A Descending Vesicopressor Pathway in the Monkey[1] (34399)

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The purpose of this investigation was to locate the descending vesicopressor pathway at some of the more rostral spinal cord levels in the monkey (*Macaca mulatta*) for comparative purposes and for possible clinical cordotomy correlation. Bilateral anterolateral cordotomy in man is most often performed at cervical and high thoracic spinal cord levels and is frequently followed by temporary or permanent urinary retention and incontinence. The urinary complications may be caused by surgical damage of both, or either the afferent or the efferent limb of the micturition reflex. The course of the descending fibers involved on the efferent side of the micturition reflex has not been adequately studied in primates.

Materials and Methods. Five adult female monkeys (*Macaca mulatta*), weighing between 3.6 and 4.5 kg, were used in five chronic and five acute experiments. Laminectomy was performed at least 48 hr before any experiment to minimize surgical shock. Antiseptic technique was employed except during acute experiments. Anesthesia was induced by pentobarbital (30 mg/kg i.v.) supplemented with intramuscular injections as needed.

Intravesical pressure was measured in the catheterized animal with a Statham pressure transducer (P23AC) and a Grass model V polygraph. Arterial pressure measured at the level of the aorta through a catheterized femoral artery was similarly recorded. The animal's head and pelvis were fixed in a stereotaxic frame. A pneumatic cuff around the lower thorax monitored respiration and respiratory changes provided additional proof that stimuli were being delivered. The existing laminectomy wound was opened with minimal bleeding and shock, exposing the dura over spinal cord segments to be explored by stimulating microelectrodes. Spinous processes immediately rostral and caudal to the exposed dura were fixed in the stereotaxic frame for immobilization of the vertebral column. The dura was then opened exposing the dorsal surface of the spinal cord between the denticulate ligaments.

Microelectrodes, coated with INSL-X, were prepared following the method of Green (6). The maximum diameter of the exposed tips was approximately 20 μ; resistances were near 1 megohm. With the microelectrode in a micromanipulator, the left lateral funiculus of the chronic animal was explored dorsoventrally following transverse planes. Microelectrodes were moved 250 to 500 μ between stimuli. "Just-above-threshold" stimuli were defined in terms of physiologic responses. Square wave, monophasic pulses (up to 0.8 mA) with frequencies of either 40 or 60 /sec and a duration of 1 msec were delivered through a constant current stimulator. Maximum duration for any stimulus was 40 sec. Electrolytic lesions produced by DC, 100 μA currents for 15–30 sec were placed at some of the points where stimulation produced increased bladder pressure. These lesions were created only to provide further proof of electrode position and not to destroy fiber pathways. The descending vesicopressor pathway, if injured by lesion, was never injured bilaterally in a chronic experiment and therefore no neurologic deficit was encountered. After exploration of the left lateral column at several segmental levels, the wound was closed and the chronic animal was allowed

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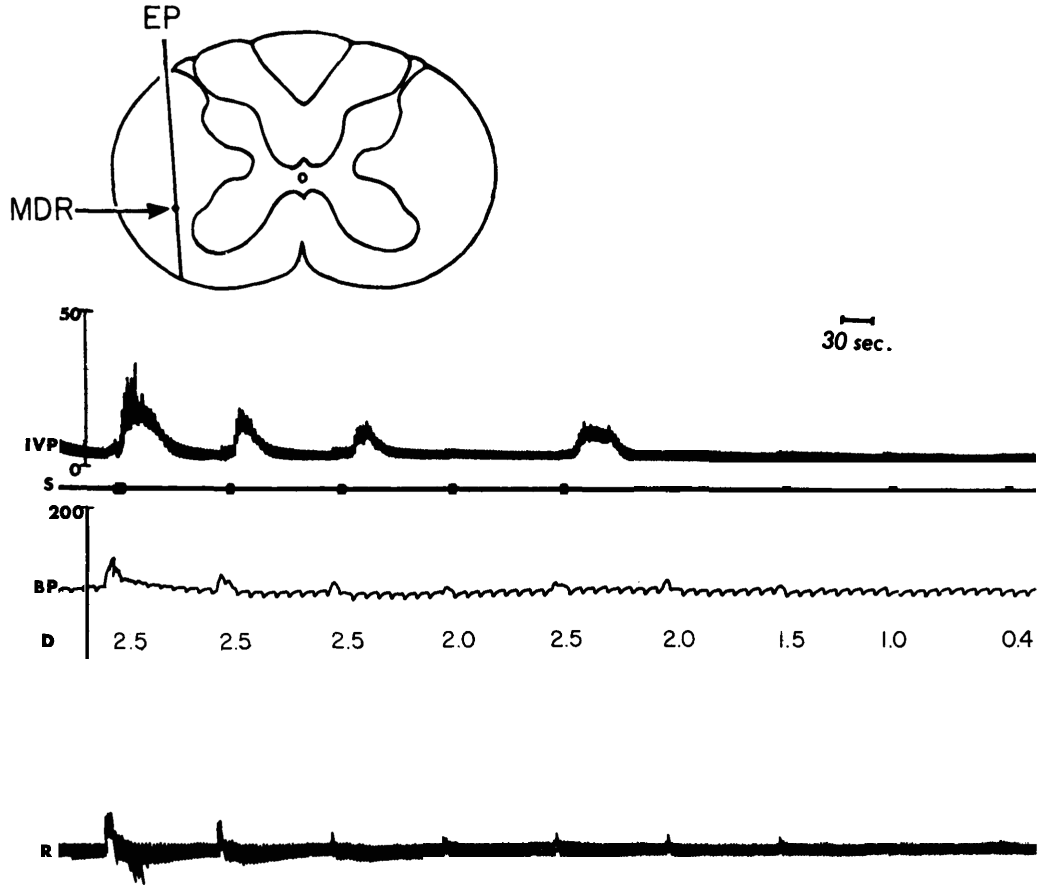

