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TAYLOR, ROBERT F., AND LAWRENCE P. SCHRAMM. *Spinally mediated inhibition of abdominal and lumbar sympathetic activities.* Am. J. Physiol. 254 (Regulatory Integrative Comp. Physiol. 23): R655–R658, 1988.—Renal, splenic, and lumbar sympathetic nerve activities were recorded in the paralyzed, anesthetized, artificially ventilated, and spinally transected rat. Electrical stimulation of the dorsolateral funiculus caudal to the spinal transection was used to generate stimulus-response curves for changes in sympathetic activity in each of the three sympathetic nerves using five stimulus frequencies. In all rats, spinal stimulation inhibited sympathetic activity in renal and splenogastric nerves by ~50%. In grouped data, threshold frequency for inhibition of renal and splenogastric sympathetic nerve activity was 5 Hz, and inhibitions were maximal (50–60%) at 10 Hz. In contrast, activity in the lumbar sympathetic chain was inhibited in only two of five rats, and grouped data did not exhibit any statistically significant inhibitions. We conclude that lumbar sympathetic activity which remains after spinal transection can be inhibited only marginally by spinal stimulation, which substantially reduces renal and splenogastric sympathetic activity.

sympathetic activity; renal; splenic; gastric; transection; dorsal horn; dorsolateral funiculus

SYMPATHETIC NERVE ACTIVITY is regulated by both descending and ascending spinal pathways (6). Sympathoinhibition may be mediated by projections of supraspinal origin (1, 2, 4) or by intraspinal pathways (4, 8). At spinal levels, these inhibitory systems are widely distributed in the dorsal horn and in dorsolateral and ventrolateral funiculi (1, 3, 8).

Renal nerve sympathetic activity in the chloralose-anesthetized rat nearly doubles after C_1 spinal transection (10). This observation suggests the presence of potent tonic inhibition of some spinal sympathetic systems in the intact rat. Electrical stimulation of the dorsolateral surface of the cervical spinal cord, caudal to the transection, reduces renal nerve sympathetic activity by ~50% (7, 8). Stimulation produces a concomitant decrease in arterial pressure of ~10–15 mmHg (5). The magnitude of this depressor response suggests the evoked sympathoinhibition might not be restricted to the renal vascular bed. The purpose of the present study is to determine whether sympathetic vasomotor discharge to other abdominal viscera, to pelvic viscera, and to skin and skeletal muscle of the hindquarters might be affected by this sympathoinhibitory system.

METHODS

Surgical procedures. Male Sprague-Dawley rats (Charles River), weighing between 210 and 300 g, were anesthetized with ether followed by α-chloralose (100 mg/kg iv). Supplemental doses of chloralose (25 mg/kg) were administered via a femoral venous cannula when necessary to maintain an adequate level of anesthesia. A ventral midline incision was made in the neck, and a cannula was placed in the right carotid artery for the measurement of arterial blood pressure. Animals were paralyzed with gallamine triethiodide (Flaxedil 30 mg/kg) and artificially ventilated through a tracheal cannula. Body temperature was maintained between 36 and 37°C by a servo-controlled heating pad.

The lumbar sympathetic chain was approached via a ventral midline laparotomy and the subsequent ligation, section, and retraction of the left ileolumbar artery and vein. This retraction deflected the descending aorta and exposed the lumbar sympathetic chain, which was marked with a loose loop of suture. This marker was used later to locate the lumbar chain via a dorsolateral surgical approach (see below). The ventral incision was securely sutured, and the animal was repositioned on its right side. Rats were placed in a stereotaxic frame (David Kopf Instruments), and the spinal cord was exposed via a C_1–C_6 laminectomy. Once the dura was removed, the exposed spinal cord was kept moist with warm mineral oil.

The spinal cord was completely transected at C_1, and blood pressure was allowed to recover to steady state. Completeness of the transection was confirmed at the end of each experiment by careful dissection of vertebrae near the lesion.

Nerve recording and signal processing. Renal, splenogastric, and lumbar sympathetic nerves were all approached dorsolaterally through an incision in the left flank. The spleen and the kidney were retracted ventrad. This allowed the dissection of nerves coursing along their respective blood vessels. The lumbar chain was identified dorsolateral to the aorta by locating the marker loop of suture. In each experiment, sympathetic nerve activity from two of the three nerves (renal and splenogastric or renal and lumbar) was recorded simultaneously from the proximal end of the cut nerves by use of stainless steel, bipolar, hook electrodes. Recordings were made from renal and splenogastric nerve pairs in eight animals. Recordings were made from renal and lumbar sympa-

thetic nerve pairs in five animals. Nerve activity was amplified (Grass Instruments P15 and P511 amplifiers), rectified, integrated, and then displayed on two channels of a Beckman polygraph along with arterial blood pressure. Data were also stored on magnetic tape for subsequent computer analysis.

