Electrophysiological Study of Cardiovascular Neurons in the Rostral Ventrolateral Medulla in Rats

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SUMMARY. In urethane-anesthetized rats, electrophysiological recordings of spontaneously active neurons in the vasopressor area of the rostral ventrolateral medulla were analyzed for participation in cardiovascular regulation. A total of 138 units were found which were inhibited by transient increases in mean arterial pressure elicited by intravenous injection of norepinephrine, aortic occlusion, or electrical stimulation of the hypothalamus, with 100% inhibition occurring at 148 mm Hg. Histograms of postsystolic activity showed that these units had pulse-synchronous rhythms which grew more prominent as arterial pressure increased. Furthermore, electrical stimulation of the superior laryngeal nerve, which elicited a vasodepressor response, strongly inhibited these units. Thus, these neurons were termed negatively correlated cardiovascular units. At least half of these cells project to or through the thoracic spinal cord. In addition, arterial pressure sensitivity is conveyed through carotid sinus and aortic arch afferents. Approximately half of the cardiovascular units are also excited by hypothalamic stimulation. Finally, analysis of neighboring cells showed that it is possible to distinguish between cardiovascular and respiratory units. These data are consistent with the concept of a medullary center which supports tonic sympathetic vasomotor tone and which mediates baroreceptor reflexes, as well as vascular responses of the defense reaction. (Circ Res 56: 359-369, 1985)

THE importance of the rostral ventrolateral medulla oblongata in cardiovascular regulation has been demonstrated repeatedly. Tonic arterial pressure maintenance requires the integrity of this area (Reis and Cuenod, 1965; Dampney and Moon, 1980). Electrical and chemical stimulation of the area elicits a powerful vasopressor response comprised, in part, of femoral and renal vasoconstriction (Dampney and Moon, 1980; Ross et al., 1984a). Microinjection of muscimol, an agonist at receptors for 7-aminobutyric acid (GABA), in the vasopressor area of the rostral medulla reduces arterial pressure to basal levels (Willette et al., 1983). Finally, anatomical evidence indicates that reticulospinal neurons of the area project specifically to the intermediolateral cell column and the central autonomic area of the spinal cord (Amendt et al., 1983; Ross et al., 1984b).

Similarly, the rostral ventrolateral medulla participates in baroreceptor reflex control of arterial pressure. Application of glycine to the surface of the medulla just ventral to the rostral pressor area not only reduces resting arterial pressure, but also greatly reduces the vasoconstrictor response to carotid occlusion (Winnergren and Oberg, 1980). Furthermore, microinjection of muscimol into the vasopressor area blocks the depressor response to aortic nerve stimulation (Willette et al., 1983).

In addition, the rostral ventrolateral medulla integrates cardiovascular responses originating in the hypothalamus. Microinjection of bicuculline methiodide, an antagonist at receptors for GABA, into the vasopressor area enhances pressor responses elicited by anterior hypothalamic stimulation (Willette et al., 1984). Topical applications of glycine to the medullary surface greatly attenuates the vasoconstrictor components of the defense reaction (Hilton et al., 1984). Because of the concomitant reduction of resting arterial pressure, Hilton et al. proposed that the same pool of medullary neurons that integrates the defense reaction also provides basal sympathetic tone; they also suggested that the medullary neurons are tonically excited by hypothalamic drive.

Electrophysiological recordings in the intermediate portion of the nucleus paragigantocellularis lateralis have shown the existence of neurons with axonal projections to the thoracic spinal cord and with pulse-synchronous rhythms (Brown and Guyenet, 1984). These cells are also acutely sensitive to pharmacologically induced changes in arterial pressure. Thus, these neurons were proposed to be cardiovascular neurons mediating baroreceptor signals to the spinal preganglionic neurons. The purpose of the present study was to further examine the role of these cardiovascular neurons in baroreceptor reflexes and in the integration of hypothalamic vasopressor responses.

