1947 – (25)

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Reprinted from the Archives of Neurology and Psychiatry
October 1947, Vol. 58, pp. 452-473

Printed and Published in the United States of America

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CROSSING of nerves to antagonistic limb muscles or transplantation of the muscles themselves has been found to produce in the rat disorders of motor coordination directly correlated with the anatomic rearrangements. For example, transposition of the flexor and extensor muscles of the shank [1] or interchange of the nerve supply of these muscles [2] produced in each case a full reversal of the flexor-extensor movements of the ankle. A comparable reversal of motor action in the forelimb was shown to follow the crossing of nerves and the transposition of muscles acting on the elbow joint.[3] Sensory nerve crosses from one hindfoot into the contralateral hindfoot also were found to result in false reference of sensations and a maladaptive reversal of the withdrawal reflexes.[4] All these functional derangements persisted permanently in the rat without correction by reeducation.

Numerous clinical reports indicate, however, that man is capable of achieving motor readjustments considerably more complex than those called for by the foregoing nerve-muscle operations on the rat.[5] Consequently, it seemed imperative to conduct experiments of the sort

This work was done at the Yerkes Laboratories of Primate Biology as part of a project directed by Dr. Paul Weiss under contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Chicago.

1. Sperry, R. W.: The Functional Results of Muscle Transposition in the Hind Limb of the Rat, Anat. Rec. (supp.) **73**:51, 1939; J. Comp. Neurol. **73**:379-404, 1940.

2. Sperry, R. W.: The Effect of Crossing Nerves to Antagonistic Muscles in the Hind Limb of the Rat, J. Comp. Neurol. **75**:1-19, 1941.

3. Sperry, R. W.: Transplantation of Motor Nerves and Muscles in the Forelimb of the Rat, J. Comp. Neurol. **76**:283-321, 1942.

4. Sperry, R. W.: Functional Results of Crossing Sensory Nerves in the Rat, J. Comp. Neurol. **78**:59-90, 1943; Fixed Persistence in the Rat of Spinal Reflex Patterns Rendered Extremely Maladaptive by Cross Union of Sensory Nerves, Federation Proc. **5**:98, 1946.

5. Sperry, R. W.: The Problem of Central Nervous Reorganization After Nerve Regeneration and Muscle Transposition: A Critical Review, Quart. Rev. Biol. **20**:311-369, 1945.

described for the rat on an intermediate form, such as the monkey. It was not intended in the present investigation to try to explore in full quantitative detail the capacities of the monkey for readjustment under such conditions. This would be a tremendous task, requiring, among other things, a preliminary analysis of normal muscle kinesiology beyond anything yet available, even for man. The object was, rather, to disclose, if possible, any basic and major differences in capacity for readaptation between the rat and the monkey that might appear under experimental conditions which were roughly similar, and to find out whether the results in the monkey would not approach closely those reported for man. It was hoped that such a comparison of the monkey and the rat might yield some clues to fundamental differences in organization of the central nervous system of these two forms which might explain in part the superior adaptability of the primates.

METHOD AND MATERIALS

The nerve branches to the primary flexor and extensor muscles of the elbow were dissected free, divided and cross united, so that the nerves were forced to regenerate into muscles antagonistic to those which they had formerly supplied. Nerves of the arm, rather than of the leg, were chosen because, other things being equal, motor readjustment should occur more readily in the arm.[5] Selection of these particular nerves and muscles acting on the elbow joint was made because of anatomic advantages for the type of operation involved, because the muscle function at this hinge joint is relatively uncomplicated and because the same nerves and muscles had been used in previous experiments on the rat.

After sufficient time had been allowed for nerve regeneration, the movements of the elbow were examined in natural and in trained activities, first for reversed movements and discoordination and later for evidence of correction of these abnormal movements. Because the animals soon learned to use the elbow joint by various trick methods without any active contraction of the test muscles, it became necessary to test coordination and to train for reeducation under special conditions in which such trick movements would not be possible. This was satisfactorily accomplished by making the monkeys reach through a metal tube for their food (figure). The tube was about the length of the monkey's upper arm and was large enough so that the fist partly closed over a small object could easily be drawn through it. The tube was mounted over a hole in the center of a large screen of hardware cloth, the mesh of which was too small to permit passage of the fingers but permitted the animal to see easily the object for which it was reaching. The screen and tube could be placed on the sides or on the top of the training cages. Pieces of food impaled on a stick were held outside the screen in such a position that they could be reached only if the monkey extended the arm into the tube all the way to the shoulder, with the elbow protruding slightly beyond the outer edge of the tube. In this position the elbow could be flexed and extended freely, but the upper arm and the shoulder were well stabilized in and against the tube. Elbow movement was easily observed under these conditions, and most of the trick movements depending on shoulder action, momentum or inertia of the forearm or special postures with respect to gravity were excluded. By holding the lure in different positions with respect to the end of the tube, by moving the lure after the animal had started to reach for it, and by using the tube in vertical as well as in horizontal positions, one could test satisfactorily the monkey's capacity to flex and extend the elbow under a variety of conditions.

Use of the tube was begun shortly after recovery of function in the second arm in the bilateral cases. Approximately twenty trials per day for each arm were given through the first seven weeks. Thereafter the tests were administered over ten day periods at intervals beginning about once in every two months and increasing to once in six months at the end of the third year

Observations were carried out over a total period of a little more than three years. Most of the data were obtained from 4 red spider monkeys (Ateles geoffroyi), 3 of them with nerves crossed in both arms and 1 with nerves crossed in one arm only. These full-grown animals had been kept in captivity at least six years prior to their use in these experiments. Additional results obtained on

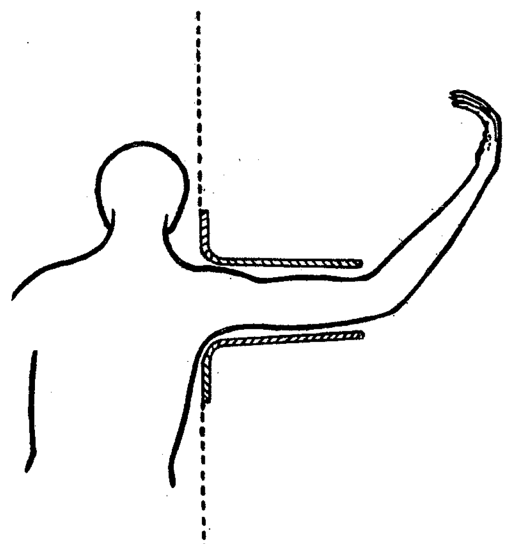

Diagram showing how elbow movements were tested by having the monkey reach through a short rigid tube.