Integrated neural signals stored on magnetic tape were digitized by a computer every 5 ms, before and during inhibitory stimulation, and expressed in arbitrary units. At the end of each experiment, proximal ends of nerves were cut and left on recording electrodes to measure a "zero" value for nerve activity. This background level was then digitized and subtracted from measured nerve activity to obtain an estimate of true sympathetic nerve activity.

Inhibitory stimulation. The transected spinal cord was electrically stimulated with a concentric bipolar electrode (Rhodes, SNE100) mounted on a micromanipulator. Inhibitions were elicited by stimulation of the medial portion of the dorsal horn, distal to the C_2 dorsal root entry zone, as previously described by Schramm and Livingstone (8). Inhibitory response curves were generated for each nerve recording using stimulus trains at 2, 5, 10, 20, and 50 Hz (pulse duration, 300 μs; intensity, 300–400 μA) and lasting 60–75 s. Sympathetic activity during inhibitions was compared with the preceding 50 s of activity. Stimulation was followed by 5–10 min of recovery to steady state.

Data analysis. In all experiments, mean activity during the inhibitory period was compared with that recorded during the preceding control period. Significant inhibitions were determined by use of a one-way analysis of variance with a Duncan's post hoc multiple comparison test. $P < 0.05$ was considered statistically significant (11). Threshold of the inhibitory response for the group data corresponded to the lowest stimulation frequency that elicited a statistically significant decrease in mean nerve activity compared with the preceding control period.

RESULTS

Renal and splenogastric nerve activity. Sympathoinhibitory stimulation decreased activity in both the renal and splenogastric nerves (Fig. 1). Responses were nearly maximal at stimulation frequencies of 10 and 20 Hz. Individual responses in both nerves exhibited some "adaptation" after 20 s of stimulation. Absolute magnitude of this adaptation increased with frequency of stimulation. Small decreases in arterial blood pressure (10–15 mmHg) accompanied inhibitions at stimulus frequencies >2 Hz.

In eight rats, stimulus thresholds for inhibitions in both nerves occurred at 5 Hz (Fig. 2). Significant inhibitory responses in both renal and splenogastric nerves saturated at 10 Hz, achieving decreases between 50 and 60% of control activity.

Renal and lumbar nerve activity. In the second group of five rats, renal nerve inhibitions were comparable to those seen in the previous group. In contrast, responses in the lumbar chain varied between very modest inhibitions in two rats to a small amount of excitation at several stimulus frequencies in the remaining three rats. Analysis of variance indicated that none of the responses

