THE EFFECT OF CROSSING NERVES TO
ANTAGONISTIC MUSCLES IN THE
HIND LIMB OF THE RAT

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When nerves to limb muscles are forced by operative measures to activate opposing muscles in amphibians, no corresponding disturbance results in the response pattern of the limb muscles (Weiss, '36). Contrary to the view that specific connections between nerve centers and end organs are important in determining the pattern of response, the muscles or limbs so operated contract normally in timing and in intensity regardless of the experimental distortion of their nerve connections. It has been demonstrated further that this return to normal function after crossing of limb nerves in amphibians is not the result of reeducation or of any kind of automatic reflex adjustment (Weiss, '37).

The only tenable explanation of the phenomenon yet suggested is that offered by Weiss himself in terms of modulation of nerve by muscle. When nerve fibers growing out in ontogenetic development make contact with peripheral organs, they are presumably induced by those end organs to undergo a further cell differentiation according to the specific biochemical properties of the end organ. Nerves to different muscles thus become differentiated qualitatively from each other. When a nerve is severed from its muscle and forced to

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The visual system is highly sensitive to motion, even in the absence of ongoing movement. Although the brain can accurately perceive and track moving objects, the process of motion perception is complex and involves multiple brain regions. The visual cortex, particularly the primary visual cortex (V1), plays a crucial role in processing motion information.

Motion perception involves the analysis of visual motion stimuli, which can include both movement in the environment and self-motion. The brain uses various mechanisms to extract motion information from visual inputs. These mechanisms include the use of optical flow, a transformation that maps the apparent movement of objects in the visual field to changes in the neural activity of the visual cortex.

The brain's ability to perceive motion is essential for navigation and spatial orientation. Motion perception is also critical for the perception of depth and spatial relationships, as well as for the perception of三维 objects. The brain uses motion information to build a 3D representation of the environment, which is essential for navigation and spatial cognition.

Motion perception is not limited to the visual cortex. Other brain regions, such as the parietal and frontal lobes, are also involved in the processing of motion information. These regions help to integrate motion information with other sensory inputs, such as audition and touch, to create a coherent and meaningful representation of the environment.

The brain's ability to perceive motion is also influenced by attention and context. For example, the brain can selectively attend to moving objects in the visual field, and this attentional focus can influence the perceived motion of those objects.

In summary, motion perception is a complex process that involves multiple brain regions and is essential for navigation, spatial orientation, and perception of the environment.
ON/ion transduction under certain conditions and the discovery

of hormone-sensitive ion channels that could hardly be interpreted

NORMAL TO PERSERION IN VITRO
crossing of chromosomes in rats

In the crossing of chromosomes in rats, the genetic material is exchanged between homologous chromosomes during meiosis, leading to genetic diversity. This process is crucial for the evolution and adaptation of species.

Heretics

The term "heretic" refers to a person who holds or promotes religious or ideological views that are considered to be outside the accepted norms or teachings of a particular group or society. The term has been used historically to label individuals who differ from accepted beliefs or practices, often leading to social and religious conflicts.

Time

The concept of "time" encompasses the measurement and experience of duration, often associated with the sequence of events and the passage of moments. In physics, time is considered a fundamental quantity, while in human experience, it is often perceived subjectively.

Tears

Tears are produced by the lacrimal glands and travel along the tears ducts to the conjunctival sac. They serve various functions, including the lubrication of the eyes, the removal of foreign substances, and the production of a mucous layer to aid in vision.

Tension

Tension refers to the state of being stretched or pulled taut, often associated with physical or mental stress. In physics, tension is a force that acts along a cord, string, or other flexible material, opposing the elongation caused by an applied force.

Test

A test is a method or procedure used to determine whether a given hypothesis is correct. Tests can be designed to assess various aspects of knowledge, abilities, or conditions, often involving the evaluation of responses or performance.

Microscope

A microscope is an optical instrument used to magnify and view small objects or samples that are too small to be seen with the naked eye. Microscopes are essential tools in fields such as biology, chemistry, and engineering for detailed examination of specimens.