2 macaques (Macaca mulatta) both operated on unilaterally, were in essential aspects similar to those obtained on the spider monkeys. The macaques were approximately 3 years old at the time of operation. They proved to be somewhat less satisfactory than the spider monkeys with regard both to the operation and recovery and to functional examination. One of the spider monkeys died at the end of one year and another at the end of the second year. The other 4 animals were killed about three and one-half years after their initial nerve-crossing operation. An additional spider monkey and a macaque, in both of which the elbow joint became ankylosed after operation, were discarded from the experiment.

The following control measures were taken: In all animals all extra muscles acting directly on the elbow joint were excised in order that their action might not counteract or obscure that of the test muscles. In the contralateral arm of the spider monkey with unilateral nerve cross, nerve splices were made but failed to hold, and the nerves regenerated back into their proper muscle groups instead of into antagonistic muscles. Otherwise, this arm was operated on in the same way as in the other spider monkeys. It therefore made a good control and was used as such. To overcome the animals' tendency not to use an arm that had been operated on, the other arm was either similarly operated on, or, in the unilateral cases, paralyzed by repeated nerve crushing. Special care was taken throughout all tests to distinguish movement of the elbow caused by active contraction of the test muscles from movement produced by other methods. Biopsy was performed about two years after the first operation to check, by dissection and by electrical stimulation of the nerves proximal to the point of cross union, for the intended cross innervation as well as for any possible misregeneration of nerve fibers back into their original muscles. Again, when the animals were killed, the arms were dissected carefully, and electrical stimulation was employed to test once more for the existence of stray nerve fibers innervating their own, instead of antagonistic, muscles.

OPERATION PROCEDURE

The main trunk of the musculocutaneous nerve, which supplies the biceps and brachialis (flexor) muscles of the elbow, was dissected free and cut. Likewise, the nerve branches to the triceps (extensor) muscles were dissected free and cut at the same level. In freeing the extensor nerves, it was frequently necessary to split the nerve branches for several centimeters into their constituent loosely bound fascicles. This was done under a dissecting microscope with almost no difficulty in this region from intraneural plexuses. The central end of the musculocutaneous nerve was then united to the collected distal ends of the triceps nerves; conversely, the central ends of the triceps nerves were united to the distal end of the musculocutaneous nerve. Because there was no slack in the nerve lengths, the crossed stumps were fastened together, with only a small gap between them, by a single suture of fine silk through the epineurium. A tube of preserved monkey artery about 1.7 cm. in length was then pulled over each union. Finally, further to prevent any fibers from misregenerating into their original channels, a large sheet of allantoic membrane [6] ("insultoic membrane") was laid between the two splices.

The coracobrachialis muscle was excised, and its nerve was split proximally away from the musculocutaneous trunk, so that no nerve fibers to this muscle were included in the nerve cross. The end of this nerve was ligated and fastened proximally to prevent regeneration into the test muscles. The anastomotic nerve branch from the median nerve to the brachialis muscle was also severed, ligated and tied posteriorly, where it could not regenerate into its original muscle. The epitrochlearis (extensor) muscle and its nerve were left intact to help prevent ankyosis of the joint during the period of muscular paralysis. About six months after the primary operation this muscle was excised and its nerve ligated and fastened as far dorsally as possible. At the same time the muscles of the forearm which overlap the elbow joint and have their origin on the humerus, such as the brachioradialis, the pronator teres and the extensor carpi radialis longus, were excised to prevent their aiding in movement of the elbow. It has been shown that

6. "Insultoic Membrane" (Bauer and Black).

flexion of the elbow can be accomplished in man by some of these muscles after complete paralysis of the brachial flexors,[7] and such action is even more favored by the mechanical relations of these muscles in the monkey.

The method just described was used in crossing the nerves in the right arm of the 4 spider monkeys. An alternative procedure was used on the left arm of these animals and also on the left arm of the 2 macques as follows: The overlapping muscles of the forearm were excised in a preliminary operation about one month before the nerves were crossed. In the main operation, the central ends of some of the more proximal branches of the nerves to the triceps muscle were collected and crossed to the distal stump of the isolated nerve to the biceps muscle. The central end of the nerve to the brachialis muscle was crossed to the collected distal stumps of some of the more peripheral branches to the triceps muscle. When crossed in this way, the nerve stump could be joined with plenty of slack, and no silk suture was required. The nerves were trimmed to an appropriate length and joined in an arterial tube by a method similar to that advocated by Weiss.[8] The unused nerve stumps were ligated tightly and tied to tissues as far away from their original terminations as possible. The epitrochlearis muscle and nerve were left intact, to be excised about six months later. All operations were carried out with the subject under deep pentobarbital anesthesia.

No essential differences in the functional results were noted which could reliably be attributed to the different surgical methods of crossing. The essential effect of the operations by either method was to cause the flexor muscles of the elbow to become innervated only by what were originally extensor motoneurons, and the extensor muscles to be innervated only by flexor motoneurons such that a reversal of elbow movement should result in the absence of central nervous reorganization. Such terms as "reversed movement" and "reversed action" refer throughout to the unadjusted maladaptive action of the reinnervated muscles.

RECOVERY WITH REVERSED MOVEMENTS

Immediately after the operation on the right arm, the animals used the contralateral arm almost entirely. After the wound had healed, and while the nerves were still regenerating, the use of the experimental arm gradually increased, although the left arm remained dominant and preferred. The onset of recovery in the test muscles of the right arm was thus obscured by the tendency to use the normal (left) arm, as well as by the action of extrabrachial and antibrachial muscles left intact during the period of muscular paralysis to help prevent ankylosis of the joint. Removal of these extra brachial muscles again decreased the use of the right arm. Even when the overlapping muscles of the forearm had been freshly excised from the left arm, in the preliminary operation for the alternative surgical procedure previously described, the animal still preferred immediately afterward to use the left arm.

