Visceromotor Organization within Descending Spinal Sympathetic Pathways in the Dog

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ABSTRACT
The organization within the descending sympathetic pathways on the surface of the dorsolateral funiculus of the spinal cord was investigated in anesthetized dogs. Changes in heart rate and carotid, renal, and femoral resistances were calculated during electrical stimulation of the descending spinal sympathetic pathways; the location within the pathway of the maximum change in each of these parameters was then determined. Blood pressure increased at each stimulation point with the maximum increase at 3–3.5 mm ventrolateral to the dorsolateral sulcus (DLS). The maximum increases in carotid, renal, and femoral resistances occurred with stimulation at 0.5–1.5, 2, and 3 mm ventrolateral to the DLS, respectively. Maximum heart rate responses were elicited by stimulation 2 mm ventrolateral to the sulcus. These data demonstrate that the pathway is organized in a dorsal-to-ventral manner, with the most rostral parts of the body being represented most dorsally and the more caudal parts being represented more ventrally.

In recent years many investigators have provided evidence for a discrete or regional control of the cardiovascular system by stimulation of the central nervous system. Lofving (1) has observed marked differences in changes in intestinal, skeletal muscle, skin, and renal vascular resistances when the subcallosal depressor areas are stimulated. Nino-miya and co-workers (2) have reported that hypothalamic stimulation has a differential effect on sympathetic discharge to the heart, kidney, and spleen. Forsyth (3) has noted variations in resistance changes in the absence of pressor changes in 15 vascular beds due to stimulation of anterior hypothalamic pressor regions. These studies confirm the notion that central nervous system structures regulating the cardiovascular system are capable of eliciting a discrete activation of the sympathetic nervous system. The possibility that spinal sympathetic pathways are also capable of regional cardiovascular regulation has not been evaluated.

The present investigation was designed to determine the functional organization of the descending sympathetic pathways (4–7) on the surface of the dorsolateral funiculus in the cervical spinal cord of dogs. Changes in resistance from the carotid, renal, and femoral vascular beds and changes in heart rate were compared during electrical stimulations of descending spinal sympathetic pathways carrying fibers from supraspinal regions that regulate the cardiovascular system to the preganglionic neurons.

Methods

Animal Preparations.—Experiments were performed on 22 mongrel dogs (15–22 kg) anesthetized with phencyclidine hydrochloride (2 mg/kg, im) and alpha-chloralose (80 mg/kg, iv). A tracheotomy was performed, and the femoral artery and the external jugular vein were cannulated and connected to pressure transducers to record systemic arterial blood pressure and central venous pressure, respectively. A flow probe was placed around the right carotid, renal, or femoral artery and connected to an electromagnetic flowmeter (Carolina Medical Electronics). Zero flow was determined by clamping the artery distal to the probe and was periodically checked for stability throughout the experiments. The transducers and the flowmeter were connected to an oscillograph (Grass model 7) to provide a continuous recording of pulsatile and mean blood pressures and blood flow. Heart rate responses were determined from the pressure and flow recordings.

A laminectomy was performed at the C3–C5 region. The dura mater was resected, and the dorsal roots were cut at these segments. The dogs were ventilated with a positive-pressure respirator and immobilized with gallamine triethiodide (2 mg/kg. initially followed by 1 mg/kg every 0.5–1 hour as needed). A bilateral vagotomy was performed on all of the dogs except those used for the carotid resistance studies. Rectal temperature was maintained at 38 ± 1°C by a heating pad on the animal table.

To verify that changes in resistance were not due to increased levels of circulating catecholamines, the sympathetic innervation was interrupted in several experiments, and the descending spinal sympathetic pathway was again stimulated. The sciatic nerve, containing the majority of vasoconstrictor fibers to the femoral vascular bed (8), was cut when changes in femoral resistance were being studied. The renal nerves traversing the connective tissue surrounding the kidney were cut when changes in renal resistance were being studied. Since the cervical
sympathetic nerves to the carotid vascular bed are contained within the vagal sheath in the dog, vagotomy interrupts the sympathetic innervation to the head.