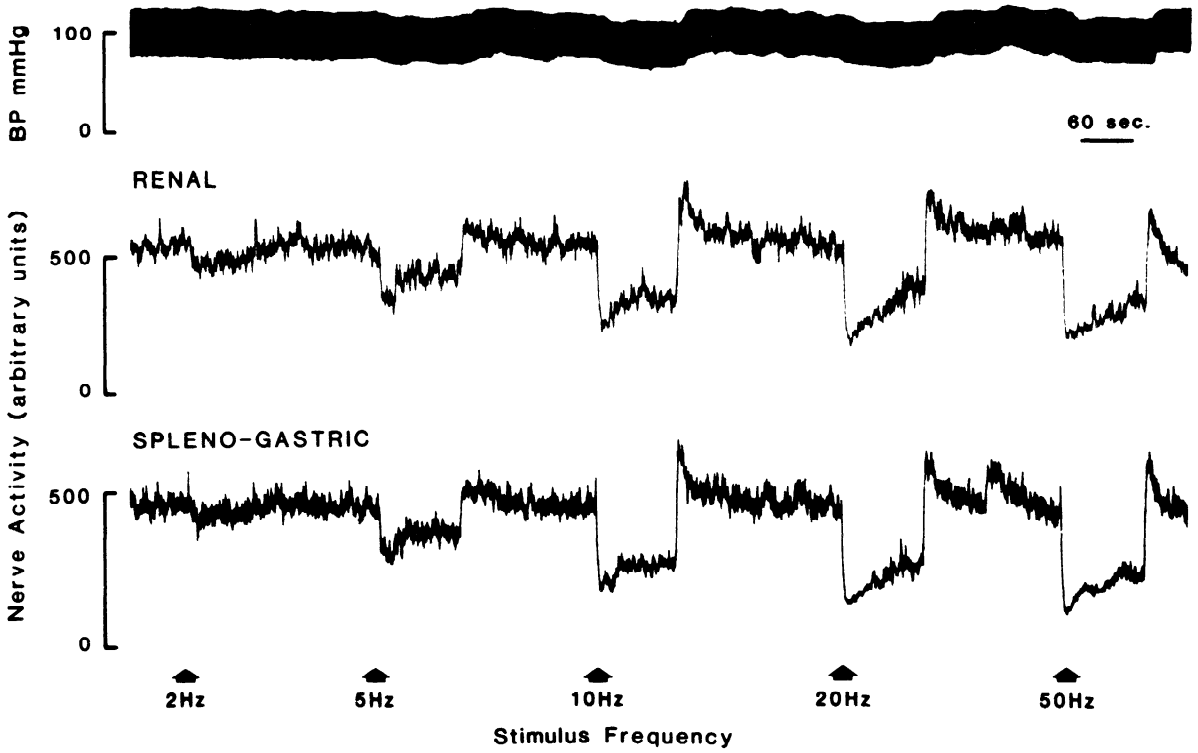

FIG. 1. Sympathoinhibitory responses of integrated renal and splenogastric sympathetic nerve activity to dorsolateral spinal cord stimulation. Onset of stimulation (300 μA) at given frequency is indicated (↑). BP, blood pressure.

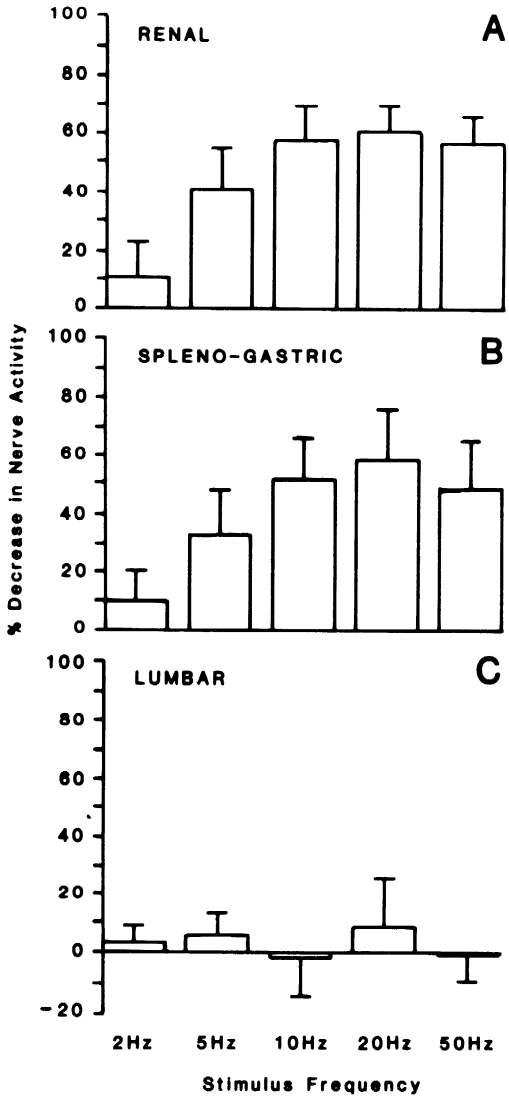

FIG. 2. Percent decreases in sympathetic nerve activity in response to spinal cord stimulation. *A*: mean ± SD renal nerve activity (n = 8). *B*: mean ± SD splenogastric nerve activity (n = 8). *C*: mean ± SD lumbar chain nerve activity (n = 5).

to inhibitory stimulation in lumbar chain were statistically significant.

DISCUSSION

Renal and splenogastric nerve activity. The sympathoinhibitory stimulus-response relationship for the splenogastric nerve was almost identical to that for the renal nerve. This finding suggests that the dorsolateral funicular sympathoinhibitory system in the rat inhibits sympathetic activity to a variety of tissues. Indeed, Schramm and Livingstone (8) reported that bradycardia frequently accompanied inhibitions of renal sympathetic activity. Because their rats were functionally vagotomized due to paralysis with Flaxedil (30 mg/kg), the bradycardia was probably due to inhibition of cardiac sympathetic activity. Inhibition was widespread enough that, in both the present and previous study (5), small decreases in arterial pressure were observed.