It was only later, after the nerves had been crossed or crushed in the contralateral arm, approximately eight months after the primary

7. Wright, W. G.: Muscle Function, New York, Paul B. Hoeber, Inc., 1928.

8. Weiss, P.: The Technology of Nerve Regeneration: A Review; Sutureless Tubulation and Related Methods of Nerve Repair, J. Neurosurg. **1**:400-450, 1944.

operation in all cases, that signs of function of the crossed nerves became apparent. When the animals were thus suddenly forced to use the arm with the cross innervated muscles in ways to which they had not been accustomed, they displayed reversed flexion and extension movements of the elbow. For example, in an attempt to extend the arm outward and forward horizontally for food, the forearm was, instead, flexed upward against gravity toward the chin. When the monkey tried to catch food impaled on the end of a stick, which was moved about slowly in front of the cage within easy reach, the elbow showed extension when flexion was called for, and vice versa. When the arm was being withdrawn through the wires of the cage, the forearm often flexed at right angles instead of straightening, thus becoming caught at the elbow. Efforts to straighten the arm only caused it to bend more acutely. Caught in this position, the animal would continue to tug and pull for some moments, until eventually the flexor muscles relaxed, the elbow straightened and the arm was pulled inside the cage.

Reversed movements of the sort just described appeared in all the 4 spider monkeys and in 2 macques, varying in intensity and frequency, however, in the different animals. They were most conspicuous in a spider monkey in which the muscles of the forearm and hand, as well as the test muscles of the upper arm, were paralyzed during the period of regeneration. This paralysis was probably caused by overstretching of the main nerve trunks, particularly of the radial nerve, at the time of operation. Consequently, this animal used the right arm hardly at all during the period of regeneration and, unlike the other animals, had had no practice in inhibiting the reversed action of the test muscles or in using the elbow passively during the preceding months.

In animals with bilateral crossed innervation the time of onset of functional recovery in the left arm was obscured in the spider monkeys mainly by trick methods of using the elbow joint passively and, in part, by preferential use of the right arm, which had previously been operated on. The animals were not suddenly forced to use the left arm in new ways, as had been the case with the right arm. There was plenty of time during recovery to adjust gradually to the postoperative conditions; consequently, reversed action was not seen in the left arm of these monkeys under natural cage conditions. It was only when they were forced to use the left arm in reaching through the metal tube, where the trick movements on which they had been relying were impossible, that reversal of elbow action on the left side became definitely apparent.

In 1 spider monkey recovery on the left side was exceptional in that no reversal of movement appeared under any conditions. On the contrary, well coordinated flexion and extension of the elbow in the proper direction occurred even in comparatively rapid movements. Biopsy, as well as examination after the animal had been killed, revealed that in this instance the nerve crosses had not been successful. The nerve splices had pulled apart, and extensive misregeneration of nerve fibers into their original flexor and extensor muscle groups had taken place. Almost no crossed innervation was observed. The action of the reinnervated muscles of this limb therefore presented a good control for comparison with the function in those animals in which the nerve crosses had been successful.

On the whole, the reversed movements in the monkeys were much less conspicuous than had been the reversed limb movements in the rat after similar nerve crossing operations. In the rat the reversed responses were carried out with full intensity and scope persistently throughout all activities, the animals seemingly insensible of the reversal. In the monkey, on the other hand, the occurrence of a movement in reverse direction usually caused a break in the general activity going on at the moment. The erroneous reaction was halted and attention was turned to the abnormally acting member. After repeated attempts to improve the arm movement, the animal either succeeded somehow in getting the hand into a satisfactory position, or ceased trying altogether. As a result, and because of other factors to be mentioned, the reversed elbow movements tended to be weak in the monkey and in most instances to be brief or only incipient, without being carried through to completion

The idea that central nervous reorganization to suit the new peripheral relations under such conditions occurs immediately and spontaneously, without any practice,[9] a view which has clearly been discredited in the case of the rat and lower vertebrates,[10] is also refuted by these results in the monkey. Not only did reversed movements appear during the early stages following nerve regeneration but, as will be described, the reversed action persisted in some instances for months, and even years.

After the early stages of recovery the test and observation program proceeded in an exploratory manner, with considerable irregularity and variation from animal to animal and from time to time. It would be prohibitive to recount in any detail the histories and specific findings for the individual animals throughout the three year period. An attempt is made, therefore to present the essential aspect of the results under the following topical headings, with examples illustrating the principal points in each instance.

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9. Marina, A.: Die Relationen des Paläencephalons (Edinger) sind nicht fix, Neurol. Centralbl. **34**:338-345, 1915. Bethe, A., and Fischer, E.: Die Anpassungsfähigkeit (Plastisität) des Nervensystems, in Bethe, A.; von Bergmann, G.; Einbden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1931, vol. 15, pp. 1045-1130. Goldstein, K.: The Organism, New York, American Book Co., 1939.

10. Sperry.[5] Weiss, P.: Self-Differentiation of the Basic Patterns of Co-Ordination, Comp. Psychol. Monogr. **17**:1-96, 1941.

TRICK MOVEMENTS AND SUBSTITUTIONARY REACTIONS

The monkeys were quick to find ways of using the experimental limb advantageously without contracting the test muscles. These compensatory, or "trick," methods of using the elbow passively were largely acquired early in the regeneration period, while the test muscles were completely paralyzed, and were then carried over with gradual improvement after the crossed nerves had regenerated. The ability to use the arm in such a way that the elbow would flex and extend passively as early as three weeks after the final removal of the extrabrachial muscles in the cases of bilateral crossed innervation was so good that a casual observer might well have failed to notice any motor disability. The efficiency with which the arms were used in regular cage activities suggested at first glance that complete central nervous reorganization must already have occurred, enabling the test muscles to contract in their proper action phase despite the abnormal innervation. With more careful analysis of the movements, however, it became apparent that this elbow action was not necessarily dependent on active contraction of the test muscles. In every situation observed, all flexor movements and all but a few rare extensor movements (see section on "Positive Readaptation") could be accounted for on the basis of other factors, such as gravity, inertia or secondary effects of muscles at other joints.