Methods

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hindlimb toe pinch until termination of the experiment, at which time the animals were killed with a bolus injection of a saturated solution of potassium chloride. The animals were placed on a heating pad to maintain rectal temperature at 37°C. After tracheal intubation, the animals were respirated with a minute volume of 600-780 ml/kg. End tidal CO₂ was continuously monitored and regulated between 3.5 and 5.0% by adjusting tidal volume. Arterial pressure was monitored through a catheter in the femoral artery or the brachial artery in experiments utilizing aortic occlusion. The tapered tip of a second large catheter which housed five smaller catheters was placed in the femoral vein or into the tubing of a butterfly catheter inserted into a tail vein; this catheter was used for the injection of small boluses (10-50 µl) of norepinephrine (150 M\(\text{g} \text{ml}^{-1}\)) or the vasodilator, sodium nitroprusside (0.5 M\(\text{g} \text{ml}^{-1}\)).

The right marginal mandibular branch of the facial nerve was exposed and the tip of a concentric bipolar stimulating electrode (David Kopf Instruments, NE100) was implanted in the fascia surrounding the nerve. Typical stimulation parameters for antidromic activation of the facial nerve were: 1-2 mA, 200 \(\mu\)sec, 1 Hz. At this intensity, orthodromic activation of muscles underlying the vibrissae (several centimeters distal) was observed and provided an index for successful stimulation of the nerve. Direct activation of muscles adjacent to the electrode usually required a stronger stimulus.

For hypothalamic stimulation, a small opening was drilled in the parietal bone 5.7 mm rostral to lambda. This permitted placement of an electrode in the ipsilateral dorsomedial hypothalamus at 10 mm lateral to the midline and 9.0 mm below the cerebral surface, according to the atlas of Paxinos and Watson (1982). The location of the electrode could be confirmed by the large pressor response—up to 100 mm Hg—produced by electrical stimulation (10-sec train, 250 Hz, 100 Hz, 300 Hz). Stimulation sites were verified histologically.

Another stimulating electrode was implanted in the spinal cord, following a laminectomy at thoracic (T3-T4) levels. The tip of the electrode was placed 0.5-1.0 mm lateral to the midline and 1.0-1.5 mm below the dorsal surface of the spinal cord. These coordinates approximate the location of the intermediolateral cell column; however, histological verification was not attempted. Stimulation parameters were 10-50 \(\mu\)A, 10 Hz, 100 Hz, 500 \(\mu\)sec. Stimulation sites were verified histologically.

In two experiments, baroreceptor nerves were transiently blocked with a local anesthetic. Bilaterally, catheters were gently inserted into the nerve sheath of the vagosympathetic nerve trunk and pushed rostrally to the region of the nodose ganglion. The carotid sinus nerves were denervated and the superior laryngeal nerves were transected. After identification of a cardiovascular neuron, 50 \(\mu\)A of chloroprocaine (Nesacaine, 20 mg/ml) was superfused onto the region of the nodose ganglion. Several washes with normal saline (1 ml total) through the same catheter over the next 30 minutes was sufficient for recovery of properties of cardiovascular neurons. The animals in these experiments were initially anesthetized with ether, rapidly tracheotomized and intubated, and subsequently anesthetized with halothane (Fluothane, 0.8%) and maintained anesthetized by inhalation of 4% halothane, 66% nitrous oxide,N₂O, and 26% oxygen.

In one experiment, the brainstem was hemisected with a retractable wire knife lowered on a micromanipulator. The transection was made at the midcollular level. Post-mortem examination of the brain confirmed the completeness of the transection. At the end of an experiment, a deposit of fast green dye was made by passing a 20-\(\mu\)A current for 20 minutes. Subsequent histological processing permitted location of the recording sites, which were then mapped on standardized sections adapted from an atlas (Paxinos and Watson, 1982).

Post-event histograms of unit activity and averaged arterial pressure or tidal CO₂ waveforms were generated with a computer (Tracor Northern TN-1505). The latter was triggered with the gate output of an oscilloscope which was itself triggered from the arterial pressure or tidal CO₂ signals. Cardiac electrical activity could be evaluated by electrocardiogram (ECG) waveform generated by signal averaging the recording electrode signal over more than 200 cycles. Statistical comparisons were made using analysis of variance techniques (Yamane, 1964). Values are reported as mean ± SD.

