Recovery of Motor Function in Rhesus Monkeys: H. G. J. M. Kuypers

Kuypers's experiments centered on motor control executed by the descending pathways from the brainstem and cerebral cortex to the spinal cord (Kuypers, 1964). The brainstem pathways consist of a lateral and a medial group that terminate preferentially in the dorsolateral and ventromedial parts of the intermediate zone respectively, i.e., mainly on interneurons. The connections of the cells in these different parts of the intermediate zone suggest that the lateral brainstem pathways to the dorsolateral part of the intermediate zone influence especially motoneurons of distal extremity muscles, while the medial brainstem pathways to the ventromedial parts influence especially motoneurons of axial and proximal extremity muscles (Sterling and Kuypers, 1968; Rustioni et al., 1971). The corticospinal fibers probably amplify these brainstem controls, because they share their termination area in the intermediate zone with both groups of brainstem pathways. In addition, many corticospinal fibers terminate directly in motoneuronal cell groups of distal extremity muscles, in contrast to the termination of the brainstem pathways (Bernhard and Bohm, 1954; Kuypers, 1960; Phillips and Porter, 1964).

Prompted by these anatomical findings, Kuypers and his co-workers studied the functional capacities of the various descending pathways in rhesus monkeys. In one series of experiments, both pyramidal tracts were interrupted at medullary levels (Lawrence and Kuypers, 1968a). Following surgery, the monkeys could walk and climb but initially had difficulty using their individual limbs independently in picking up food (Figure 21). Two to 3 weeks later the animals began to perform this task by executing a hooking motion of the extremity, consisting of a combined movement of arm and hand. Four to 5 weeks postoperatively they began to do this first by bringing the hand to the food by stretching the arm, and then closing the whole hand independently, without accompanying arm movements. Yet, at least one year after the operation, they were still unable to execute relatively independent finger movements, as demonstrated by their failure to pry food pellets from small holes by insertion and movement of an individual finger (see Beck and Chambers, 1970). In 5 animals, however, in which the pyramidal transections were incomplete, some recovery of independent finger control occurred.

The motor control that is recovered after bilateral pyramidotomy probably depends on the descending brainstem pathways that

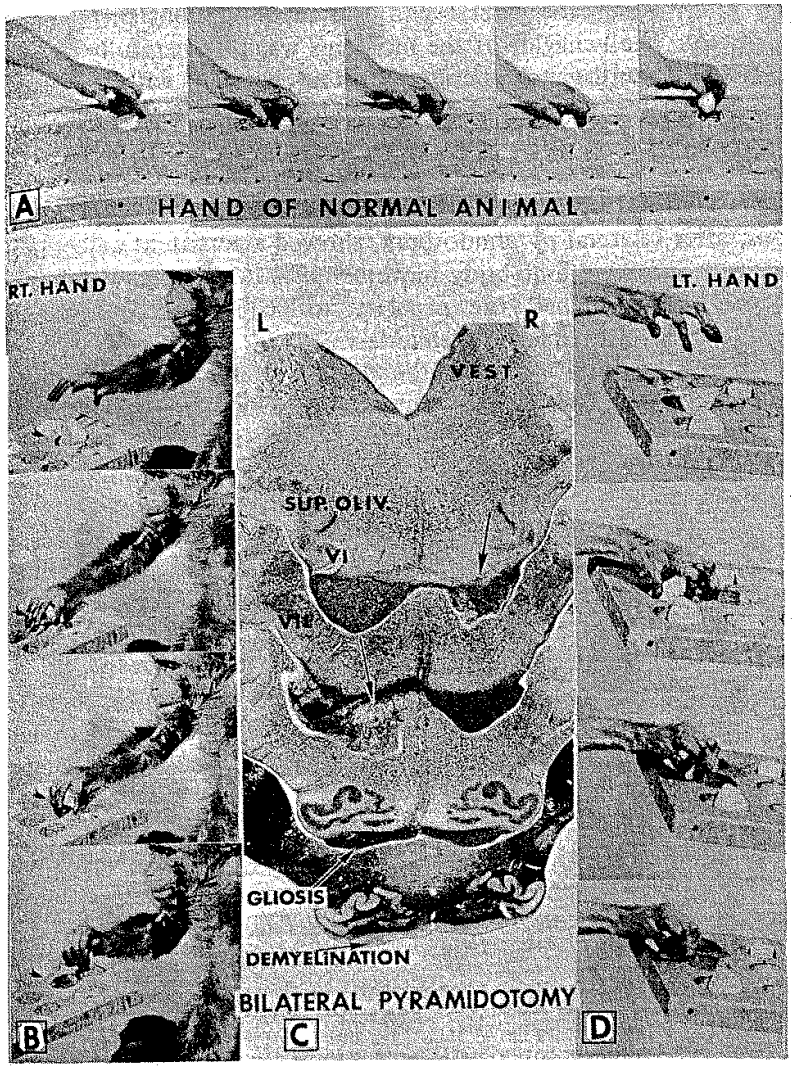

Figure 21. Hand and finger action of a normal (A) and a bilaterally pyramidotomized monkey (B and D) picking up pieces of food. Histological sections show the bilateral pyramidal tract interruption as well as the gliosis and demyelination below the lesion (C). [Lawrence and Kuypers, 1968a]