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ing the skin and pulling the hair over all regions of the shank, ankle, and foot, and to flexing the toes and ankle about a month after return of function showed that the operation had not impaired the sensitivity of the limb.

CROSSES BETWEEN PERONEAL AND TIBIAL NERVES

Since regeneration of nerves is unsel ective (Weiss, '36), the crossing of large nerve trunks such as the peroneal and tibial must result in a random redistribution of the motor fibers of any one muscle of the shank or foot to a large number of foreign muscles. Likewise any one foreign muscle must be reinnervated by a heterogeneous lot of fibers that originally were spread among many different muscles. A similar random dispersal must occur among the sensory fibers. For reeducation or reflex regulation to occur in the face of such confused reinnervation would imply an extreme plasticity, homogeneity, and adaptability on the part of the nerve centers that is directly negated by the results of muscle transposition and nerve crosses between individual muscular nerve branches. The latter results show that contraction of the shank muscles as a group cannot be dissociated in the nerve centers from that of the rest of the leg musculature. It seems improbable that this same dissociation plus the much finer dissociations between different groups of shank and intrinsic foot muscles and even between individual neurons, as would be required after unsel ective regeneration of the peroneal and tibial nerve trunks, could be made after crossing these nerves. Learning would be simpler presumably after reconnecting the fibers of one muscle directly to another single muscle. However, since reeducational adjustment has been reported to follow the crossing of the compound peroneal and tibial nerve trunks in dogs by Osborne and Kilvington and in dogs, cats, rabbits, and pigs by Rawn, this operation also was performed on a number of rats.

Anatomically the dorsi-flexor muscles of the foot are supplied by the peroneal nerve and the plantar flexors by the tibial nerve. In the normal rat electrical stimulation under
light anesthesia of the distal cut end of the peroneal nerve causes sharp strong dorsi-flexion of the foot. Likewise, stimulation of the tibial nerve causes vigorous clear-cut plantar flexion of the foot.

Twenty cases were prepared. They were operated at ages ranging from 15 to 80 days. After cutting the nerves the proximal end of the peroneal was sutured to the distal end of the tibial and the proximal end of the tibial to the distal end of the peroneal. The sutures were enclosed in artery tubes and, because the nerve trunks lie side by side, a long sheet of beef allantoic membrane (Bauer and Black's "insultoic membrane") was placed between the sutured nerves to prevent cross regeneration of fibers to their original branches.

Regeneration occurred as intended. When the legs were reopened after 2½ months, the two nerve trunks were distinctly separable with no sign of stray fibers crossing from one suture to the other. The shank muscles had regained their full size. After cutting the nerve trunks proximal to the point of suture in three cases, electrical stimulation of the cut ends produced dorsi-flexion when the crossed tibial nerve was stimulated, and plantar flexion when the crossed peroneal nerve was stimulated. Clearly the mass of structures normally supplied by the tibial fibers had been reinnervated by the peroneal fibers, and vice-versa.

Placid paralysis with muscular atrophy immediately followed the operation. On regeneration of the nerves with resultant recovery of muscular strength and tonus, the foot was moved abnormally but not in reverse as after crosses between individual muscles. There were no loose free reciprocal movements of the foot. Active dorsi-flexion was never seen. Only when the rats were at rest with the leg muscles relaxed did the foot attain a normal position of dorsi-flexion, passively flexed underneath the animal by the body weight. Whenever leg movement occurred, the foot was held rather stiffly and moved only through varying degrees of plantar flexion. As time went on, the plantar flexion became more predominant. During activity the foot was kept stiffly extended. In the supporting
phase of locomotion the body weight was supported on the
digits instead of on the sole of the foot. The result of this
rigid plantar flexion in locomotion was to make the leg coordi-
nation of the rats similar to that of digitigrade mammals such
as the cat, dog and pig. In the rat, however, the toes are
long and become permanently curled after the operation so
that the rats walked on the dorsal rather than on the plantar
surface of the toes.