**Results**

**Electrophysiological Location of the Vasopressor Center in the Ventrolateral Medulla Oblongata**

Stimulation of the facial nerve elicited a field potential with a latency of 2 \(\mu\)sec (peak) in the nucleus of the facial nerve (Fig. 1). This field poten-
was used to map the medial, lateral, ventral, and posterior boundaries of the facial nucleus. The stereotaxic coordinates of these boundaries permitted reliable location of the powerful "vasopressor" area which lies immediately caudal to the facial nucleus, close to the ventral surface of the medulla. Stimulation of this area with recording electrodes using 12.7 ± 3.2 mA (0.2 msec, 50 Hz for 3 sec) (Fig. 1) produced increases in mean arterial pressure of 33.3 ± 4.7 mm Hg (n = 3). Neurons with cardiovascular properties (described below) were found in a region which coincided precisely with the focus of this vasopressor region, within a column approximately 400 um in diameter and 600 mm long, extending from the caudal end of the facial nucleus to the rostral end of the inferior olivary complex. The middle panel of Figure 1A shows the rostral end of the recording area. At this level, a few motorneurons of facial nucleus can still be seen.

Cardiovascular Neurons of the Vasopressor Center

Single-unit recordings identified a total of 138 cardiovascular neurons, characterized by their immediate and complete decrease in activity (as a result of either inhibition or disfacilitation) during the rapid rise of arterial pressure produced by a bolus injection of norepinephrine and by the recovery of activity to basal levels that followed closely in time the return of arterial pressure to resting levels (Fig. 2A). Figure 2B shows the response curve of a typical unit: there is a relatively linear region of high sensitivity to changes in mean arterial pressure and a cut-off pressure above which the unit is completely silenced. When arterial pressure was reduced below resting levels with vasodilator drugs, unit activity reached a maximum at pressures of 60-85 mm Hg and did not increase further, as pressure decreased. These cardiovascular neurons were called 'negatively correlated' because of the negative slope of the pressure sensitive portion of the response curve.

A second characteristic of these cardiovascular neurons was a cardiac rhythm manifested only at elevated arterial pressures, which shifted unit activity to the highly sensitive portion of its response curve (Fig. 2D). At lower pressures, for which unit activity lies in its pressure-insensitive region, pulse-synchronous rhythms were diminished or absent (Fig. 2C). Maximal inhibition of unit activity occurred at 74.3 ± 7.8 msec after the R-wave, with 80% inhibition occurring approximately 8 msec earlier (n = 21).

Three cardiovascular neurons were analyzed for pulse-synchronous rhythms when impulses in nerves carrying baroreceptor signals were transiently blocked. In animals with bilateral carotid sinus denervation and superior laryngeal nerve transection, the remaining baroreceptor nerves—vagus, aortic nerve, and sympathetic chain—were anesthetized with chloroprocaine. The cells lost virtually all sensitivity to changes in arterial pressure and displayed only slight pulse-synchronous activity in one case (Fig. 3B) and none in two other cases. Activity which was both pressure-sensitive and pulse-synchronous returned after washing out the anesthetic (Fig. 3C).
Respiratory Neurons

Neurons with prominent rhythms synchronized to the respiratory cycle were commonly encountered in the region 200-300 μm dorsal to the region where the cardiovascular neurons were found (Fig. 4B). These cells commonly showed an acute sensitivity to plasma CO2 levels. Because these cells are located in the region of well-defined respiratory cell groups and have a prominent sensitivity to events linked to respiration, we have classified them as respiratory units. The response of respiratory cells to changes in arterial pressure was highly variable between cells (Fig. 4A). Frequently, activity decreased when arterial pressure increased, but with a generally poor temporal correlation of the two events. Furthermore, unit activity never displayed any cardiac rhythm, even when examined at elevated pressures (Fig. 4C).