share a termination with the pyramidal fibers in the spinal intermediate zone (Kuypers, 1964). In order to test this hypothesis, monkeys with bilateral pyramidotomies were allowed to recover for at least 6 weeks (Lawrence and Kuypers, 1968b). Subsequently, brainstem lesions were

made interrupting the lateral and the medial brainstem pathways respectively. The behavior of the monkeys was then carefully observed for 4 to 5 months postoperatively. The animals with the lateral brainstem lesions, after bilateral pyramidotomy, took their food by a combined movement of arm and hand, apparently having lost the recovered capacity to execute independent movement of the extremities, especially their distal part. Animals with medial brainstem lesions, after bilateral pyramidotomy, showed a persistent defect in the control of body and limb-body movements as in righting, walking, and turning but maintained the capacity to acquire food morsels by independent arm and hand movements.

In the rhesus monkey, the direct pyramidal connections to motoneurons of distal extremity muscles (individual digit control) are not present at birth but develop during the first 6 to 8 months of postnatal life (Kuypers, 1962; Dominik and Wiesendanger, 1971). Correspondingly, in picking up food, monkeys under 2 months of age do not execute relatively independent finger movements. Recently Lawrence and Hopkins (1972) completely interrupted both pyramidal tracts in neonatal monkeys. Two years later the animals showed very little general motor defect but had failed to develop the normal individual finger control, i.e., there was no functional recovery.

These and other findings led to the following conclusions: The medial brainstem system provides postural control of body and limbs, while the lateral brainstem system provides the capacity for independent movements of the extremities, especially their distal parts. The corticospinal fibers amplify these brainstem controls and in addition uniquely provide individual finger control that probably depends on the direct pyramidal connections to motoneurons of distal extremity muscles.

This hypothesis was also tested without interrupting these pathways by studying the motor control in the split-brain monkeys in which the optic chiasm, the forebrain commissures, and dorsal mesencephalic commissures had been transected. This approach was suggested by the fact that anatomically each half of the brain is connected bilaterally with the ventromedial parts of the intermediate zone and contralaterally with the dorsolateral parts of the intermediate zone and the motoneurons of distal extremity muscles (Figure 22). Brinkman and Kuypers (1972) observed that, consistent with the original hypothesis, in performing a visuomotor task the extremity contralateral to the open eye could execute visually controlled

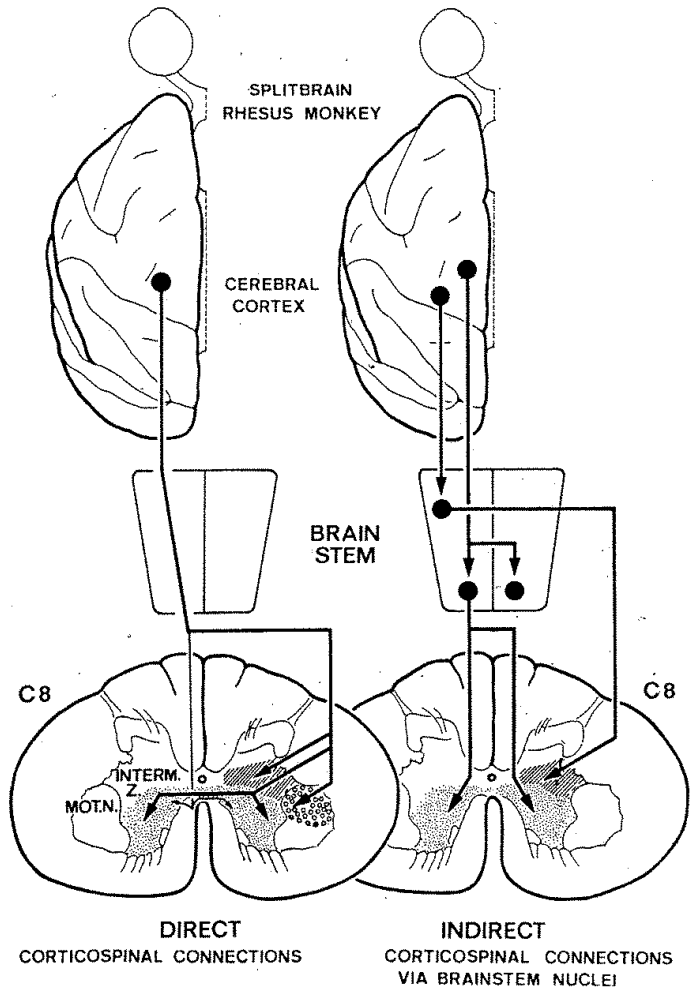

Figure 22. Diagram of the cortical connections to the spinal cord, both directly (*left*) and indirectly by way of the brainstem pathways (*right*) in the rhesus monkey. Ipsilaterally, the direct and indirect connections lead to the ventromedial part of the intermediate zone (stippled). Contralaterally the direct and indirect connections lead to both the dorsolateral (shaded) and the ventromedial (stippled) parts of the intermediate zone. Many direct connections are established contralaterally with motoneurons of distal extremity muscles (open circles). [Brinkman and Kuypers, 1972]

independent arm, hand, and finger movements, whereas the ipsilateral extremity executed mainly visually controlled arm movements and combined arm-hand movements.

