardiac and sympathetic rhythms were uncoupled (1). These characteristics of the SND did not change during sequential elimination of the preganglionic input to the sympathetic ganglia (see Figs. 1 and 3).

The changes in the activity of two nerves originating from the left stellate ganglion after sectioning of different WR are demonstrated in two representative examples in Fig. 1. In the experiment shown in Fig. 1A, in a baroreceptor-intact cat, we first cut WR T1, T2, T8,
T9, and the sympathetic trunk between T8 and T9 (Fig. 1Aa). There were no changes in the power or the character of either the cardiac or vertebral SNDs, indicating that the tonic activity of neurons in the stellate ganglion was entirely maintained by the remaining thoracic segments. The power of vertebral SND was reduced by 30% after sectioning of WR T7 and was completely eliminated after the WR T6 was also cut. At the same time, cardiac SND was not affected by sectioning of WR T7 and only slightly decreased by severing the preganglionic fibers travelling through WR T6 (by 15%) or WR T4 (19%). The largest decrease in the power of cardiac SND followed the elimination of the segmental output at level T5 (by 61%).

The other example (Fig. 1B) shows a baroreceptor-denervated cat in which sectioning of thoracic WR started at the rostral segments and followed caudally. In this experiment, cardiac SND was drastically reduced in power by sectioning of WR T4 while vertebral SND gradually decreased after cutting of WR T5 and T6.

Composite histograms summarizing the results of 22 experiments (Fig. 2) indicate that tonically active SPNs projecting to the stellate ganglion for the most part can be found from T3 through T8. Under chloralose-urethan anesthesia, resting activity of the two efferents originating from this ganglion were driven by SPNs located in 4–5 segments each, with a considerable overlap at levels T4–T6. The distributions were unimodal, with peaks located at different segments for the two nerves. On average, the largest input to cardiac SND was conveyed through WR T4, but significant cardiac activity originated also from segments T5 and T3. The origin of the vertebral SND was found more caudally, at segments T5–T7, with a maximum located at T6. In cats anesthetized with urethan, the distribution of tonically active SPNs appeared even more concentrated. Resting cardiac SND, in these experiments, mostly originated from two segments (T3 and T4), and the distributions of active vertebral SPNs were strongly concentrated in T6 with smaller contributions of segments T4–T7. As a consequence, there was less overlap between the two SND distributions in T4 and T5 than under chloralose-urethan anesthesia.

The width of the distribution histograms is determined by two factors, i.e., not only by the width of the individual histograms found in individual experiments.

Fig. 2. Distribution of power of tonic sympathetic activity transmitted to the inferior cardiac (A and B) and vertebral (C and D) nerves through different segments of the spinal cord in 16 cats anesthetized with chloralose-urethan (A and C) and 6 cats anesthetized with urethan (B and D). Bars show the percent decrease in power of sympathetic nerve discharge (SND) (mean and SE) after sectioning of corresponding WR.
but by the between-experiment variations as well. It was noticed, indeed, that the segment sending the strongest input to different postganglionic nerves varied between cats (compare, for example, cardiac SNDs, but not vertebral SNDs, in Fig. 1, A and B). Therefore, to estimate the relative role of these factors, a quantitative analysis of the autospectra and RMS values was performed for each experiment separately.

In most cats, the distribution of active segments had a very narrow peak confined to one or two spinal cord segments. This can be discerned from the overlapping autospectra calculated at different stages of elimination of the segmental input. In the experiment shown in Fig. 3A, vertebral autospectra calculated for control conditions and for recordings taken after sectioning WR from T1 through T5 were similar in magnitude and contained much more power than those calculated after sectioning of WR T6 and T7. Because the latter autospectra were also similar, it is evident that most of vertebral SND power was lost when WR T6 was cut. For the cardiac SND, this dominant segment turned out to be T4 because the amplitude of cardiac autospectra only changed when WR T4 was sectioned.