Cardiovascular neurons were examined for possible involvement in respiration. At resting arterial pressures, these cells never showed any detectable respiratory rhythm (Fig. 2E). At elevated arterial pressures, an apparent respiratory modulation of unit activity appeared (Fig. 2F). However, closer examination revealed that arterial pressure was modulated during the respiratory cycle (Fig. 2F) and that the change in unit activity was appropriate for the respiration-related changes in arterial pressure at the new operating point on the response curve (Fig. 2B). These observations were confirmed for five cardiovascular units, and suggest that the respiratory modulation of unit discharge is a result of respiratory modulation of arterial baroreceptor activity.

Responses to Aortic Occlusion

Occlusion of the abdominal aorta with a snare produced a rapid, transient rise in arterial pressure. This stimulus was used to examine the responses of six cardiovascular units; all units showed a decreased activity, proportional to the increased pressure (Fig. 5A). Moreover, the activity-pressure response curve for the snare coincided with the response curve generated with a bolus injection of norepinephrine (Fig. 5B). In the immediate vicinity of the cardiovascular neurons, the responses of four non-respiratory, non-cardiovascular units were examined; these cells did not respond to the snare-induced pressure rise (Fig. 5C).
Responses to Superior Laryngeal Nerve Stimulation

A total of 18 units were studied for responses to a short electrical stimulation of the superior laryngeal nerve (2-5 sec train, 100-400 nA, 100 Hz, 200 μsec), which caused an immediate, transient decrease in arterial pressure to approximately 50-60 mm Hg. Nine cardiovascular neurons were tested, and all responded with an immediate reduction of activity, ranging from 70-100% (Fig. 6A). Five respiratory neurons were tested and all were unresponsive. Four neurons that did not have respiratory rhythms and were not sensitive to norepinephrine-induced changes in arterial pressure were also tested; three were unresponsive (Fig. 6B) and one was excited.

The Effects of Selective Deafferentation on Cardiovascular Neurons

Arterial baroreceptor fibers are known to travel in the vagus/aortic nerve/cervical sympathetic chain complex, carotid sinus and superior laryngeal nerves (Krieger and Marseillan, 1964). Cardiovascular neurons were studied in three different groups of partially baroreceptor-innervated animals: (1) carotid sinus afferents intact (vagus/aortic nerve/sympathetic chain complex, and superior laryngeal nerve transected); (2) aortic arch afferents partially intact and carotid sinus afferents intact (vagus/aortic nerve/sympathetic chain complex transected); (3) vagus/aortic nerve/sympathetic chain afferents intact (carotid sinus denervated). In all cases, cardiovascular neurons could be identified; however, many cells could not be fully silenced at pressures obtained by bolus injection of norepinephrine. For these cells, cut-off pressures were estimated by extrapolating the highly pressure-sensitive portion of the curve to the abscissa. With only carotid sinus afferents intact, cut-off pressure was 178.5 ± 32.7 mm Hg (n = 10). With carotid sinus and superior laryngeal nerve afferents intact, cut-off pressure was 169.8 ± 16.6 mm Hg (n = 10). In both groups of
vagotomized animals, cardiovascular neurons displayed prominent pulse-synchronous rhythms when histograms of post-systolic activity during elevated arterial pressure were examined. With only carotid sinus afferents denervated, cut-off pressure was 142 ± 20.3 mm Hg (n = 3). In fully innervated animals cut-off pressure was 148.3 ± 21.3 mm Hg (q.v. Table 1).

Responses to Hypothalamic Stimulation and Midbrain Transection

Stimulation of the dorsomedial hypothalamus at moderate intensities (less than 250 μA) caused large increases in arterial pressure. All cardiovascular neurons tested were inhibited subsequent to the pressure increase, with a time course similar to that seen with pharmacological pressor responses (Fig. 7 A). During the stimulus train, however, some units (10 of 19) were excited (Figs. 7 A, 10C), and other units (9 of 19) were either inhibited (Fig. 10D) or unaffected. Respiratory neurons were uniformly excited by the same stimulation, and the excitation lasted several seconds beyond the stimulation (Fig. 7B).