Extension of the elbow was easily achieved and maintained in most postures by the action of gravity. The forearm was simply allowed to fall loosely from the elbow into the extended position. In some postures the relative positions of elbow and forearm were adjusted by movement of the upper arm from the shoulder, so as to increase the effectiveness of gravity. At times the movement from the shoulder, combined with the inertia of the forearm, was sufficient to bring about extension of the elbow without the aid of gravity. When it was necessary to extend the arm upward against gravity, as in climbing, the elbow was usually extended first by gravity, and then the whole arm, straightly extended, was raised from the shoulder. At the same time the upper arm was properly rotated so that the weight and inertia of the forearm and hand tended always passively to extend the elbow, which, of course, would not bend beyond the straight position because of the structure of the bones and ligaments. With the upper arm in a horizontal position or at a downward angle, the flexed elbow could be extended simply by outward rotation of the arm from the shoulder, in which case the rotation of the upper arm swung the forearm into a position from which it was forced into extension by gravity.

Flexion of the elbow, which has to occur against gravity in most upright postures, was not achieved as frequently as extension. To flex the elbow upward to bring food to the mouth, the animal usually propped the forearm against the knees in the sitting position. The elbow was sometimes flexed by gravity when the upper arm was raised. The spider monkeys frequently picked up food and put it in the mouth while hanging upside down from their tails. In this position the forearm hung vertically from the elbow and was flexed or extended passively as the elbow was raised or lowered. Occasionally the forearm was swung into a position of flexion by a flail-like motion. When the hand grasped the wires of the cage, flexion or extension of the elbow might occur, depending on movements of the upper arm and shoulder. Incidental and transient flexor, as well as extensor, movements of this sort occurred continually.

By these and similar methods adaptive flexion and extension of the elbow were achieved without active participation of the test muscles. These movements came to be performed quite smoothly, so that the monkeys appeared to get along in their natural cage activities without obvious motor impairment. Such movements tended to obscure whatever action of the test muscles may have been present and, at the same time, reduced the urgency of learning new motor patterns involving the cross innervated muscles.

Besides trick methods of using the elbow passively, many less direct substitutionary reactions were employed, such as increased use of the contralateral arm or of the ipsilateral shoulder and wrist to make up for the defective action of the elbow or use of the mouth, instead of the hands, to pick up food. Many of these substitutionary and trick adjustments probably required no learning at all, whereas others, particularly some of those involving movements of the elbow itself, undoubtedly required practice and learning in varying degrees. Adjustments of the sort described, involving shifts in the function of the normally innervated musculature, constitute the simplest means of readaptation to rearrangement of motor nerves. Even the rat showed some simple readaptation of this kind. The variety and scope of such readjustments, however, were obviously much greater in the monkey.

INHIBITION OF REVERSED MOVEMENTS

Complete readjustment in the action of abnormally innervated muscles requires, first, inhibition of old contraction patterns and, second, positive activation in new patterns. Both may be learned in a single step, or the two may be learned separately. Where learning of the two takes place independently, it is necessary to distinguish between them, because the type of central nervous adjustment may be quite different for the two processes. Undifferentiated inhibition of the arm muscles involves no more difficult an adjustment than would be necessary if the muscles had their normal nerve supply. To inhibit action at the elbow while, at the same time, retaining movement of the wrist and shoulder is a more complex readjustment and apparently required some practice in the present cases. This still does not involve, however, the more specialized, and presumably more complicated, reversal of relations between the flexors and the extensors, as well as other arm and trunk muscles that would be required for positive readjustment of the contraction phase of the muscles. Also, the ability to halt reversed movements which are already under way ought to be distinguished from the ability to inhibit the initiation of reversed action. The interruption of adverse movements took place readily in most instances, apparently as a result of the visual and kinesthetic effects of the movement in reverse. It is the inhibition of the tendency to start reversed action that required practice and which is the main concern in the following discussion.

Many of the trick reactions mentioned in the foregoing section required that the reversed action of the test muscles be inhibited to permit loose passive movement of the elbow. These trick reactions were learned largely during the period when the test muscles were paralyzed and their active inhibition, therefore, not required. Later, however, when function was restored through reinnervation, active inhibition of the test muscles became necessary. The learning involved in this instance may have been aided considerably by the opportunity to acquire first the positive part of the coordination pattern while the test muscles were still paralyzed.

In some cases it was clear that the monkey learned to inhibit the reversed action of the test muscles rather quickly. For example, the reversed movements in the right arm that appeared immediately after the left arm was rendered useless did not last more than about three or four days in most of the animals. The reversals were most pronounced on the first two days and on the first trials of each test session on succeeding days. In 1 of the spider monkeys clear reversed movements appeared only in the first few attempts to elicit them on the first day and in the first trial on the second day. The animal refused to use the arm thereafter except in performances in which trick movements of various kinds were adequate. In another spider monkey, at the other extreme, the reversals remained conspicuous for about two weeks. The reversed reactions in this exceptional case were eliminated in large part by the end of the first month, but relapses remained common through the succeeding two months. This animal was the one which had had no practice in the use of the arm during the period of nerve regeneration because of temporary paralysis of the muscles of the forearm and hand. The notable difference between this animal and the others indicated that the more rapid inhibition of reversed elbow movement in the other animals could be ascribed to the practice which they had already had in the preceding months, both before and after the reinnervation of the test muscles.

The disappearance of reversed elbow movements after a short learning period under the foregoing conditions does not imply the onset of correct reactions in the test muscles. At first the animals simply refused to employ the arm in circumstances in which it had moved in reverse direction. Later they hesitantly began to use it, gradually dropping out all reversed action at the elbow. This inhibition of reversed action merely made it possible to use the joint passively by various trick methods of the kind described in the preceding section.