Stimulations.—A unipolar stainless steel electrode with a tip diameter of 50μ or a coaxial electrode (100μ, o.d.) was connected to an isolated stimulator (Grass SD9) and placed on the surface of the dorsolateral funiculus on the right side of the spinal cord. The surface of the cord was stimulated randomly in 0.5-mm increments between the dorsolateral sulcus (DLS) and the dentate ligament, a distance of approximately 4.5 mm in all of the dogs studied. The distances were measured by placing a small millimeter ruler near the surface of the cord and observing the preparation with a 16x dissecting microscope. Stimulation parameters of 4-8 v, 1 msec duration, and 50 Hz were applied for approximately 20-30 seconds.

In each dog, to verify that the response was due to stimulation of an efferent pathway, a lesion was made about 1-1.5 mm in depth between the DLS and the dentate ligament. Stimulation rostral to this lesion did not evoke a response; however, responses to stimulation caudal to the lesion were not changed. Stimulation of descending spinal sympathetic pathways on the contralateral spinal cord had no consistent effects on vascular resistance changes in the blood supply to the right side of the body. This finding supports the conclusion by Foreman and Wurster (4) that the pathway does not decussate in the spinal cord.

Resistance Calculations.—Resistance was calculated from the pressure drop (systemic arterial blood pressure minus central venous pressure) divided by flow; it was expressed as percent change from the control level.

Results

Systemic arterial blood pressure, central venous pressure, and right femoral, renal, or carotid flow responses were recorded during stimulations of the ipsilateral descending sympathetic pathway on the surface of the dorsolateral funiculus of the cervical spinal cord. Changes in resistance and heart rate could then be analyzed while various regions within the pathway were stimulated, and regional variations in sympathetic activation could be described.

Blood pressure increases were obtained from every stimulation point, with the maximum responses occurring in all dogs from stimulation 3-3.5 mm ventrolateral to the DLS.

Femoral flow was measured in seven dogs to determine the changes in resistance during stimulation of the descending spinal sympathetic pathway. A decreased resistance resulted during stimulation between 0.5 and 2.5 mm ventrolateral to the DLS. Maximum increases in femoral vascular resistance occurred when the cord was stimulated between 3 and 3.5 mm ventrolateral to the DLS in all seven dogs. The range for the maximum increase in resistance was between 150 and 850% above control levels, with an average of 330%.

To verify that the femoral resistance response was not due to circulating adrenal catecholamines, the sciatic and femoral nerves were cut, and the pathway was again stimulated. Figure 1 shows representative blood pressure and blood flow responses to stimulation of the spinal sympathetic pathway 3 mm ventrolateral to the sulcus before and after the sympathetic nerves were cut. Central venous pressure did not change as a result of sympathetic stimulation and, therefore, is not shown on the figures. Prior to cutting the nerves, stimulation increased resistance to 156% above the control level. Cutting the femoral nerve did not affect the vasomotor response during stimulation. After the sciatic nerve had been cut, stimulation increased the flow and resulted in a passive decrease in resistance to more than 33% below the control level. Pressor responses were not significantly influenced by cutting the sciatic nerve. In addition to interrupting the sympathetic nerve supply to the femoral vascular bed, in a few experiments the adrenal medulla was clamped, and the pathway was again stimulated. There was no change in the response, indicating that the adrenal medulla did not play a significant role in this response.

Renal flow was measured in five dogs during stimulation of the spinal sympathetic pathway. Figure 2 shows representative blood pressure and
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Responses in renal artery flow and systemic arterial blood pressure during stimulation of descending spinal sympathetic pathways 2 mm (left) and 3 mm (right) below the dorsolateral sulcus (DLS).