The contribution of the nondominant segments was weak, comprising only a few percent of the SND power. Nevertheless, the 1- to 6-Hz peak was present in the autospectra until all SNDs were completely eliminated, i.e., after WR from T1 to T7 or T8 were all cut or (as, e.g., experiment in Fig. 3A) after ganglionic blockade. Although the contribution to power by nondominant segments rarely exceeded the range of variations between control recordings, their significance was indicated by the fact that these residual SNDs showed high coherence with signals recorded from the other nerves with intact segmental inputs, e.g., the renal nerve, which was usually not affected by sectioning thoracic WR above T8 (see, e.g., Fig. 3A). Note, for example, that the shape and amplitude of the coherence function between vertebral and renal SNDs shown in Fig. 3B were strikingly similar for all recordings with the exception of the one taken after ganglionic blockade. Similarly, the coherence between cardiac and the other two nerves (renal and vertebral) decreased in this cat to near the significance level only after severing of WR T7, indicating that WR T5 and T6 still made a weak but significant contribution to cardiac SND.

The location of dominant segments in different cats is demonstrated in Table 1. For each cat, the WR contributing at least 20% of SND power are marked for both nerves. In some experiments (see for example expt 418 for vertebral and 514 for cardiac nerve), there was only one such segment; in others there were two (e.g., cardiac and vertebral in expt 711) or three (e.g., vertebral in expt 118). Even in these latter cases, however, the contribution of one segment was usually much higher than those of other segments. The extent of disparity between the neighboring segments contributing more than 20% to vertebral and cardiac SND is shown in Table 1. In the majority of experiments, one WR carried most of the SND power: RMS ~ 50% was found in 12 of 20 cardiac and 17 of 22 vertebral SNDs.

Fig. 3. Power spectra (A) of vertebral (VNA), inferior cardiac (CNA), and renal (RNA) sympathetic activities and pairwise coherences between these neurograms (B) during control, after sequential elimination of preganglionic input through WR T1 to T7, and after ganglionic blockade. Autospectra are scaled to the highest peak of power in each nerve signal recorded during the control period. Hex, hexamethonium bromide injection.
baroreceptors. Changes in heart rate, not exceeding
pressure never dropped below the threshold of the
in all recordings in baroreceptor-intact cats, the blood
indicated by significant SND-blood pressure coherence
and the recording taken after cutting all 7 or 8 WR. As
significant variations between different experiments
eral resistance. The decrease in blood pressure showed
hindered on a constant level through the series of manipula-
tions influencing both the cardiac output and periph-
eral resistance. The primary finding of this study is that, in contrast
5–10%, however, occurred usually after cutting the WR
exiting the dominant segment of the cardiac SND.

The separation of the dominant segments was not
affected by the order of sectioning the WR. This is
indicated in Table 1 by “random” mingling of experi-
ments in which sectioning started from the rostral or
caudal WR. (Note that the listing of experiments fol-
low the order of increasing values of the vertebral-
cardiac separation). The effect of the order of sectioning
on the location of the dominant segment was not
unequivocal, however. Although the largest effect on
vertebral SND appeared after cutting WR of T6 in most
experiments (n = 12) independent of the direction, T5
was found dominant (n = 2) only in experiments with
caudorostral and T7 in more experiments (n = 2 vs. 1)
with rostrocaudal direction of cutting the WR. The low
number of these observations did not allow for statisti-
cal analysis, but this finding suggests that in some
experiments convergence of SPN from different seg-
ments might have played a certain role. No such effect
was noted for the cardiac SND, and in some cats (e.g.,
expt 423, in which most of vertebral SND power was
lost on first cutting WR T7) it was evident even for
vertebral nerve that SPN convergence was not a con-
stant factor determining resting SND.

To further test the possible role of SPN convergence,
in three cats we first cut the WR originating from the
“expected” dominant segments (i.e., T4 and T6), fol-
lowed by WR T3, T5, T7, T1, T2, and T8. Figure 4 shows
the percent decrease of cardiac and vertebral SND
power both in anatomic order (Fig. 4, A and C) and in
order of WR sectioning (Fig. 4, B and D). The largest
decrease in cardiac SND power occurred on first cutting
WR T4 in two out of three experiments. Then, sec-
tioning WR T6 and T5 did not cause a considerable drop in
SND, but at T3 there was a second peak in the SND
power-WR curve. Two peaks were even more obvious in
Fig. 4D, representing vertebral SND corresponding to
large decreases of SND power after sectioning of WR T6
and T7 separated by no change after cutting of WR T5
and T3.

Coherence between vertebral and cardiac nerve sig-
als was between 0.70 and 0.95 in baroreceptor-intact
cats and between 0.15 and 0.77 after baroreceptor
denervation, similar to that reported in previous stud-
ies (18). The separation between the dominant seg-
ments supplying the two SNDs had no influence on the
nerve-to-nerve coherence.