Five cardiovascular neurons were identified in one animal with a midcollicular transection. Maximal firing rates ranged from 10-42 spikes/sec, and cut-off pressures ranged from 124-152. These values were similar to those found in animals with intact neuraxes.

Electrophysiological Characteristics of Cardiovascular Neurons

The recorded spikes of cardiovascular neurons commonly displayed biphasic (positive/negative) waveforms. Frequently, constant latency spikes were evoked by electrical stimulation of the upper thoracic spinal cord; these spikes followed high frequency stimulation. A total of 84 negatively correlated cardiovascular neurons were tested for antidromic activation from the thoracic spinal cord: 44 were identified as antidromically activated (52%) on the basis of collision of spontaneous spikes and evoked spikes. Latencies were quite variable between cells, ranging from 4.5-95 msec. A natural consequence of the high level of activity of many of these cells was the collision of most antidromic impulses with spontaneous impulses. Only when
the cells were tested at elevated pressures were antidromic impulses reliably observed.

Calculated axonal conduction velocities varied from 0.4-8.5 m/sec (Fig. 8). This wide range of conduction velocities is not characteristic of any single fiber type. Indeed, a natural division of conduction velocities appeared between 1.1 and 2.0 m/sec, suggesting that at least two fiber types may be represented in the data. Thus, the data were further analyzed on the basis of this arbitrary division (Table 1). The maximal firing rates and sensitivities of the two groups were markedly different. Cut-off pressures were not different. These results are illustrated in Figure 9 with response curves based on the averaged data. Threshold pressures (the arterial pressure at which inhibition is first apparent) can be estimated from the response curves: 62 mm Hg for group 1 and 88 mm Hg for group 2.

Spike Amplitude Modulation
A striking and consistent characteristic of the cardiovascular neurons was the modulation of spike amplitude according to the ongoing activity of the units (Fig. 10). Spike amplitude was minimal when

<table>
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<th>TABLE 1</th>
<th>Electrophysiological Properties of Antidromically Identified Cardiovascular Neurons</th>
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<tr>
<td>Group</td>
<td>Conduction velocity (m/sec)</td>
</tr>
<tr>
<td>Pooled</td>
<td>2.33 ± 2.04 (44)</td>
</tr>
<tr>
<td>1</td>
<td>0.64 ± 0.21 (20)</td>
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<tr>
<td>2</td>
<td>3.83 ± 1.75 (24)</td>
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Results are expressed as mean ± SD.
* P < 0.05, comparing group 1 and group 2.
unit activity was high as a result of low arterial pressures (Fig. 10A). When hypothalamic stimulation further increased the activity of cardiovascular units, further reduction in spike amplitude was seen (Fig. 10C). In contrast, spike amplitude increased whenever unit activity decreased. This situation was observed without exception: when pressure was increased by norepinephrine injections or by hypothalamic stimulation (Fig. 10, A and C); when stimulation of the superior laryngeal nerve reduced arterial pressure (Fig. 10E); when hypothalamic stimulation reduced unit activity prior to pressure changes (Fig. 10D). Finally, a train of high frequency antidromic spikes showed the same gradual reduction in amplitude between initial and final spikes, whether at resting or elevated arterial pressures (Fig. 10, F-H).

Discussion

This study demonstrates that, within the potent vasopressor region of the rostral ventrolateral me-

dulla, there exists a group of neurons that are spontaneously active, are strongly inhibited by increases in arterial pressure, and project to the spinal cord. The pressure sensitivity is observed within the cardiac cycle, as well as in transient changes in mean arterial pressure. Moreover, these cells have properties that are distinctly different from respiratory neurons in the same vicinity. Because the cells are found in close association with the region of the medulla which controls basal vasomotor tone, have spinal projections, are acutely baro-sensitive in a wide variety of circumstances, and do not display
any significant respiration-linked properties; they are likely candidates for cardiovascular neurons controlling sympathetic vasomotor outflow.