At low stimulation frequencies, inhibitions were well-sustained, confirming previous reports from this laboratory (5, 7, 8). At higher stimulation frequencies, inhibitions exhibited some "adaptation," and they were less well sustained. Was this "adaptation" a property of the sympathoinhibitory system itself, or did it result from the slow onset of a concomitantly stimulated sympathoexcitatory system that had a reduced threshold at higher stimulation frequencies? The latter possibility seems unlikely because we have never observed spinally mediated renal sympathoexcitations with slow onsets. Indeed, as shown by Schramm and Chornoboy (7), renal sympathoexcitations elicited by cervical spinal stimulation begin with a relatively large increase in activity, which is followed by a return to an elevated, but much lower, steady-state level of sympathetic activity.

Renal and lumbar nerve activity. In another group of rats in which inhibitions of renal nerve activity were invariably observed, spinal stimulation did not consistently reduce lumbar sympathetic activity. This observation suggests several hypotheses. First, differential inhibition of renal and lumbar sympathetic activity may represent a truly differential regulation by the dorsolateral funicular sympathoinhibitory system. Sympathetic activity in the lumbar sympathetic chain may be selectively inhibited by some other system. Such differential regulation of sympathetic activity is thought to underlie complex cardiovascular responses to environmental or behavioral situations.

Second, the differential effect of spinal stimulation could have resulted, in reality, from differential effects of spinal transection on sympathetic activity. Sympathetic inhibition can be elicited by electrical stimulation of the dorsolateral funiculus only after spinal transection (8). In the chloralose-anesthetized rat, spinal transection doubles renal sympathetic activity, but it halves lumbar sympathetic activity (12). Sympathetic activity may simply have been too low to observe inhibitions in our spinally transected rats. Were this hypothesis correct, we would have observed a direct relationship between the level of ongoing sympathetic activity and the magnitude or incidence of evoked sympathoinhibitions and sympathoexcitations in the lumbar chain. No such relationship was observed.

Spinal transection could also have created the observed differential responses by selectively abolishing only that sympathetic activity which would normally be inhibited by this system. The lumbar chain transmits sympathetic activity to many tissues, and it might be suspected that activity to only some tissues responds to this inhibitory system. Single-unit studies, now in progress, will be necessary to distinguish between the differential effects of spinal transection and differential effects of spinal stimulation.

A third hypothesis suggests that differential effects of inhibitory stimulation result from costimulation of cervical excitatory and inhibitory systems. Indeed, at the stimulation intensities used in these experiments, it is plausible that costimulation of some sympathoexcitatory systems might have occurred. Schramm and Livingstone (9) studied interactions between dorsolateral funicular sympathoinhibitory systems and dorsolateral funicular sympathoexcitatory systems. They showed that, at stim-

ulation frequencies as high as 50 Hz, renal sympathoinhibitions could still be observed, even in the presence of substantial sympathoexcitations. Therefore, if lumbar sympathetic activity exhibits similar interactions, it seems unlikely that costimulated excitation and inhibition, especially at lower frequencies, would have exactly balanced so that, on the average, cervical stimulation would have had no significant effect.

Finally, a fourth hypothesis suggests that the differential effect of inhibitory stimulation on renal and lumbar sympathetic activities was a function of relative proportions of preganglionic fibers in renal and lumbar nerves. Renal nerves are largely postganglionic. On the other hand, activity in the lumbar chain is reduced by ~50% after ganglionic blockade (12), manifesting a substantial population of preganglionic fibers. Synaptic divergence and the nonlinear transmission properties of sympathetic ganglia might enhance the ability to observe inhibitions in postganglionic fibers. Conversely, inhibitions might be more difficult to observe in preganglionic fibers. This explanation for differential responses seems unlikely. Even if postganglionic fibers generated only 50% of the observed lumbar activity and that postganglionic activity were reduced 50% by inhibitory stimulation (as are renal and splenogastric activities), we would have observed a 25% reduction in lumbar sympathetic activity on spinal stimulation. Inhibitions of this magnitude were not observed (Fig. 2).

We conclude that, after spinal transection, electrical stimulation of the dorsolateral spinal cord produces quantitatively similar inhibitions of renal and splenogastric sympathetic activity. Identical stimulation is far less effective in reducing lumbar sympathetic activity. If, as has been suggested by Schramm and Livingstone (8), this inhibitory system is tonically active in the intact rat, then it may be more important in regulating the ongoing sympathetic activity to the abdominal viscera than in regulating ongoing activity to the pelvic viscera or to muscles of the hindlimbs.

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