In the special test situation in which the animals were forced to reach for things through a tube, inhibition of reversed movements came somewhat more slowly. Under these conditions it was not so easy to resort to trick movements, nor was there as much opportunity for practice. In the animal which learned most rapidly it was almost two weeks before the reversed movements were clearly beginning to be inhibited. With most of the animals it was more nearly three to four weeks before they had begun to learn to inhibit reversed action of the elbow in simply reaching for a stationary lure. The reversed action thereafter became less frequent and extensive, but obvious reversals were still not uncommon as late as six, eight, nine and sixteen months after training had been started in different cases. Improvement took place in both arms with about equal speed in 1 of the 3 monkeys with bilateral crossed innervation. In the other 2 monkeys the right arm improved more rapidly than the left, especially in the early stages of training. This was to be expected, for the right arm had recovered first from the operation and had had more practice than the left. The superiority of one side over the other could be taken as evidence either that there was lack of transfer of learning from one side to the other or that the motor coordination used on the two sides was somewhat different.

One spider monkey was exceptional in that it persistently continued to exhibit predominantly reversed action throughout two and one-half years without evidence of any appreciable improvement by learning. This animal was unable to obtain a lure even in a position in which it was merely necessary to relax the test muscles so that the forearm would fall into flexion passively by its own weight. Under these conditions, with the animal obviously straining with full effort to flex the elbow downward, the forearm remained stiffly extended against gravity. Learning appeared abruptly toward the end of the second year of training in this case, and, once started, it proceeded fully as rapidly as in the others. This exceptional monkey was the one in which the left arm was the control. Its slowness in learning may, therefore, have been due to the fact that it used the more proficient control arm regularly and did not give practice to the experimental arm.

The steps by which the different animals learned to reach through a horizontal tube and flex the elbow downward 90 degrees were surprisingly similar, and in some respects not unlike the method of learning described by Weiss and Brown [11] after muscle transplantation in man. At first there was only stiff extension of the elbow straight outward against gravity, and after a moment the monkey usually stopped trying to flex the arm and withdrew it from the tube. With sufficient hunger the animal persisted in its efforts for a longer time, in the course of which there were momentary relaxations of the extensor muscles, which may possibly have been accompanied with active contraction of the flexor muscles. In any case, the result was short, sudden flexor movements of the elbow imposed on the predominant extension. These sudden, almost spasmodic, flexor movements were then increased in frequency and extent during the second and third weeks of training, the forearm swinging up and down through an angle of 90 degrees. At the bottom of the downward stroke the hand and fingers came in contact with the lure, but at this stage of learning the hand movements were not coordinated with the elbow movements, and the lure was usually missed because the fingers failed to close at the proper moment. Eventually, after two or three months, the monkey managed to inhibit the predominating extension, so that the forearm, after it had fallen into the flexed position, was not immediately jerked back into extension. There was then time for the fingers and hand to grope for and grasp the lure. At the end of three years the downward flexion of the forearm and the opening and closing of the hand had become coordinated into a single movement, but at best it still lacked in all cases the speed and sureness of the same movement in the control arm.

There was thus a striking difference between the monkey and the rat with respect to the inhibition of reversed movements. In the rat the reversed movements persisted indefinitely. In the monkey, on the contrary, they were quickly halted and inhibited. In only 1 monkey, under particular conditions already described, did the reversal persist in a manner at all resembling that in the rat. This was in an animal which had used its arm comparatively little because of the proficiency of the contralateral arm.

POSITIVE READAPTATION

Readaptation went further than the mere acquisition of various trick movements and inhibition of reversed action. Positive readjustment in the active contraction of the muscles supplied by the crossed nerves was eventually achieved to some degree in all animals. It generally came later and more slowly than inhibition of reversed patterns, although in some reactions the two occurred simultaneously. There was con-

11. Weiss, P., and Brown, P.: Electromyographic Studies on Recoordination of Leg Movements in Poliomyelitis Patients with Transposed Tendons, Proc. Soc. Exper. Biol. & Med. **48**:284-287, 1941.

siderable variation in the time required for such readjustments to occur in the various animals and in the level of efficiency finally achieved. Such differences seemed best ascribed to accidents of learning.

Adaptive extension of the elbow against gravity appeared in the right arm of 2 spider monkeys and in the left arm of 1 macaque when they were induced to reach for food in the early months following completion of nerve regeneration. This active extension of the elbow in the correct direction, however, was slow, weak, accompanied with pronounced tremors and generally rather inefficient in all cases. The monkeys were observed to use this extension of the elbow only when food was offered in such a position that it could not be reached otherwise. They preferred to extend the elbow passively and then raise the whole arm from the shoulder whenever possible. Along with these correct extensor actions the animals exhibited as well flexor and extensor movements in reverse in other performances.

When biopsy was performed, it was observed that some extensor fibers had escaped and misregenerated into the extensor muscles in the animals that had first shown adaptive active extension. Similar misregeneration was also observed, however, in 2 other animals which had not shown these early extensor movements. The extent of this unintended reinnervation of the original muscles appeared to be quite small, for only a small twitch of the triceps muscles was elicited with maximum electrical stimulation. In only 1 case was the contraction strong enough to cause a short extensor movement of the elbow. Because the extensor nerves were numerous and some of them very fine, and because the proximal nerve stumps were almost surrounded by extensor muscles, it was difficult to prevent at least a few fibers from escaping back into the extensor muscles. An effort was made at the time of biopsy to search out, cut and ligate all these misregenerated fibers. Afterward, the animals were still able to extend the arm actively at the proper time, however, indicating that by this stage of recovery, at least, the adaptive extension involved function of the nerves successfully crossed. It remained uncertain whether or not the early extensor movements had been effected by the misregenerated nerves.

There was much less chance for the flexor nerves to regenerate back into their proper muscles, and no misregeneration of this sort was seen at biopsy among the experimental animals except in 1 monkey, in which a fine thread of fibers had misregenerated from the median nerve into the brachialis muscle. The function in this case was not significantly different from that in the others. The following data on positive readaptation on the flexor side are, therefore, not complicated by the presence of unintended nerve regeneration.

