Decussation of hind-limb and fore-limb fibers in the monkey corticospinal tract: relevance to cruciate paralysis

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Cruciate paralysis is a clinical entity in which patients with trauma to the anterior cervicomedullary junction present with weakness of the upper-extremity greater than that of the lower extremity. The underlying mechanism of this paralysis is commonly thought to be selective damage affecting upper-extremity nerve fibers more than lower-extremity fibers. Both Nielsen and Bell proposed a differential decussation of upper- and lower-extremity fibers in the pyramidal tract at the cervicomedullary junction as the causative pathology. According to their theory, the upper-extremity fibers would cross in the rostral and medial part of the decussation; hence, damage in this region would selectively affect the upper limbs. Only Barnard and Woolsey and Coxe and Landau have specifically analyzed the course of upper- and lower-extremity fibers in the region of the pyramidal decussation. They used Marchi degeneration techniques to trace degenerating fibers from discrete lesions of the motor cortex in the cynomolgus monkey. They found no evidence that the fiber populations were segregated, thus failing to support the differential decussation theory. Nonetheless, damage in the region of the cervicomedullary junction of humans does affect the limbs differentially. Either the course of pyramidal tract fibers differs across species or the mechanism underlying cruciate paralysis does not rely on differential decussation of upper- and lower-extremity fibers.

We re-examined the anatomical basis of cruciate paralysis in Old World and New World primates using the neuroanatomical tracer, wheat germ agglutinin (WGA) conjugated with horseradish peroxidase (HRP), which defines fiber terminations as well as trajectories. Anterograde transport of WGA-HRP depends upon its incorporation by the cell soma. With this method, potential confusion by fiber pickup underlying injection sites is not a factor. In contrast, confounding pickup is always a possibility with degeneration techniques because of incidental fiber damage as well as degeneration resulting from compromised vasculature and edema. In clarifying the corticospinal tract, WGA-HRP is the tracer of choice. The well-defined terminal label resulting from WGA-HRP transport also provides additional information about injection site uptake. Therefore, it is important to use a refined technique such as WGA-HRP imaging to study the corticospinal decussation. Our results support those of Coxe and Landau and Barnard and Woolsey and suggest two alternative explanations for the basis of cruciate paralysis.

Materials and Methods

Six New World squirrel monkeys (Saimiri sciureus) and two Old World cynomolgus monkeys (Macaca fascicularis) were anesthetized with intravenous sodium pentobarbital and placed in a stereotactic frame.
Sterile technique was used to perform a bilateral craniectomy to expose the precentral cortex. After the dura was opened, tungsten microelectrodes with a 20-μm tip exposure were used both to stimulate (maximum stimulus parameters: −0.5 mA, 200 Hz, 0.1 msec in 100-msec trains) and to record responses from the precentral cortex. The resulting movements and sensory responses allowed accurate definition of precentral cortex serving specific limb joints. The results agree well with previously published data.

Once an appropriate injection site was determined, the metal microelectrode was cross-referenced to a glass pipette for injection of WGA-HRP into the same location. A solution of 2% or 4% WGA-HRP in distilled water was injected approximately 2 mm below the cortical surface by applying brief air pulses (15 msec) to the back of the pipette while the meniscus of the WGA-HRP was observed under a x 50 microscope. The microscope was filled with a calibrated reticule that allowed accurate volumes to be injected. Total injected volumes ranged from 0.1 to 1.0 μl spread across cortex serving one limb by using multiple small injections. The incision was then sutured and the animal was allowed to recover in an incubator under observation.

After 48 hours, the animals were given a lethal dose of sodium pentobarbital intravenously. They were then perfused through the aorta with warm saline (approximately 500 ml at 43°C) containing 0.01% H₂O₂. This prewash was followed by perfusion with cold 3% paraformaldehyde in a phosphate buffer (pH 7.4) that was allowed to flow for 30 minutes. After fixation, the animals were perfused with a graded series of sucrose phosphate-buffer solutions (1000 ml of 10%, 500 ml of 20%, and 500 ml of 30%). The brain and spinal cord were removed and stored overnight in a 30% buffer solution. The tissue was then frozen and sectioned. The sections were reacted with tetramethylbenzidine at 37°C and then stained with neutral red, mounted, and examined with polarized-light microscopy.