Kuypers concluded from these findings that recovery of function does not occur in motor systems that do not share functions with other systems and that, after interruption of the various systems sharing a function, little recovery ensues. In his opinion the apparent recovery in such circumstances may be the result of nonspecific testing, which fails to show the loss of a specific function because the animal is allowed to employ different tactics in performing the task.

Functional Compensation in the Vestibular System: W. Precht

Unilateral removal of a labyrinth, or section of the corresponding vestibular nerve, produces the well-known postural asymmetries and "spontaneous" ocular nystagmus. The latter disappears a few days after the lesion, although rotation of the head still reveals asymmetries in ocular nystagmus. Asymmetries in evoked nystagmus subside in the following 4 to 6 weeks (compensated state). Bechterew (1883) observed that a lesion in the second labyrinth or vestibular nerve then produces nystagmus in the direction opposite to that produced by the first lesion. This second, or compensatory, nystagmus develops even when the forebrain and cerebellum are removed and the spinal cord cut, as long as the vestibular nucleus on the side of the first lesion is intact The usual explanation for the phenomenon assumes an increase in excitability in the vestibular nuclei on the side of the first lesion to balance the asymmetric input.

Precht and his collaborators investigated the problem anew by recording from single cells in the vestibular nuclei during the acute and compensated states after vestibular nerve section (Precht and Shimazu, 1965; Shimazu and Precht, 1965, 1966; Precht et al., 1966). They had previously shown that, in the normal cat, type I vestibular neurons, which project to eye motoneurons, are excited by homolateral and inhibited by contralateral labyrinthine stimulation. They also demonstrated that contralateral inhibition is mediated by commissural fibers and type II cells (interneurons), which do not project to the oculomotor nuclei and do not receive ipsilateral vestibular input.

In the acute stage after hemilabyrinthectomy, the spontaneous and rotation-evoked activity of type I cells was almost absent on the deafferented side, while on the intact side spontaneous activity was higher than normal and acceleration threshold higher than in bilateral

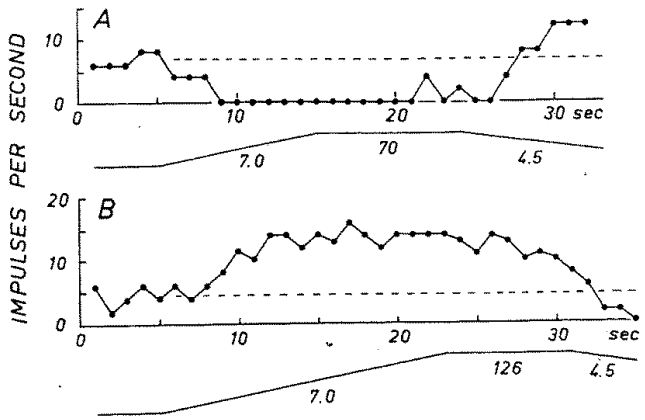

Figure 23. Frequency diagrams of discharges of a type I vestibular neuron in response to contralateral (A) and ipsilateral (B) horizontal angular acceleration and deceleration. Ipsilateral labyrinth was destroyed 30 days before recording. In each diagram the ordinate represents spikes/sec of single unit discharges measured in each sec. Horizontal broken line in each diagram represents the average frequency over 10 sec before rotation. Curve below each frequency diagram indicates the speed of rotation. Numbers below the rotation curve indicate, from left to right, the acceleration rate (degree/sec^2), velocity of constant rotation (degree/sec), and deceleration rate. [Precht]

intact preparations. Type II activity could be detected on the deafferented side but not on the intact side.

In the compensated state (Figure 23), spontaneous activity as well as responsiveness to rotation returned in the type I cells of the deafferented side, although their acceleration threshold was higher than normal and of the same order of magnitude as the threshold for the type II cells.

Electrical stimulation of the remaining intact VIIIth nerve showed that the threshold for commissural inhibition of type I neurons was significantly lower as compared to the bilateral intact preparation. The threshold for type II activation remained unaltered.

Thus two major changes occur with vestibular neurons during the process of compensation: (1) Type I neurons in the deafferented nucleus regain spontaneous activity, the origin of which is unknown. Disappearance of postoperative spontaneous nystagmus might be readily explained by the recovery of tonic activity in type I neurons, because it establishes a new symmetry between the bilateral vestibular output to the ocular motoneurons. (2) During recovery, commissural inhibition increases its efficacy. This effect assures that the spontaneous