There was no evidence of active adaptive flexion of the forearm in any of the animals in the course of ordinary cage activities during the early months following the completion of nerve regeneration. It was not until the monkeys had been trained for varying periods to reach through the tube that the first signs of adaptive flexor action appeared. All the animals eventually learned to flex the forearm against gravity in this situation. At first the flexor movements in the proper direction occurred accidentally and were peculiarly sudden and spasmodic. For example, in an attempt to flex the forearm upward with the upper arm stabilized horizontally in the tube, the predominant reversed extension was occasionally broken by a sudden upward flexion of the forearm, which immediately was snapped back into extension. There seemed to be little or no control over these early accidental movements in the proper direction. Even when the arm flexed sufficiently for the hand to come in contact with the lure, the lure was not grasped. It was as though the correct movement had caught the monkey by surprise, so that it was not prepared to grasp with the hand at that moment. In time the animal learned to grab at the lure at the height of these sudden upward swings. Later still, some control was acquired over the flexion itself, so that the movement could be made more slowly and steadily, allowing time for the wrist, fingers and angle of the fore-arm to be shifted in adaptation to the particular position of the lure.

In the case of these active flexor movements against gravity, the time required for learning was not appreciably different from that involved in flexion with gravity, where only inhibition was required. By the end of a month the monkeys, with 1 exception, had clearly begun to flex the elbow when flexion was called for, 90 degrees and sometimes more. They were not able to do so consistently and the movements were still rather spasmodic and poorly controlled, but there was unmistakable advancement over the reactions made during the first week of training. The final step to be learned in this performance by most of the animals was the coordination between finger and elbow movements. A point was reached at which the elbow could be flexed properly to bring the hand into the vicinity of the lure and held there, but as soon as the fingers were opened and an attempt was made to grasp the lure, the elbow simultaneously extended, carrying the hand out of reach. By the end of eighteen months this difficulty was overcome. The animals were able to flex the forearm upward to an angle of 90 degrees and to hold the flexed position while the lure was grasped with the fingers. The movements still showed pronounced tremors in 2 monkeys and all the animals had occasional relapses in which the elbow would extend repeatedly when flexion was attempted. In these particular conditions, apparently, the active contraction against gravity was learned about as readily as the downward movement with gravity. With regard to the relative speed of learning on the two sides in the 3 bilateral preparations, the conditions paralleled those already given for learning to flex the arm downward. Thus, in this respect, also, the learning processes involved in flexing downward with gravity and in flexing upward against it were closely related, suggesting that the coordinations were not much different in the two situations.

The 1 exceptional animal mentioned had not progressed at the end of eighteen months beyond the point where the forearm displayed repeated spasmodic flexions to about 40 degrees at most, with the hand attempting to grasp the lure when it was held within this range. Often the hand failed to close on the lure even when the palm or volar surface of the fingers made contact with it. This was the same animal which had not even learned by this time to relax the brachial muscles so that the forearm could flex downward passively by its own weight. Ability to flex the forearm was acquired suddenly during the second day of a training session near the end of the second year. For the first time the monkey managed to flex the forearm upward a full 90 degrees. The capacity to flex the elbow was retained on immediately succeeding trials in horizontal and downward directions, as well as in the upward direction. In the course of the next two days the flexor movements, which first had been abrupt, spasmodic jerks, became slower and steadier. Positive readaptation in this instance, then, was established directly, without an intermediate stage of indifferent inhibition. As mentioned, this animal in which learning was exceptionally retarded was the one whose other arm served as a control, and it is probable that the delay in learning was causally related to the fact that the experimental arm did not get as much practice as in the other animals.

In the left arm of 2 of the spider monkeys upward flexion of the forearm was conspicuously associated with pronation of the hand. If the hand was in a position of supination, the elbow extended when flexion was attempted. As soon as the hand turned into pronation, the elbow flexed. If the elbow were already in the flexed position and the hand became supinated in an attempt to grasp the lure, the elbow immediately extended, carrying the hand in a reverse direction away from the lure. This association of pronation and supination with flexion and extension of the elbow was rather strict in the first stages of learning but had almost disappeared by the beginning of the third year.

When the lure was moved slowly about with erratic changes in direction after the animal had started to reach for it, the monkey was quite unable to follow it in the early training sessions. Reversed flexor and extensor action at the elbow caused a great deal of excess waving of the arm, with overreaching and false starts, until the monkey either chanced to hit against the lure or ceased trying altogether. Eventually the monkeys all acquired the ability to make their movements predominantly in the correct direction, but complete elimination of reversed action was never achieved in any case. The animal in which the learning of simple flexion had been exceptionally delayed was greatly retarded in this performance also. Even in the animal with most advanced recovery, the movements after three years remained abnormally slow and hesitant, with pronounced tremors, overreaching and starts in the wrong direction. By contrast, the control arm under similar conditions could immediately snatch a piece of food off the end of the moving stick with no difficulty whatever. Even in simple flexion or extension of the arm to reach a stationary object, there remained to the end an obvious contrast between the quick, sure movements of the control arm and the slow, uncertain movements of the experimental arm.

In their regular cage activities the monkeys continued throughout the three year period of observation to rely primarily on trick methods of using the elbow. However, by the end of two years they had all acquired at least a few movements which involved active participation of the test muscles. For example, in certain positions in which they scratched themselves active elbow flexion against gravity was required. In reaching underneath the cage walls to steal food from neighboring cages, an awkward action in which trick movements were of little help, the animals managed to extend and flex the elbow without aid of gravity. On rare occasions, especially when the animals were competing for food, they would sometimes pick up food and lift it directly to the mouth by flexing the elbow against gravity without bothering to use the knee as a prop. The natural reactions of this kind in which adaptive function of the test muscles was involved were few. Those used most frequently were carried out in a smooth, and apparently automatic, manner without hesitation or tremors, such as were present in the specially trained movements with the tube. The better quality of coordination in these common cage activities may be attributed to the much greater amount of practice which they received. Vision was used to help guide the elbow movements to a large degree, but it was not necessary. The scratching reactions were regularly carried out without visual aid. Also, in reaching through the tube, it was common for the monkeys, after locating the position of the lure visually, to turn the head sideways in the act of reaching, so that the eyes could not be used further in guiding the arm movements.

