FURTHER EXPERIMENTS WITH DEPLANTED AND DERANGED NERVE CENTERS IN AMPHIBIANS.

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Further Experiments with Deplanted and Deranged Nerve Centers in Amphibians.*

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A previous communication1 has described the appearance of rhythmic spontaneous (=endogenous) activity, and later of reflexes, in fragments of spinal cord transplanted ("deplanted") to the dorsal fin of amphibian larvae and provided with grafted limbs as effectors. A continuation of these studies has brought the following results.

A large section of spinal cord was deplanted to the fin and made to innervate 2 limbs, one grafted anteriorly and the other posteriorly. After re-innervation, prolonged seizures of spontaneous activity appeared in both limb grafts. During all major fits the beats of the 2 limbs occurred synchronously and with approximately proportional strength. This proves that in all actions, except very weak ones, the whole neurone pool of the grafted center discharges in unison. Reflexes likewise spread through the whole grafted center without localization.

Some limbs were deplanted along with their own spinal ganglia and cord segments, with all peripheral nerve connections being left intact. During the days following the operation this isolated reflex preparation gave orderly reflex responses. Gradually, however, the response deteriorated, assuming undifferentiated mass character with prolonged after-discharges, while at the same time spontaneous rhythmic

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seizures began to appear. This result demonstrates the direct relation between endogenous activity and central disorganization.

In order to intensify the structural break-down normally occurring in the deplanted centers, fragments were mutilated in various ways prior to their transplantation (slashing; sucking through pipettes too small in diameter; mincing). Such grafts behaved in the same way as undisrupted ones: spontaneous seizures and reflexes appeared within a few weeks.

Spontaneous activity has also been obtained from deplanted fragments of the spinal cord of adult animals; it is not, therefore, restricted to the larval stage in which the previous observations were made.

In testing dorsal and ventral cord fragments separately, it was found that both can exhibit spontaneous seizures, although more experiments will be needed to determine whether their responses are exactly alike. At any rate, the fact that dorsal gray devoid of specialized motor cells does exhibit spontaneous activity, is in itself noteworthy. Similarly, reflexes were obtained from purely ventral fragments.

Deplanted fragments of medulla oblongata exhibit spontaneous activity of great intensity and usually very pronounced periodicity. However, none of the 8 cases thus far observed have shown reflexes of the kind regularly obtained in spinal cord grafts.

In confirmation of earlier observations, the composition of the blood was again found to affect the discharge threshold: invariably, exercise of the host body is followed by a marked intensification of spontaneous activity and reflex sensitivity in the deplants. Whether this effect is caused by anoxemia, CO₂, acidity, or metabolites, is for the future to decide.

In conclusion, these experiments amplify previously reported results in showing that deplanted pools of central neurones from a wide variety of sources display rhythmic spontaneous activity. We may assume that the factors generating this activity and determining its pulse are present in all gray matter, but are normally prevented from reaching discharge threshold by harnessing effects lying in the organization of the intact nervous system. The appearance of the rhythmic spontaneous discharges in the deplanted fragments may therefore be ascribed to the break-down (degradation) of the finer central organization. One factor affecting the discharge threshold has definitely been identified as humoral, inasmuch as the threshold fluctuates with the composition of the blood.
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**Does Sensory Control Play a Constructive Role in the Development of Motor Coordination?**

By Paul Weiss

Nobody in his senses would think of questioning the importance of sensory control of movement. But just what is the precise scope of that control? Is the sensory influx a constructive agent, instrumental in building up the motor patterns, or is it a regulative agent, merely controlling the expression of autonomous patterns without contributing to their differentiation? There have been advocates of either view. Some pertinent experiments in favor of the latter will be reported below. But before presenting them, let us first specify what we mean by „sensory control“ and „motor patterns“.

Sensory stimuli, through afferent impulses, can a) initiate a central response; b) decide the type of response; c) condition the centers for subsequent responses; d) alter the excitability of the centers; e) inform the centers of the state of muscles (myotatic reflexes); f) furnish the centers with cues of behavioral significance.