FIG. 1. Intravesical pressure (IVP; cm H_2O), blood pressure (BP; mm Hg), and respiration (R) are shown for stimulation periods (S) at different depths (D) at segment C_6 of monkey AC-128; (insert) EP= electrode path; MDR = maximum detrusor response.

3–5 days for recovery and for determination that neurologic deficits were not present.

The second set of experiments for each animal involved microelectrode exploration of the right lateral column in an acute preparation. Intracardiac heparin was then given followed by perfusion, first with normal saline, then with 10% formalin. The spinal cords and lower brain stems were sectioned at 25 μ and stained by the Weil method to locate electrolytic lesions and planes of exploration which established points of stimulation yielding detrusor activity. Eighteen transverse planes were examined from chronic and 22 from acute animals.

Results. The area in the lateral funiculus which produced the greatest intravesical pressure changes to "just-above-threshold" stimuli will be called the "area of maximum detrusor response." The maximum bladder response varied greatly both within a preparation and between animals. The greatest vasopressor responses were obtained from stimulation points which also produced maximum vesicopressor responses; however, thresholds for vasopressor responses were lower than for vesicopressor changes. Where vesicopressor responses were not present, the vasopressor changes showed that stimuli were being delivered and also indicated a change in depth of the microelectrode.

Figure 1 shows an electrode path at C_6 level of acute monkey AC-128 and reports representative polygraph tracings. The first three stimuli delivered at electrode depths of 2.5 mm show the results of decreasing stimulus strengths used to define the "just-above-threshold" shock. The fourth stimulus at "just-above-threshold" strength was at 2.0-mm depth and produced no detrusor response. The electrode tip was returned to 2.5 mm (fifth shock), and stimulation produced a rise in intravesical pressure similar to that recorded at the third stimulus. Sixth through ninth stimuli were delivered at indicated depths. The detrusor response was maximal at 2.5 mm and the vasomotor response decreased directly with stimulus strength and electrode depth. The vasopressor changes indicate a greater concentration of fibers between 2.0 and 2.5 mm than at lesser or greater depths along this pathway, and the respiratory record shows that vesicopressor and vasopressor changes are independent of respiratory movements.

Stimulations of the lateral columns in transverse planes through the seventh and eighth cervical and first thoracic spinal cord segments yielded data similar to those shown for the sixth cervical level in Fig. 1. The vesicopressor responses were greatest in the junctional area of the dorsal and ventral halves of the lateral funiculus. Figure 2A-D report the location of the vesicopressor pathway at the junction of dorsal and ventral halves of the lateral funiculus for C_6 through T_1 levels of the macaque spinal cord, located more ventrally at C_6 than at T_1 segment.

Discussion. Figure 1 reports detrusor responses to "just-above-threshold" stimuli, only from the area of the lateral funiculus ventral to the lateral corticospinal tract for the levels investigated (C_6 through T_1). These data also indicate that vasopressor fibers share a common area of the spinal cord with vesicopressor fibers, and that a lower threshold exists for the recorded vasopressor responses than for vesicopressor changes. The data shown in Fig. 2 indicate that vesicopressor fibers are more dorsally positioned in the spinal cord at the lower levels (C_8 and T_1) than at the higher level (C_6 and C_7). Stimulation following cervical cord transection in monkey AC-128 support the view of Kerr and Alexander (8) that these stimulation procedures produced only descending vesicopressor effects in the intact animal,

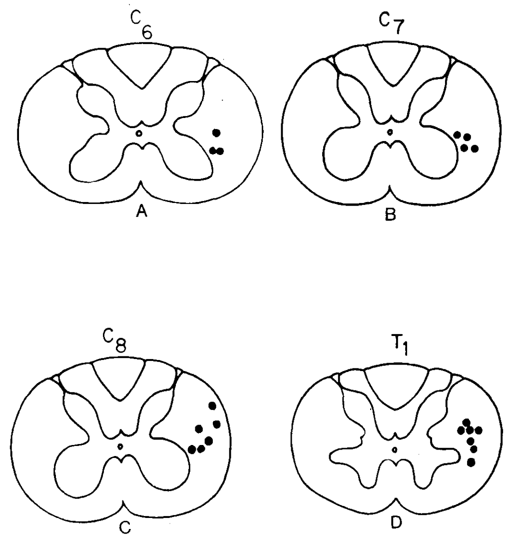

FIG. 2. Vesicopressor pathway (●) stimulation points productive of maximum detrusor response: (A) C_6 spinal cord level; (B) C_7 spinal cord level; (C) C_8 spinal cord level; and (D) T_1 spinal cord level.

since detrusor response to stimulation 30 min after transection was similar to that elicited before section.