Figure 1 shows a dorsal view of the squirrel monkey brain further depicted in Fig. 2. The injection sites in the precentral areas involved with hind-limb (foot) and fore-limb (hand) motor function are delineated. This illustration was made by enlarging the negative of a photograph of the dorsal view of the brain with an optical projector. By enlarging the stained coronal sections to the same magnification, the injection site was mapped using the central sulcus, sylvian fissure, and interhemisphere sulcus as landmarks.

Results

Decussation of Fore- and Hind-Limb Fibers

Two squirrel monkeys received single injections of WGA-HRP into either the fore-limb or the hind-limb area of the precentral cortex. The brain stems were sectioned parasagittally. The pyramidal decussations were found to extend approximately 3.5 mm along the long axis of the brain stem at the level of the obex. There was no difference in the location of the decussation in the specimens with fore-limb and hind-limb injections.

An additional six monkeys (four squirrel and two cynomolgus monkeys) received bilateral injections in the precentral cortex in the fore-limb area on one side and in the hind-limb area on the other. These bilaterally examined specimens were sectioned in the transverse plane so that the location of decussating fore-limb and hind-limb fibers could be compared in the same sections. Again, none exhibited evidence of a differential location of hind-limb and fore-limb fibers at the decussation.

Figure 2 illustrates the WGA-HRP labeling in a single squirrel monkey. Figure 2A shows a section at the level of the precentral cortical injection sites. Notice that the resulting thalamic labels from the two sides are complementary with little overlap, indicating no overlap of the cortical areas' transporting labels. Labeled medullary pyramids are visible in the most ventral portion of the section and labeled fibers are evenly distributed throughout the pyramids. This even distribution is more clearly seen in Fig. 2B, which shows the pyramids just rostral to their decussation. Figure 2C and D illustrates the decussation. The labeled fibers form a symmetrical pattern, indicating no differential decussation of the fore-limb and hind-limb fibers. Figure 2E illustrates a medullary section immediately after the decussation. The labeled fibers are symmetrically located and distributed evenly throughout the corticospinal tract.

Smaller injections into the precentral cortex labeled fewer fibers, but the labeled fibers were evenly distributed throughout the pyramids, as illustrated in Fig. 3. A variable feature is the number of labeled fibers in the ventral corticospinal tract. In most cases, a few labeled fibers could be seen in the ventral funiculus, but two squirrel monkeys showed a substantial number of
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**Fig. 2.** Photographs of sections from the brain of a squirrel monkey (Monkey SM3) showing the injection sites of 0.05 μl 2% WGA-HRP per side. A: Polarized light dark-field photograph showing a frontal section through the cortical WGA-HRP injection sites, thalamus (th), and brain stem. Labeled areas appear light. The lateral injection site (FL) on the left was placed where microstimulation elicited finger movement; the medial injection site (HL) on the right was placed where stimulation produced toe movement. The columns of label in motor cortex are the result of transcallosal transport from the contralateral injection site (callosal fibers were heavily labeled in more anterior sections). Extremely dense label (both anterograde and retrograde) is visible in the thalamus. The thalamic labels are in complementary and largely non-overlapping regions, thus indicating that the injection sites did not overlap in the cortical areas that transported the labeling agent. Labeled corticospinal fibers are visible in the ventrally located medullary pyramids (p). Labeled fibers are distributed evenly throughout the pyramids on both sides. Scale bar = 1 cm. B: Higher-power photograph of a transverse section through the medulla at the level of the inferior olive. The evenness in the fiber labeling of the pyramids is easily seen. Fine fibers leaving the pyramid (p) on the left side correspond to the fore-limb injection and cross the brain stem to terminate the lateral reticular formation (lrn). Scale bar = 1 mm. C: Transverse section through the rostral part of the pyramidal decussation. Heavy terminal labeling is visible in the gracile nucleus (gr) on the left while more scattered labeling is seen in and around the cuneate nucleus (cu) on the right. The pyramidal tracts (px) decussate symmetrically. Scale bar = 1 mm. D: Photograph of a slightly more caudal section than shown in C, but still in the pyramidal decussation. The gracile nucleus (gr) is still heavily labeled; the label in the cuneate nucleus (cu) has become more focused and has shifted medially. Decussating pyramidal fibers (px) have moved dorsally and laterally but still occupy symmetrical positions in their respective halves of the brain stem. Scale bar = 1 mm. E: Transverse section immediately caudal to the pyramidal decussation. The labeled corticospinal (cs) tracts form roughly circular patterns that occupy symmetrical areas on both sides. The gracile label (gr) is largely absent, while the cuneate label (cu) is dense and sharply defined. A second area of corticospinal termination (curved arrow) is visible on the medial border of the right corticospinal tract. This label lies in Kuypers' internuncial region. Some of the corticospinal terminals are present in the cuneate (long arrow) and the rest are in the central gray area (short arrow). Scale bar = 1 mm.
labeled ventral corticospinal fibers. Figure 3 right illustrates a specimen from a case with moderate labeling in the ventral corticospinal tract. Notice the complete absence of a ventral corticospinal tract in the squirrel monkey depicted in Fig. 2E. Neither cynomolgus monkey specimen showed a significant ventral corticospinal tract.