GENERALIZATION AND TRANSFER OF LEARNED REACTIONS

It is theoretically conceivable that, having once learned in a particular performance to flex the elbow with cross innervated muscles, the animal might thereafter be able to flex the elbow properly in any other performance. On the other hand, it is possible that flexion and extension of the elbow would have to be relearned separately for each performance. The actual results came much nearer the latter extreme than the former. There were a number of instances in which the learning clearly failed to be transferred spontaneously from one performance to another. For example, after animals had learned to inhibit reversed flexion when trying to extend the arm horizontally for food in front of the cage, they again exhibited reversed flexion when induced to reach under similar conditions through the side of the cage or from a height or posture different from that in which the original learning had occurred. Most of the animals had learned to inhibit reversed action of the test muscles before they were tested with the tube. When these tests were started, however, the same reversal of elbow movement reappeared, and its inhibition had to be learned again in the new situation. The animal which was exceptionally slow in learning to flex the elbow when reaching through the tube had been able to flex the elbow to scratch itself or to pull food through the cage wires for almost a year before it finally learned to flex the elbow similarly in the tube situation. There was, thus, a striking lack of transfer in many instances.

If the learning process involved rearrangements in the relationships, of the primary or secondary neurons with the spinal centers, as contended at times in the past, one would expect a complete transfer of learning from one performance to all. Once the basic relationships of the spinal limb centers had been readjusted, the adjustment should be effective for all limb movements. The fact that learning to flex or to extend the elbow in one situation did not necessarily become generalized for other performances indicated that the neural readjustment was not localized in the spinal centers but involved, instead, reorganization of cerebral processes specialized for the different performances.

EFFECT OF PENTOBARBITAL AND CORTICAL LESIONS

To see whether it would cause a breakdown in the new coordination patterns and a return of reversed movement, 2 of the animals were given a three-fourths anesthetic dose of pentobarbital sodium subcutaneously. This was done on two separate occasions near the end of the third year. When the monkeys had reached a stage at which they were beginning to be unsteady in their movements, the elbow coordinations were tested. In 1 case there was a definite increase in the amount of reversed action at the elbow, but not a complete breakdown of the adaptive movements. It looked as though the animal was quite indifferent, and not concentrating on the arm movement as much as usual. In the second case the drug seemed to improve the elbow coordination. Under the influence of pentobarbital, this animal used the elbow more frequently than usual and with less tension. The animal seemed to be better relaxed, and the arm did not show the stiff extension which characteristically occurred under normal training conditions when flexion was attempted. This animal was the exceptionally slow learner. Apparently, the relaxation produced by pentobarbital may have either a beneficial or a deleterious effect, depending on whether the animal in normal circumstances is sufficiently or too little relaxed for optimal performance.

An attempt was also made to produce a relapse into reversed movements by making lesions in the cerebral cortex. In 1 animal bilateral destruction of arm area 6 and the anterior half of arm area 4, as given on architectonic charts, caused so severe a paralysis that meaningful tests could not be made. In 2 additional animals the frontal lobes were removed bilaterally, and in another operation extensive lesions were made in postcentral arm areas 1, 2, 5 and 7. In 1 of these animals the frontal lobes were removed first, and in the other the postcentral lesions were made first. In both animals the removal of the frontal lobes produced a temporary increase in the amount of reversed action, from which there was recovery by the end of two weeks. The postcentral lesions made it difficult for the monkeys to aim the arm movements accurately. They had great difficulty, for example, in getting the hand into the tube. In the flexor-extensor movement of the elbow, however, there was no sign of increased reversal. The results showed that the habit was not dependent on the frontal lobes and suggested that kinesthetic stimuli from the arm were not of major importance in the control of the adapted elbow coordinations.

ANATOMIC CHECKS

When the animals were killed, the brachial nerves were dissected free, with the use of anesthesia, and stimulated electrically to test for the presence of nerve fibers innervating their original muscles. All animals seemed to be free of such fibers except for the control monkey. Apparently, all unintended regeneration that had been present was successfully eliminated in the biopsies earlier in the experiments. The brachialis muscle in 1 of the macaques was not completely atrophic but did not contract to stimulation of any of the flexor nerve trunks. In the right arm of 1 of the spider monkeys the triceps muscles were not more than one-eighth their normal size. In the left arm of another spider monkey only the medial head of the triceps muscle was reinnervated, the other parts being atrophic. The test muscles were otherwise in good condition and ranged roughly from about two-thirds normal to normal in size. Stimulation of the nerves proximal to the region of cross union produced quick, vigorous responses of the forearm in the direction opposite the normal. Further dissection of the nerves disclosed nicely crossed nerve connections with no further evidence of unintended regeneration. Microscopic examination of samples of the crossed nerves from 3 of the animals showed rich reinnervation of the distal nerve stumps. In the region of the scar the fibers followed rather erratic courses, but this was not of much consequence because the motor components of the nerves were functionally homogeneous.

COMMENT

When the foregoing results are compared with those obtained after the interchange of limb nerves in the rat, the superior readaptive capacity of the monkey is very apparent. The monkey is quick to halt reversed movements, as well as to find new ways of accomplishing various acts without using the abnormally innervated muscles. Positive correction in the contraction phase of the test muscles was also eventually achieved. The active coordination of the cross innervated muscles became smooth and automatic in the course of two years in some reactions which received constant daily practice in regular cage activities. The rat, on the other hand, was found to repeat the reversed movements indefinitely without correction and even without inhibition of the reversed action.

Regarding the problem of the neurologic basis of the monkey's superiority, there are a number of known factors that appear significant. First, there are the obvious advancements in the structure of the primate nervous system and its associated end organs,[12] of which the following may be listed as particularly pertinent: (*a*) the more highly developed sensorimotor cortex; (*b*) the more elaborate connection systems between the spinal limb centers and the higher levels of the brain, especially the corticospinal tracts and the dorsal funiculi and medial lemniscus system; (*c*) the increased ratio of sensory to motor fibers in the limb nerves; (*d*) the increase in number and differentiation of sensory nerve terminations in the skin, tendons, muscles and joints, and (*e*) the mechanical arrangement of the muscles and skeleton of the primate limb so as to permit a much greater range of variation in limb movements than is possible in the rat.