DISCUSSION

The primary finding of this study is that, in contrast
to total SPN populations, the distribution of active
SPNs regulating different organs did not overlap, i.e.,
tonic SND in different nerves originated from different
segments even though the spinal maps containing all
SPNs projecting to these postganglionic nerves were
similar and extensively overlapping. The separation
between dominant segments determining tonic cardiac
and vertebral SNDs varied from animal to animal from
one to three segments and was found, on average,
higher under urethan than chloralose-urethan anesthe-
tively rare (e.g., expt 711), and three segments were
involved in maintaining cardiac SND in only two (expts
1,016 and 418) and the vertebral SND in 3 (expts 710,
918, and 1,118; Table 1), all under chloralose-urethan
anesthesia.

The dominant segments of the two nerves exiting the
stellate ganglion did not overlap in any of the 22 cats.
The separation between the primary sources of verte-
bral and cardiac SNDs varied from one to three seg-
ments. It should be noted, however, that in three
chloralose-urethan-anesthetized cats, although the
dominant segments remained well separated, signifi-
cant power was transmitted to both nerves by the same
WR (T5 in expts 502 and 710 and T6 in 1,016; Table 1).

Because the connections between 2- to 6-Hz SND
generators may change depending on different factors
such as anesthesia, baroreceptor input, etc., the effect
of the state of the central sympathetic networks on the
location of the segments activated in the spinal cord
was tested by comparison between groups of cats
anesthetized with different anesthetics and groups
with intact and denervated baroreceptors. We men-
tioned earlier that the distribution of SND power
carried by different WR appeared more focused when
urethan was used without chloralose for anesthesia
(Fig. 2). Data in Table 1 indicate that such concen-
tration of active SPN to fewer segments in this group
was due to both narrower distribution of active SPNs in
individual experiments and less variability between
different cats. As a consequence, the average separa-
tions of the dominant segments were also significantly
higher for urethan than chloralose-urethan anesthe-
tized cats (2.07 and 2.75 segments, respectively). It
should be noted that all differences between the two
groups reflected different features of the 2- to 6-Hz SND
generators because cats anesthetized with urethan
were only considered in this study if 10-Hz rhythm
appeared in none of the SND autospectra (see METH-
ODS).

There was no significant difference between the
separation of segments in baroreceptor-intact and -de-
nervated cats tested under chloralose-urethan anesthe-
sia. There seemed to be a possible shift of the vertebral
SPN population to more rostral segments after barode-
nervation (i.e., T5 was only dominant in barodener-
vated cats whereas T7 was dominant in intact cats), but
the sample size was too small to draw statistically
reliable conclusion. In addition, it was difficult to
evaluate the effect of baroreceptor input from these
experiments because the blood pressure could not be
held on a constant level through the series of manipula-
tions influencing both the cardiac output and periph-
eral resistance. The decrease in blood pressure showed
significant variations between different experiments
and measured up to 40% between the control recording
and the recording taken after cutting all 7 or 8 WR. As
indicated by significant SND-blood pressure coherence
in all recordings in baroreceptor-intact cats, the blood
pressure never dropped below the threshold of the
baroreceptors. Changes in heart rate, not exceeding
sia. The separation of active cardiac and vertebral SPNs did not significantly influence the nerve-to-nerve coherence. The differences between total and tonically active SPN populations concerned some other characteristics of their distribution functions as well. Active SPNs were confined to fewer segments, indicating unequal proportions in different segments of the active and nonactive SPNs projecting to the same organ. The peaks of the active segmental maps appeared at more caudal levels than those of the total SPN population, suggesting that segments on the falling limb of SPN distribution histogram containing fewer SPNs are mainly responsible for driving target-specific groups of postganglionic neurons at rest.

Segmental distribution of SPNs driving SND in the vertebral and inferior cardiac nerves. The signature of wide overlapping distribution of SPNs projecting to vertebral and cardiac nerves could be detected from our experiments as well. The nerve-to-nerve coherence is a very sensitive measure and could be used for this purpose. After cutting of the majority of WR projecting to a certain nerve, the coherence between the residual neurogram and an intact SND (renal in this study) remained significant. Thus we conclude that the signal still contained sympathetic activity. With the use of this parameter, SPNs projecting to the cardiac nerve were located at levels from T1 to T6/T7 and vertebral SPNs between T1/T2 and T8, i.e., well in line with available anatomic data (13, 20, 26, 30, 31).