In the specimens with a sizable ventral corticospinal tract, the fibers were present on the side corresponding to the fore-limb injection (this cannot be seen in Fig. 3 right since the ventral portions of the two sides overlap at the midline), and did not course beyond upper thoracic levels. The uncrossed fibers could be seen crossing at segmental levels, and no terminations were noted on the ipsilateral side.

**Fore-Limb and Hind-Limb Fiber Terminations**

Unlike the course of the decussating fibers, the terminations of hind-limb and fore-limb fibers were well separated. At the beginning of the decussation (Fig. 2B), heavy hind-limb fiber terminations were seen in the gracile nucleus. Lighter and more widely spread terminations of fore-limb fibers were visible in the cuneate and bulbar reticular formation at the same level. Caudally, the fore-limb fiber terminations became more distinct; at the C-1 level, fore-limb fiber terminations were more prominent than hind-limb terminations. Heavy termination bands were visible (Fig. 2D and E) just medial to the lateral corticospinal tract (Kuypers' internuncial region, curved arrow), in the caudal cuneate (long arrow), and in the central gray area (small arrow). The fore-limb fiber terminations merged into spinal laminae V, VI, and VII and continued to the upper thoracic levels. Thus, caudal to the decussation and continuing into the cervical cord, terminals from injections into fore-limb regions of the motor cortex predominate. At these levels, there is no hind-limb equivalent to the fore-limb internuncial, central gray area, and cuneate terminations.

**Discussion**

Cruciate paralysis, characterized by midline involvement of the rostral portion of the pyramidal decussation, occurs after the cervicomedullary junction is injured by trauma, odontoid fracture, tuberculosis, or cervical spine injury. The proposed neuroanatomical mechanism underlying cruciate paralysis places the motor axons of the upper extremities in the more rostral and medial parts of the medullary decussation and the axons of the lower extremities more caudally and laterally.

In 1947, Nielsen first described isolated paralysis of the upper extremities. He attributed this finding to the proposed somatotopic organization of the pyramidal decussation. In 1970, Bell again described this clinical phenomenon. More recently, Dumitru and Lang and Marano, et al., reported cases of bilateral upper-extremity paralysis resulting from a deacceleration motor-vehicle injury and from a gunshot wound to the cervicomedullary junction, respectively. These investigators proposed that medially decussating upper-limb fibers were affected while laterally placed lower-limb fibers were spared.

In contrast, Barnard and Woolsey and Coxe and Landau found no evidence for a differential decussation of fore-limb fibers in the monkey. Our results support their findings, and extend the observation to another primate species. Fore-limb and hind-limb fibers in the pyramidal tract appear to be completely inter-
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mingled and to decussate together. In fact, the even distribution of fore-limb and hind-limb fibers across the pyramids suggests that the intermingling might be an organizational principle of the corticospinal pathway. This uniform distribution of fibers would preclude a severe deficit of any one limb resulting from a partial lesion of the pathway. Clearly, damage to the corticospinal tract at the decussation could not selectively influence hind-limb or fore-limb performance in humans unless human anatomy differs markedly from other primates. Thus, there is no obvious anatomical explanation for cruciate palsy. Our results, however, do suggest two alternative explanations for cruciate paralysis.