The reason for the predominance of plantar flexion with
curling of the toes and rigidity of the ankle joint is not entirely
clear, though the following factors are probably in part re-
 sponsible. The peroneal and tibial trunks contain, besides
fibers to the directly opposed flexor and extensor muscles,
fibers to the peroneal group of muscles and to the group of
deep flexor muscles and also to all the small muscles intrinsic
to the foot which groups probably do not all function in per-
f ect synchrony with the primary plantar and dorsi-flexors. If,
for example, the posterior tibial and the short and long pero-
neal muscles contract during plantar flexion as they appar-
etly do in man (Wright, ’28), then, after crossing their fibers
along with those of the dorsi-flexors into the plantar flexor
muscles, one would expect to get a continuous plantar-flexor
contraction persisting through both phases of locomotion.
Also, because the plantar flexors are much more powerful than
the dorsi-flexors, any generalized pull on all muscles produced
by prolonged contraction, contracture, or even by muscle
tonus, after disruption of the myotatic reflex mechanisms for
controlling that tonus, would tend to result in predomination
of plantar flexion. Whether cause or result, there was an
anatomical shortening of the plantar flexor muscles. This
shortening was not so severe in the majority of cases as to
prevent reeducational adjustment since good dorsi-flexion of
the foot could be obtained by electrical stimulation of the
nerve. In most of those cases operated at about 15 days of
age, however, when growth is still very rapid, the condition
became so severe that complete dorsi-flexion was impossible
even by forcible manipulation.
The leg coordination following the crossing of peroneal and tibial nerves was quite similar in all twenty rats save for the age difference mentioned above. Fifteen of the animals were kept longer than a year, nine of them as long as 18 months after the operation. Foot movement remained abnormal to the end with no evidence of correction.

One must conclude either that the nervous system of cats, dogs, rabbits, and pigs is considerably more efficient in regard to reeducation than that of rats, which seems very unlikely particularly in the case of pigs whose central nervous system is decidedly more primitive (Kappers, Huber and Crosby, '36), or that the adjustment observed in these other animals was actually due to anatomical and mechanical peripheral effects rather than to central adjustment. In this regard it should be noted that passive extension of a dog’s, cat’s, rabbit’s, or pig’s knee mechanically forces an extension of the foot because of the pronounced two-joint action of the plantar-flexor muscles. Dorsiflexion is mechanically impossible with the knee extended and can occur only, as it does normally, when the knee is flexed. After crossing peroneal and tibial nerves, knee movement which is unaffected by the operation would thus tend on regeneration of the nerves to control foot movement mechanically as the two-joint muscles gradually recovered their strength and tonus. The effects observed after crossing the peroneal and tibial nerves in the rat, obviously not normal in this animal, would be functionally very adaptive in a short-toed digitigrade animal, and might easily be mistaken for a restoration of normal coordination.

There was no indication of nerve modulation in these cases. Unfortunately the effect of modulation of the few fibers that had not yet reached their end-organs at the time of operation in the youngest animals would have been so weak that it would have been overshadowed by the action of the fibers already established.

CONCLUSION

No adaptive functional adjustment of the nervous system took place in these rats after the connections from the spinal
centers to antagonistic limb muscles had been exchanged. The crossing of the peroneal and tibial nerves and the crossing of the pure muscular branches of these nerves resulted in an awkward and thoroughly abnormal foot movement in the former case and in a complete reversal of foot movement in the latter, neither of which was ever corrected by automatic reflex regulation or by a gradual learning or conditioning process. These results are in agreement with those of Cunningham (1898) who crossed the median and ulnar nerves in dogs and stood alone in maintaining that recovery of normal muscular coordination does not follow the crossing of limb nerves. They indicate that the more numerous reports implying a surprising plasticity and regulatory adaptability of the central nervous system to disarrangements of the normal peripheral relations are not to be accepted without question, and show in contrast an extremely unplastic fixation of the basic motor patterns for hind limb coordination.

Persistence of the original patterns of discharge to the limb musculature after peripheral alterations that thoroughly disrupted the normal array of afferent stimuli from the limb supports the contention that the control of limb coordination is in large part central. As pointed out by Gray ('39), peripheral stimuli are extremely important in the timing of limb responses, in controlling the intensity of limb responses, and in determining in many cases which of various possible limb responses as wholes will be set off. But since the elementary patterns of limb coordination persist in the rat after extreme distortion of peripheral conditions produced by nerve crossing, muscle transposition, and even complete deafferentation of the limb; the organization of the intrinsic motor patterns themselves must depend primarily on central rather than peripheral factors.