Dominant segments were described in anatomic reports but these were not as sharp as the peaks in our distribution functions. For example, in the study by Pyner and Coote (27), the dominant segment (T2) contained 20% of SPNs projecting to stellate ganglion. Unfortunately, these studies mostly used total distribution histograms and did not analyze interindividual differences. Reference to the variability from animal to animal in the distribution of SPNs we could only find in one early report by Rubin and Purves (29). They noted that SPNs supplying the superior cervical ganglion shifted rostrally or caudally in different animals, indicating that the variability in our experiments probably reflected interindividual differences rather than shifting of the dominant segment in time.

The major source of afferents to the stellate ganglion is in T2/T3 segments, according to a number of studies in different species (7, 26–28, 31). A small subset of these SPNs, however, terminates on postganglionic neurons directed to effectors in the head, which places the distribution of the cardiac and vertebral population somewhat more caudal. Although transneuronal labeling data were published for cardiac SPNs (30, 35), these only reported the segmental extent (T1–T7) and did not specifically name the dominant segment. Cardioacceleration was best elicited by stimulation at level T2 (3, 32) or T3 (14), and evoked potentials in the inferior cardiac nerve reached their maximum when WR T3 was stimulated (14). It should be noted, however, that cardiac responses could be mediated in part (i.e., in a few per hundred) by postganglionic nerves other than inferior cardiac nerve and that the evoked potentials were larger from WR T4 than T2 (14). Therefore, the
degree of the caudal shift is difficult to estimate precisely. This is also emphasized by the results of Ninomiya et al. (24) reporting a 36 and 27% decrease in spontaneous cardiac SND after cutting of WR T3 and T4, respectively, in a smaller sample. The same applies to vertebral SPNs, the exact distribution of which is even less certain from previous literature (13, 20, 26, 33).

It should be noted that the contribution of different segments was estimated in this study by using an indirect measure of the decrease of SND after the corresponding WR was cut. Such an approach assumes that the activities carried by each WR are summed in the postganglionic nerve and ignores the possible consequences of the integrative function of sympathetic ganglia. Suppose, for example, that the activation of converging SPNs projecting through several WR are necessary to bring the majority of postganglionic neurons to discharge threshold. In this case, SND power would be lost before sectioning of all active WR and we should systematically find the apparent “dominant” segment more rostral in experiments in which WR were cut in a rostrocaudal order than in cats where WR sectioning started at caudal and followed to rostral segments. On the other hand, if occlusion of preganglionic inputs played a significant role in determining spontaneous output of the stellate ganglion, it would shift the dominant segment in the opposite direction. Such statistical bias was not found, however, in our experiments with sequential cutting of WR and the results of experiments in which the WR were sectioned “randomly” (Fig. 4) pointed clearly against modification of the dominant segment by ganglionic integration. Although not under the conditions of our present experiments, ganglionic integration may be important, however, and its effect has to be considered when the level of sympathetic activity changes.

Dynamic functional segmental separation of SPNs. Our study only concerned the distribution of SPNs that are spontaneously active in anesthetized cats, and even these were found different when we used different anesthetics. The wide total SPN distribution has the potential of a number of different groupings that would involve various SPN subsets up to the generalized excitation (4, 12) of the majority of SPNs in different segments. The activity of SPNs in different situations might be organized in different ways. Various reflexes or activation of distinct subsets of supraspinal premotor neurons (2, 8, 21) may influence specific groups of SPNs other than those active at rest. Alternatively, the organization may be such that changes in the level of sympathoexcitation would gradually recruit more and more SPNs controlling a certain region. In three of our cats, there was an overlap between the cardiac and vertebral SPN populations, which may have signified a certain level of a generalization of the sympathetic outflow in which neurons outside the dominant segment were recruited. In these experiments, the dominant segments remained clearly separated, but this separation may possibly become weaker at a higher level of excitation.