The question of artifact in evaluating arterial pressure sensitivity and pulse-synchronous activity must be considered. That such properties arise from peripheral baroreceptors is indicated by four types of data. First, the response curves of the cardiovascular cells show 100% modulation of activity over a range of 65–85 mm Hg and exhibit threshold pressures at which inhibition is first detectable (Fig. 9); similar thresholds for baroreceptor activity have been described (Yao and Thoren, 1983). Furthermore, the response curves can be established by several independent methods: pharmacological or mechanical maneuvers (Figs. 2A, 5B, 9). Second, these cells have cardiac rhythms that also show threshold pressure characteristics appropriate for baroreceptor signals (Fig. 2, C and D). This rhythm and pressure sensitivity are reversibly reduced or eliminated by anesthetizing the peripheral nerves carrying baroreceptor afferents (Fig. 3). Third, partial elimination of baroreceptor afferents shifts the pressure-activity response curve to the right, indicating a decrease in the potency of arterial pressure in inhibiting the cells. Finally, these cells are strongly inhibited by electrical stimulation of the superior sylvian nerve (Fig. 6A), a nerve known to carry baroreceptor fibers from the aortic arch and which buffers arterial pressure changes (Faber and Brody, 1983).

These data show that not only is baroreceptor inhibition mediated through the cardiovascular neurons of the nucleus paragigantocellularis lateralis, but also that baroreceptor signals from both carotid sinus and aortic arch regions converge on this descending pathway. Whether the convergence occurs at the level of these cells, or at some earlier synaptic junction, cannot be answered from our data. Baroreceptors are also found in the cardiopulmonary region; whether signals from such baroreceptors also converge on these cells is unknown. The present data do indicate that vagal afferents are not essential for the pressure sensitivity or pulse-synchronous activity of these neurons.

There have been many studies attempting to identify neurons in the brainstem which relay baroreceptor information to the sympathetic nervous system (q.v. Koepchen, 1975). Salmoiraghi (1962) identified a few units which he described as population-one and population-two cardiovascular neurons, based on their responses to pharmacological and reflex changes in arterial pressure. The cardiovascular neurons reported here are similar to the population-two neurons, with activities correlated negatively with mean arterial pressure levels (Fig. 2B). The term "cardiovascular" is broad and can imply the source of afferent signals or the destination of efferent outflow. With the paucity of present knowledge concerning specific pathways for integration of afferent and efferent cardiovascular information within the brain, it is justifiable to retain the term cardiovascular to describe internurons which integrate cardiovascular sensory information. Although, in the present case, the targets to which the cardiovascular cells relay baroreceptor information are not known, recent evidence shows that the spinal cord projections from the same area terminate exclusively in the autonomic nuclei of the spinal cord (Ross et al., 1984b). The results of lesion and stimulation experiments involving this portion of the medulla suggest that these neurons do relay excitatory signals to vasculature (Ross et al., 1984a). The possibility of projections to preganglionic neurons involved in regulation of targets other than vasculature is not precluded.

In spite of the general similarity of cardiovascular neuron responses to changes in arterial pressure, significant diversity exists within the cardiovascular cell group (Table 1). Two types of descending pathways from the cardiovascular neurons are suggested by these data: unmyelinated fibers (group 1 in Table 1) characterized by a lower threshold pressure for baroreceptor inhibition and small myelinated fibers (group 2) with a higher threshold. Similarly, a broad spectrum of baroreceptor fibers has been described (Coloride et al., 1980). Although there is little quantitative agreement about the specific properties of various fiber types, there is clearly consensus that different fiber types are characterized by different threshold pressures for activation. The most detailed comparative data (for a single species, using uniform techniques for analyzing the various fibers) indicates that large, myelinated fibers have a lower threshold—less than 60 mm Hg. Unmyelinated fibers have a higher threshold—greater than 84 mm Hg (Yao and Thoren, 1983). These threshold and fiber type relationships are opposite those of the cardiovascular neurons; thus, there is no apparent preservation of information, such as baroreceptor threshold, through fiber type specificity of central pathways.