Ruch (14) reviewed the literature and discussed apparently conflicting evidence regarding the location in the spinal cord of vesicopressor fibers but offered no conclusions. Crosby *et al.* (4), after study of clinical cases and review of literature, reported the position of the vesicopressor pathway for cervical levels of the human spinal cord within the lateral corticospinal tracts between the fibers to the upper and those to the lower extremity musculature. This location does not coincide with the view of Foerster and Gagel (5) or Nathan and Smith ((12), who report evidence that the vesicopressor pathway lies ventral to the lateral corticospinal tracts; nor does it agree with the findings in experimental animals (cat and monkey) of Kerr and Alexander (8) who find vesicopressor fibers in the periphery only of the dorsal half of the lateral columns.

The origin of the descending supraspinal pathways mediating vesicopressor impulses (efferent limb of micturition reflex) was reported by Barrington [(1); cat]. He demonstrated that small bilateral areas at the pontine isthmus, ventromedial to the superior cerebellar peduncles, were essential to the micturition reflex and concluded that the efferent limb of that reflex originated there. This view has been substantiated by Wang and Ranson [(17) cat], Tang and Ruch [(16) cat], and Kuru and Yamamoto [(10) cat]. Fibers have been traced from Barrington's rostral pontine vesicopressor areas caudally through the reticular formation of the brainstem by Kuru and Yamamoto [(10) cat] using the Marchi method. In the medulla they showed these fibers in the ventrolateral portion of the lateral third of the reticular formation. This has also been demonstrated by Wang and Ranson [(17) cat] with electrical stimulation and by Kuru *et al.* [(9) man] by bilateral shallow tractotomy at the level of transition of medulla to cord. At the spinobulbar junction the vesicopressor pathway passes into the cervical spinal cord and assumes a position ventral to the lateral corticospinal tracts. The vesicopressor path was reported for cervical spinal cord levels in the ventral half of the lateral funiculus by Budge [(3) dog] and by Wang and Ranson [(17) cat]. For thoracic and lumbosacral cord levels the vesicopressor fibers have been found more dorsally and peripherally in the lateral columns. Mosso and Pellacani [(11) dog] found the pathway in the dorsal half of the lateral funiculus as did Steward [(15) cat]. Barrington [(2) cat] and Kerr and Alexander [(8) cat and monkey] reported the vesicopressor pathway in the periphery only of the dorsal half of the lateral columns. Kuru and Yamamoto [(10) cat] stated that their investigations show the vesicopressor fibers mixed with rubrospinal fibers in the spinal cord. Nyberg-Hansen [(13) cat] demonstrated by the Nauta technique that rubrospinal fibers descend through cervical spinal cord levels ventral to the lateral corticospinal tracts. He also showed that these rubospinal fibers assume a more dorsal position in the lateral funiculus as they pass from cervical to thoracic levels, and at lumbosacral levels lie in the periphery only of the dorsal half of the lateral column.

Figure 2 shows for cervical levels C_6 through T_1 in the monkey (*Macaca mulatta*) the location found in this study for descending vesicopressor fibers. This position is in accord with the findings of the following investigators for these segmental levels. It is the location indicated by Budge [(3) dog] for cervical spinal cord levels. It is in agreement with the conclusions of Foerster and Gagel [(5) man] reporting their experiences with clinical cordotomy. It coincides with the position outlined by Wang and Ranson [(18) cat]. It is the location implied by Kahn and Peet [(7) man] when they noted that the deeper (medially) the anterolateral cordotomy incision, the greater was the probability of loss of the micturition reflex. It is also in agreement with the studies of Nathan and Smith [(12) man] who report the vesicopressor pathway in the equatorial plane at the junction of the dorsal and ventral halves of the lateral funiculus. Kuru and Yamamoto [(10) cat] also found vesicopressor fibers in this same area. The positions of the descending vesicopressor fiber systems appear to be similar in cat, dog, monkey, and man.

Summary. The location of a descending vesicopressor pathway in the spinal cord was investigated in *Macaca mulatta,* lightly anesthetized (pentobarbital) and immobilized in a stereotaxic frame. The lateral columns of the spinal cords were explored with stimulating microelectrodes moved 250 to 500 μ between stimuli using dorsoventral penetration. Detrusor activity was monitored using a pressure transducer connected to an intravesical catheter. A descending vesicopressor pathway was outlined in the lateral funiculus of spinal cord segments C_6 through T_1 by mapping the points of maximum detrusor response. These points of maximum detrusor response were found in an area near the junction of the dorsal and ventral halves of the lateral columns extending from the region of the denticulate ligament laterally, to the spinal cord gray medially.

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