First, because fore-limb and hind-limb fiber terminations in brain-stem nuclei are segregated along the longitudinal axis of the brain stem, hind-limb terminations lie more rostrally than fore-limb terminations. If damage near the odontoid process primarily affected terminals or cell bodies caudal to the obex, the fore limb would probably be more involved than the hind limb. However, the cells in this region are not motor neurons and it is questionable whether injury to these neurons would produce paralysis. Certainly, many of these neurons are sensory, but they (especially the intermuncial population) may also represent propriospinal neurons serving upper-limb motor function. This idea is supported by experimental studies in cats. Lower pyramidal lesions severely affect the ability of the cat to make fore-limb target-reaching movements. The movement deficits resemble those that follow dorsal column lesions. Lesions of the corticospinal tract at the C-2 level cause little impairment, therefore collateral input to the dorsal column nuclei from the pyramidal tract may have an important role in control of the fore limbs. These corticospinal tract projections to the dorsal column nuclei have been demonstrated in this study and reported in the literature.

An explanation of cruciate paralysis based on damage to the cell bodies or terminals in the region of the cuneate nucleus seems somewhat unlikely due to the relatively greater distance between the nucleus and the odontoid process. It seems that damage extending to the center of the brain stem would result in many severe deficits. However, collateral fibers are generally of quite fine caliber and may well be damaged selectively by trauma. It is also possible that cellular areas might be affected more severely than fibers passing through the same region.

A second possible explanation for cruciate paralysis is based on our observation of individual and, probably, species differences in the expression of the ventral corticospinal tract. Labeling in the ventral corticospinal tract was apparent in two squirrel monkeys but in no cynomolgus monkeys (Cox and Landau also found no degeneration in the ventral funiculus of cynomolgus monkeys after cortical lesions). Kuyppers reported no degeneration in the ventral funiculus of the rhesus monkey after cortical lesions, but clearly labeled fibers are seen in the ventral funiculus of the rat after cortical injections of HRP. The evidence supports both individual and species differences in the expression of the ventral corticospinal tract.

The labeled ventral corticospinal tract in two squirrel monkeys resulted from injections into the fore-limb but not the hind-limb cortex and did not extend far beyond the cervical enlargement. Therefore, the fibers selectively served upper-limb function, at least in these specimens. The same observation has been made for humans, chimpanzees, and monkeys. Most descriptions of the tract state that it does not project beyond upper thoracic levels, although there have been a few reports of the human tract extending throughout the length of the spinal cord. If the ventral corticospinal tract is well developed in humans, then the decussated fibers would lie along the ventral surface of the brain stem and might easily be selectively involved in the cases of odonotid fracture.

Although great individual variation in the development of the human ventral corticospinal tract has been reported, the tract is clearly often a substantial one. Indeed, one case has been reported in which the tract was developed to the exclusion of the lateral tract (presumably, it would carry both fore-limb and hind-limb fibers in that case). If damage to the ventral corticospinal tract provides the basis for cruciate paralysis, the original hypothesis of Bell and Nielsen that fore-limb and hind-limb fibers are segregated in the region of injury may well be correct. However, their specific anatomical description of the decussation is probably incorrect.

Conclusions

Our results still implicate no definitive anatomical mechanism to explain cruciate paralysis, but we offer two suggestions: 1) Selective damage to neural areas involving the intermuncial cells, the centrum gray area, and the cuneate nucleus, or input from collateral fibers of the pyramidal tract to these regions, or 2) injury to the ventral corticospinal tract. The first possibility could be investigated with animal experiments and is supported by cat studies. The second possibility is less amenable to research with animals because only a few species may have as well developed a ventral corticospinal tract as man. However, the development and extent of the human ventral corticospinal tract could be evaluated with postmortem studies.

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References


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