Permanent retention of the original incidence of discharge of the motor nerve fibers after their regeneration into foreign antagonistic muscles also demonstrates that nerve cells in juvenile and adult stages of the rat are no longer in a sufficiently labile condition to be respecified by foreign muscles.
In amphibians where modulation of nerve by muscle has been most thoroughly studied it has been shown that in larval stages respecification takes place quite readily, while in newly metamorphosed toads it occurs only very slowly (Weiss, '36, p. 516), and in fully grown toads the capacity of nerve cells to undergo modulation is completely lost (Weiss, unpublished). Mammalian tissues in general are less labile than those of amphibians and their nerves probably become irreversibly determined in an earlier stage of development soon after reaching the muscles.

The results in the rat are not necessarily contradictory to the results in larval amphibians in their implications regarding the role of inter-neuron connections in reflex activity and central nervous function. Nerve modulation may be considered an embryological inductive influence which affects development of the central connections of motor cells in the cord rather than a factor which selectively modifies the nerves' sensitivity to central excitatory agents. According to this interpretation, the formation of synaptic terminations on motor cells by the telodendria of internuclear neurons is conditioned by the specific biochemical properties induced in the different motor cells by their muscles. End-organ connection formed by outgrowing nerve fibers in ontogeny becomes, on this basis, an important factor in the laying down and differentiation of central reflex relations. The influence of peripheral organs on the quantitative development of the central nervous system has already been well demonstrated (see Detwiler, '36).

After crossing peripheral nerves, one would expect a restoration of normal function due to modulation of nerve by muscle, according to this interpretation, only in cases where the peripheral nerves had not already become irreversibly determined by their original end-organs and where the central nervous system was still in a sufficiently labile condition to permit compensatory growth readjustments in the central connections and also where the central terminations of the nerves crossed were located in the same region of the central
nervous system. At present there is no crucial evidence to indicate whether modulation affects the selective sensitivity of the motor neurons or the central connections of these neurons. But because this alternative explanation of the phenomenon of homologous response is consistent with both the amphibian and mammalian experiments and also with the classical conceptions of central nervous physiology it is mentioned here as a working hypothesis.

**SUMMARY**

1. In ten rats (eight unilateral and two bilateral cases, operated at ages ranging from 40 to 250 days) exchanging the nerve connections of flexor and extensor muscles in the shank produced a reversal of foot movement.

2. In all ten cases the foot movement remained fixedly reversed to the end with no corrective modification whatever. Seven cases were kept longer than 15 months after the operation. Immobilization of the contralateral hind foot, training the rats to rise upright on their hind legs for food, and amputation of both front legs at the shoulder all failed to induce reeducation.

3. Post-mortem examination and physiological tests showed that nerve regeneration had been as intended, that sensitivity of the shank and foot had not been impaired by the operation, and that sensory as well as motor fibers had reinnervated the muscles. Severance of the crossed nerves abolished the reversed movement. Control animals, similarly operated except that the nerves were reconnected to the original muscles, showed foot movement in normal phase in all activity.

4. In two additional rats, both unilateral; transposition of flexor and extensor muscles after the nerves to these muscles had previously been crossed resulted in foot movement in normal phase. No change toward reversal occurred after 15 months.

5. In twenty rats, ranging in age from 15 to 80 days, the peroneal and tibial nerves were crossed instead of the single nerve branches to individual muscles. This operation pro-
duced an abnormal limb coordination characterized by indiscriminate contraction of the shank muscles and a predomination of plantar flexion of the foot. This abnormal coordination persisted for 18 months without any sign of a central nervous adjustment.

6. The results furnish new evidence of the rigid organization in the rat of the basic motor patterns for hind limb coordination. They also show that, in a mammal, motor nerve cells in post-embryonic condition do not have the capacity to undergo muscle-specific modulation after regeneration into foreign muscles.

LITERATURE CITED


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