Blood flow responses to stimulation both 2 and 3 mm ventrolateral to the DLS. Although the changes in resistance were similar (216% above control at 2 mm and 210% above control at 3 mm), the rates of change in resistance were different, with the response at 2 mm occurring sooner than that at 3 mm. In addition to the rate effect, in four of the five dogs in which renal resistance was calculated, the resistance change due to stimulation 2 mm ventrolateral to the sulcus was greater than that due to stimulation 3 mm from the sulcus. However, percent changes in blood pressure were always greater at 3 mm than they were at 2 mm. The range for the maximum response was between 102 and 120% above control levels, with an average of 669%. Interrupting the sympathetic innervation to the renal vascular bed abolished the change in resistance when the sympathetic pathway was stimulated, and the flow increased with the rise in pressure.

Carotid flow was measured in five dogs while the descending spinal sympathetic pathway was stimulated. Responses were much smaller and more variable in the carotid vascular bed than they were in either the femoral or the renal vascular bed. Figure 3 illustrates blood pressure and blood flow responses in one dog due to stimulation both 1.5 and 3 mm ventrolateral to the DLS. In this dog, the flow decreased when the cord was stimulated 1.5 mm ventrolateral to the sulcus (resistance increased to 72% above control level) and increased when the stimulation was at 3 mm (resistance increased to 42% above control level). The response at 1.5 mm from the sulcus represented the maximum carotid resistance change in this dog; however, the response at 3 mm was the maximum pressor response. The maximum change in carotid resistance was elicited by stimulation 0.5 mm ventrolateral to the DLS in two dogs, 1.5 mm from the sulcus in two dogs, and 2 mm from the DLS in one dog. The range for the maximum response was between 38 and 194% above control levels, with an average of 98%. Interrupting the sympathetic nerve supply to the carotid vascular bed resulted in a large increase in flow when the descending spinal sympathetic pathways were stimulated. This increase resulted in a passive decrease in vascular resistance.

Heart rate responses were analyzed in ten dogs. The maximum increase in heart rate was elicited by stimulation 2 mm ventrolateral to the sulcus in five dogs, 1.5 mm in two dogs, 2.5 mm in two dogs, and 3 mm in one dog. The range of the maximum response was between 13 and 53% above control levels.

Figure 4 summarizes the data for all of the dogs in which changes in carotid, renal, or femoral resistance and heart rate were analyzed. Because there was a large variation in responses among the dogs, the data were normalized. The average maximum response in each dog was set equal to 100%, and all other responses were compared to the maximum response. A 0% response indicates no change from control, and a negative percent re-
Summary of normalized data for carotid, renal, and femoral resistance changes and heart rate changes. The ordinate represents the percent change in resistance or heart rate, and the abscissa represents the location of the stimulation within the descending spinal sympathetic pathways. DLS = dorsolateral sulcus. Values represent means ± SE; n is the number of dogs tested.

The purpose of this investigation was to determine the functional organization within the descending sympathetic pathways in the cervical spinal cord of dogs. Regional control of the cardiovascular system can be determined by analyzing changes in vascular resistance during stimulation of several sites within the pathway on the surface of the dorsolateral funiculus of the spinal cord. The midcervical region of the spinal cord was chosen as the site of stimulation to ensure that all sympathetic preganglionic outflow was caudal to the stimulation site. The criterion for determination of an organization within this pathway is that each vascular bed must respond maximally at a different site within the pathway. As indicated in Figure 4, the maximum change in resistance in each of the vascular beds occurred with stimulation of different locations within the descending spinal sympathetic pathway. Maximum changes in blood pressure were consistently elicited by stimulation 3-3.5 mm ventrolateral to the DLS. Thus, there appears to be evidence for a visceromotor organization within the descending sympathetic pathways in the cervical spinal cord similar to the somatomotor organization within the descending motor pathways in the spinal cord.