Segmental grouping of cardiac and vertebral SPNs does not imply homogeneous segments. There are several lines of evidence indicating that individual spinal cord segments accommodate distinct subsets of SPNs with different characteristics and regulating various tissues (6, 9, 11, 22, 28). Our present results also support intrasegmental heterogeneity of SPNs. Consider, for example, the population of SPNs in the fourth thoracic segment of the spinal cord of a cat in which the dominant segments for tonic cardiac and vertebral SNDs are T4 and T6, respectively. In this cat, T4 will contain a relatively large number of tonically active SPNs (as T6 will do, as well), and from earlier studies we know that subsets of SPNs projecting through WR T4 will terminate on vertebral as well as cardiac postganglionic neurons in the stellate ganglion. Nevertheless, at this level of the spinal cord, only those SPNs regulating the heart will be active in resting states whereas those projecting to the vertebral nerve will remain silent. Following the same logic, differential activation of vertebral SPNs but not cardiac SPNs can be shown in T6. Thus the present study provides direct evidence that specifically dedicated neurons in a certain segment may be selectively activated by the descending input maintaining tonic sympathetic outflow.

The flexibility of the pattern of activation of groups of SPNs was reflected in the differences found between chloralose-urethane- and urethan-anesthetized cats. It is known that anesthetics have a profound effect on sympathetic nerve activity. In particular, it has been demonstrated that the characteristics of synchronized SND are differentially affected by the two anesthetics used in the present study. Under chloralose-urethane anesthesia, the dominant frequency of synchronized SND is between 2 and 6 Hz, or at the heart rate (1, 18), whereas in cats anesthetized with urethan a second spectral peak may appear around 10 Hz (10), especially after baroreceptor denervation. Depending on the level of anesthesia, either one of these components may dominate the SND, or the two rhythms may coexist in the same nerve. In the present study, we were able to show that due to the actual organization of the central sympathetic generators under different types of anesthesia, their control over SPNs may differ even if the level or the basic characteristics of SNDs are similar.

Baroreceptor input has also been shown to have an important effect on both the level and the rhythmic characteristics of SND. Although the location of the dominant segments were not identical in baroreceptor-intact and -denervated cats, neither the distribution of segmental contribution to the SND power nor the separation between active cardiac and vertebral SPN populations was found significantly different. It should be noted, however, that since sectioning WR changed the blood pressure and heart rate, the baroreceptor input could not be considered constant in baroreceptor-intact cats. Therefore, comparison between the two groups could be misleading.

Although the majority of cardiac and vertebral SPNs exhibiting rhythmic SND were located in different
segments, there was always a highly significant coherence between the two SNDs. As reported previously (15–18), the coherence was higher in baroreceptor-intact than in baroreceptor-denervated animals. The coherence values, however, did not show any correlation with the relative position of SPNs driving rhythmic activity in the two nerves, i.e., the coherence was not any higher in cats with closely located dominant segments compared with those in which these were separated by 2–3 segments. Moreover, the coherence was equally high between intact SNDs and the residual signals after eliminating most of the power in the neurograms by serially cutting a number of WR, indicating that resting activity in the dominant segments and in other segments contributing minimal excitation to these nerves originated from common or strongly coupled sources (15, 18).

Perspectives

The major issue addressed in this study is whether a functional topography of SPNs exists in the spinal cord. This hypothesis has been most recently discredited by Taylor and Weaver (34) on the grounds provided by anatomic and electrophysiological studies using supramaximal stimuli. Our present results suggest that, although wide and overlapping distribution, adequate for Cannon-type reactions (4, 12), characterizes total SPN populations in general, the distribution of active subsets of SPNs does not necessarily follow this principle and may harmonize with differential sympathetic control.

The two nerves originating from the stellate ganglion serve different functions. Moreover, both are multifunctional, consisting of fibers directed to different effectors of the same organ or region. Whereas the inferior cardiac nerve is involved in the regulation of many different aspects of the cardiac function, the vertebral nerve contains fibers controlling circulatory and noncirculatory vegetative effectors in the domain of innervation of the brachial plexus. Segmental grouping of functionally related SPNs has two aspects that are advantageous for network processing. On one hand, closely positioned SPNs targeting the same effector or anatomically functionally related effectors (e.g., sinus node, ventricular muscles, coronaries, conducting system, etc., in the heart) may acquire common modulatory input through descending systems and/or segmental afferents and may participate in intrinsic circuitry with local connections, common interneurons, etc., assisting integration. On the other hand, spatial separation of neurons serving different organs would grant them a certain level of independence, facilitating their differential control.

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