Anatomical studies of the ventrolateral medulla have indicated the presence of as many as seven morphological cell types (Andrezik et al., 1981). Furthermore, many potential neurotransmitters have been found in cells in the general vicinity: epinephrine (presumed, due to the presence of phenylethanolamine-N-methyltransferase), serotonin, substance P, neuropeptide Y (Hökfelt et al., 1974, 1978, 1983; Steinbusch, 1981). In rats, some of these neurons have been demonstrated to project to the spinal cord and, specifically, to the intermediolateral cell column and central autonomic area (Bower et al., 1982; Ross et al., 1984b). Thus, it is possible that the cardiovascular cell group of the ventrolateral medulla comprises a variety of cell types, with different transmitters subserving different functions.

The observed spike amplitude modulations raise the issue of recording artifact. Traditionally, amplitude constancy has been cited as evidence for recording stability. Conversely, inconstancy has been assumed to indicate electrode movement with re-
spinal cord stimulation. The elucidation of the mechan- 
ism of amplitude modulation, however, must 
await intracellular recordings. Recent experiments 
with the dopaminergic neurons of the substantia 
nigra support the correlation between spike ampli-
tude and the level of hyperpolarization (Grace and 
Bunney, 1983).

The existence in the rostral ventrolateral medulla 
of neurons which are involved in tonic sympathetic 
vasomotor control, as well as baroreceptor reflex 
regulation, has been suggested by many studies 
using a host of pharmacological agents (Feldberg 
and Guertzenstein, 1972; Wennergren and Oberg, 
1980; Dampney et al., 1982; Willette et al., 1983; 
Hilton et al., 1984; Farlow et al., 1984; Ross et al., 
1984a). The spontaneous activity of spino-
lar cardiovascular neurons is consistent with a 
center for tonic vasomotor control. The ventrolateral 
medulla has also been described as an important 
integration area for pressor responses emanating 
from the hypothalamus (Willette et al., 1984). Hilton 
et al. (1984) have further proposed that the same 
ventrolateral medullary neurons responsible for 
tonic sympathetic vasomotor drive are also a relay 
for hypothalamic defense reaction. Indeed, the 
cardiovascular neurons reported in the present study 
do respond to electrical stimulation of hypothalamic 
areas associated with the defense reaction. The two 
types of responses—some units powerfully excited 
(Figs. 7A and 10C), others inhibited (Fig. 10D)—are 
consistent with the two patterns of vasomotor re-
responses in the defense reaction: powerful, general 
vasoconstriction and hindlimb vasodila-
tion, in part due to decreased sympathetic tone. 
However, the fact that these cells can maintain a 
high activity following midcollicular transection 
indicates that tonic excitatory drive from the hypo-
thalamus is not essential to their activity, in contrast 
to the proposal of Hilton et al. Whether the activity 
of the cardiovascular neurons arises from an excit-
atory synaptic input or is due to an inherent pace-
maker-like activity cannot be determined from the 
present experiments.

In summary, the negatively correlated cardiovas-
cular neurons of the intermediate portion of the 
nucleus paragigantocellularis are a major source of 
descending excitatory drive to spinal levels. Al-
though the target organs of these neurons remain 
to be determined more precisely, these cells are likely 
to be involved in tonic vasomotor tone setting, as 
well as baroreceptor and defense reaction vasomotor 
responses. However, this does not diminish the pos-
sible importance of other areas of the brain in inte-
grating various vasomotor functions (Hilton et al., 
1984), nor does it preclude the existence of other 
descending vasomotor pathways (Morrison and 
Gebber, 1984; Byrum et al., 1984; Guyenet, 1984).
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INDEX TERMS: Rostral ventrolateral medulla • Baroreceptor reflexes • Defense reaction • Vasomotor center • Reticulospinal neurons • Rat
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Circ Res. 1985;56:359-369
doi: 10.1161/01.RES.56.3.359

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