Vascular resistance changes occurring outside the region showing the maximum response for a particular vascular bed may be due to either fiber distribution or current spread. If they are due to current spread, low-voltage stimulation should decrease the area which elicits a response. However, no change in the spread of the response was observed when the voltage was lowered from 6 V to

Discussion

in renal resistance showed a significant (P < 0.001) trend, with the maximum response elicited by stimulation 2 mm ventrolateral to the DLS. In addition, the response at 2 mm was significantly different (P < 0.02) from the responses at all other stimulation sites except that at 2.5 mm from the DLS. Heart rate changes showed a significant (P < 0.001) trend, with the maximum increase in heart rate occurring when the cord was stimulated 2 mm ventrolateral to the DLS. In addition, the response at 2 mm was significantly different (P < 0.05) from all of the other responses. The responses in the femoral vascular bed also showed a significant (P < 0.01) trend, with the maximum response occurring with stimulation 3 mm ventrolateral to the DLS. The response at 3 mm was significantly different (P < 0.01) from those between the DLS and 2.5 mm ventrolateral to the sulcus.
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If all fibers within the descending spinal sympathetic pathway originate in the medulla, the present findings suggest that the vasomotor area of the medulla may be similarly organized. Sato and Schmidt (10) have stated that reflexes exciting the medulla result in responses which are "indeed of the more generalized variety." This statement indicates that the medulla is not capable of eliciting discrete sympathetic activation. However, Fialow (11) has speculated that diverse neuron pools in the medulla can excite different vascular beds. Such and co-workers (12) have also concluded that inhibitory and excitatory reflexes can act simultaneously in different neurons within the medullary vasomotor center, giving rise to a discrete activation of the sympathetic nervous system.

The pathway in the cervical spinal cord may carry fibers originating from several supraspinal regulatory centers. Fialow (11) has suggested that regional differences in blood flow may be due to variations in the input from several central nervous system structures to the preganglionic neuron. Thus, direct reticulospinal, tectospinal, and hypothalamospinal pathways may descend in the spinal cord, in an organized manner, along the surface of the dorsolateral funiculus. Each of these pathways may affect various vascular beds in a different manner. Loewy and co-workers (13) have suggested that autonomic pathways controlling cardiovascular, eye, and bladder functions descend in an organized manner along the lateral surface of the spinal cord. Since each of these pathways has different supraspinal origins, it is not unlikely that pathways of different origin controlling the cardiovascular system may also descend in an organized manner along the dorsolateral funiculus of the spinal cord.

As shown in Figure 4, stimulation 0.5-2.5 mm ventrolateral to the DLS decreased resistance in the femoral vascular bed. This vasodilation could be due to activation, separately or in combination, of sympathoinhibitory, cholinergic, \( \beta \)-adrenergic, or histaminergic fibers (14-17). Simultaneous activation of a mixed population of these fibers could alter the results of these experiments quantitatively. To reveal the involvement of vasodilator, sympathoinhibitory, and sympathoexcitatory fibers in the activation of descending spinal sympathetic pathways, a complex series of experiments involving pharmacological blocking agents, variations in stimulation parameters, and sympathetic nerve recordings needs to be carried out.

To summarize, Figure 5 represents a cross section of the cervical spinal cord showing the functional organization within the descending spinal sympathetic pathways on the surface of the dorsolateral funiculus. The data from this series of experiments suggest that the majority of fibers regulating the vascular supply to the head are localized between 0.5 and 1.5 mm ventrolateral to the DLS. The fibers regulating heart rate are localized around 2 mm ventrolateral to the sulcus, and the kidney vasculature is regulated by fibers located 2-2.5 mm ventrolateral to the sulcus. The hind-limb vasculature is regulated by fibers localized between 3 and 3.5 mm ventrolateral to the DLS. This study therefore indicates that the descending spinal sympathetic pathways regulating the cardiovascular system appear to be organized in a dorsal-to-ventral manner with the most rostral parts of the body being represented most dorsally and the more caudal parts being represented more ventrally.

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