To these anatomic differences may be added a number of functional differences which showed up in the course of the experiments. First, the monkey appears to have a greater capacity for detecting the presence of abnormal movements and for sensing in some degree the location and nature of the motor difficulty. Whereas the rat may continue indefinitely to repeat without modification a movement in reverse and seems meanwhile to remain oblivious of the reversed action, the monkey indicates by its behavior a more direct awareness of when and where an error has been made. The beginning of a single movement in reverse is often sufficient in the monkey to disrupt the activity going on at the moment. Sometimes it appears that the monkey stops and concentrates its attention on the member that is at fault. This is particularly true

12. Ariëns Kappers, C. U.; Huber, A. C., and Crosby, E. C.: The Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936.

when the limb is being used in a "voluntary" manner, as in reaching for or handling something.

This difference in capacity for perceiving the presence and location of adverse reactions is correlated with a second factor, namely, a difference in the way the animals naturally use their limbs. The rat is not adapted, like the monkey, for finely controlled, deliberate, delicate movements of individual limbs or separate segments of the limbs, as in manipulation. It is in movement of this sort that learning appears to occur most readily. Both the aforementioned factors are therefore probably important in the monkey's superiority: the ability to make discriminate voluntary movements of individual limbs and parts of the limb, and also the perceptual capacity to attend to such specific movements, to guide them and to note their effects.

There is a third possible factor, not unrelated to the two already indicated, which may also account in part for the monkey's quicker detection and inhibition of reversed movements, namely, a greater dependence of the motor control of limb movement on sensory cues, especially those originating within the limb itself. In the rat the adverse sensory effects resulting from movement of one joint in reverse is not sufficient, as in the monkey, to disrupt the motor sequence. The aforementioned three factors together make the reversed action of cross innervated muscles inconspicuous in the monkey as compared with the rat.

Another factor of significance is the greater diversity of limb movement present normally in the monkey. The rat tends to use a limb as a whole in a stereotyped manner, with relatively few variations of the coordination pattern. In the monkey, however, the various limb segments may act differentially, being flexed, extended or rotated in various combinations, with a large variety of possible permutations of the coordination pattern. Because dissociation in the action of cross innervated muscles is a prerequisite of readaptation, the monkey, with a high degree of such functional dissociation already present normally, has a great advantage over the rat, in which the limb muscles are more rigidly bound together in restricted functional associations.

The ability to activate the test muscles in many different combinations with other limb muscles opens the possibility for their activation in the new proper combination to suit the crossed innervation. It is necessary in learning a new motor skill to achieve the new coordination a first time, whether by directed effort or by accidental blunder. Once made, the new coordination can be reenforced by further repetition and practice. In the rat the proper coordination was apparently never achieved, even a single time. The limb always worked in the old patterns, without any trial variations. It remained questionable whether the motor system of the rodent is so organized as ever to permit the required reassociation of muscle function. The ability of the monkey to make diversified trial coordinations would seem to be an extremely important item.

Another factor favoring motor reeducation in the monkey is the fact that learning plays a much greater role in the original ontogenetic acquisition of motor coordinations. The monkey to start with is, therefore, already more experienced than the rat in learning new arm coordinations. Furthermore, it is to be expected that coordinations established largely by learning in the first place will be more easily reorganized by the learning process than those built into the system by processes of growth and maturation.

In addition to the specific items aforementioned, there remains supposedly a central intelligence factor involving the general organization and differentiation of the brain, regarding which little can be added on the basis of the present experiments.

The foregoing advancements ascribed to the monkey are, of course, to be found also in man, even better developed in most instances. Certainly, man would be far superior to the monkey in the early stages of reeducation, i. e., in the detection and understanding of the motor difficulty and, consequently, in the guidance of corrective training. In any attempt to extrapolate to man from these results in the monkey, one must remember that most of the cases of nerve crossing and nerve regeneration, as well as those of muscle transposition, met in the clinics require a different and more complicated type of motor reorganization than that demanded by the clearcut reciprocal cross of these experiments.

SUMMARY

1. In 4 spider monkeys (3 with bilateral and 1 with unilateral crossed innervation) and in 2 macaques (both with unilateral crossed innervation) reversed movements of the elbow followed the surgical interchange of the nerve connections of the elbow flexor and extensor muscles with removal of all other muscles acting on the joint.

2. These reversed movements were quickly abandoned in ordinary cage activities, and a large variety of "trick" or compensatory reactions were rapidly acquired as substitutes for the abnormal action of the test muscles.

3. After about two months' practice at most, the reversed movements could be elicited only by using special measures to force the animals to use the elbow under conditions in which trick movements were excluded and in which there had not been previous opportunity to learn to inhibit the reversed action.

4. Readaptation went farther than the development of trick movements and inhibition of reversed action. Positive readjustment in the

function of the test muscles was eventually achieved in all cases, until the monkeys could actively flex and extend the elbow in an adaptive manner. A few of these corrected reactions which received constant practice in natural cage activities seemed to be as smoothly coordinated at the end of three years as the same movements in a control case after a similar operation but in which the nerves regenerated into their original muscle groups.

5. Correct use of the cross innervated muscles learned in one performance was not transferred automatically to all other performances. Lack of such transfer was strikingly apparent in a number of instances.

6. Reversed action at the elbow persisted throughout the three year course of the experiments in certain performances which received comparatively little practice.

7. The new motor coordinations survived bilateral frontal lobectomy combined with extensive bilateral lesions in the cortical arm areas 1, 2, 5 and 7.

8. Comparison of the present results with those of similar surgical operations carried out previously on the rat indicated throughout a marked superiority of the monkey. Some of the known factors, anatomic and functional, contributing to this readaptive supremacy of the primate nervous system are discussed.

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Printed and Published in the United States of America