The list, while incomplete, indicates the variety of effects known to trail a sensory stimulus. If we add trophic effects of the sensory nerves and possible morphogenetic, pre-functional, influences of sensory neurones on the centers, we realize that experimental tampering with the sensory system must entail severe and complex consequences for the normal functioning of the organism. Does it, however, affect the patterns of motor coordination?

By „motor pattern“ we mean the orderly chronological sequence in which the several muscles of a member must be engaged in order to produce a coordinated movement — this is coordination on a lower level; or the order in which the different extremities

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1) This contribution to a volume to be presented to Prof. W. R. Hess in celebration of his sixtieth birthday gives the author a gratifying opportunity to reiterate his sincerest thanks for the hospitality and friendship extended to him by Prof. Hess on many past occasions.

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must be actuated and integrated with the trunk in order to make partial movements yield locomotion of the body — coordination on a higher level. Reciprocal innervation of antagonists is only one feature of such motor patterns.

The patterns of coordination of a normal animal lead to biologically useful effects: progression, retreat, swimming, burrowing, etc. But is the achieving of these effects really relevant and instrumental in producing the patterns of their execution? If so, the process would have to be guided by sensory control, as the only means by which the centers could judge the adequacy of the tried motor combinations. The question has been answered by previous experiments on amphibians. These have shown that coordination patterns remain the same, whether they yield the desired effects or not. A crucial test consists of disarranging the muscles in such a manner that the standard patterns of coordination lead to wholly incorrect effects, and new patterns would have to be developed to remedy the contingency. Amphibians have consistently failed in these tests (P. Weiss, 1936). Animals in which the arrangement of limb muscles has been reversed, move in reverse (P. Weiss, 1937), as the centers continue to discharge the inherited muscle „score“ for progression, which, when executed, muscle for muscle, by a reversed limb, naturally moves the body backwards. In spite of their predicament, such animals have never improved. The result is even more striking if the limbs are reversed in the embryonic, pre-functional phase (P. Weiss, 1940): Such animals walk in reverse from their very first steps. Sensory messages certainly do signal to the centers the utter inadequacy of their effects, but obviously the centers can do nothing about it. This does not speak in favor of sensory guidance in the making of motor patterns.

Recently the tests were extended to rats. The tendons of antagonistic leg muscles were crossed (Sperry, 1940). All foot movements came out in reverse and remained so without any sign of re-education, even under severe training conditions. Man under similar conditions can do better, as all surgeons well know. Yet, even his improvement does not seem to involve re-education of inherited basic motor patterns, but rather the superseding of these by newly learned patterns of cortical origin.

All these experiences emphasize the central autonomy of the basic motor coordination patterns, the argument being that, inasmuch as the centers are impotent to adjust their coordination to the peripheral needs, they are not very likely to have learned coordination by trial and error in the first place.

There is a natural temptation to supplement the evidence of these „alteration“ experiments by „elimination“ experiments, removing the central influx into the centers altogether. It must be kept in mind, however, that afferation, may be a combination of, effects and words, lack of motivation necessarily prove a contrast of motor patterns. Coordination in deeper structures includes review of other levels be activated coordinately, if been severed. This has been shown by Chase (1949) and Moldaver (1955), who damage. Recently, the length of the coordinately as merely amplifies the fishes.

An essential fact is that the sensory influx are not: certain disturbances months after the surgery have been in well-corded material seen which appears which is not (Chase, Gray). cerebration has the only fact that somehow the integrity. On the other hand, even in the long term, it may point to an excessively low sensory input. The centers, layered in time might allow cells themselves.

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kept in mind, however, that whatever deficiencies appear after de-afferentation, may be attributable to the loss of any one, or combination of, effects outlined above as „sensory control“. In other words, lack of motility following de-afferentation would not necessarily prove a constructive rôle of sensory functions in the building of motor patterns. Actually, there is no loss of basic motor coordination in desensitized limbs of amphibians (P. Weiss, 1934; includes review of other forms also). The limb muscles continue to be activated coordinately even after all sensory limb roots have been severed. This has been confirmed, though underemphasized, by Chase (1940) and Gray (1939). A report to the contrary by Moldaver (1936) can possibly be explained by post-operative damage. Recently, tadpoles, de-afferented on both sides throughout the length of the spinal cord, were found to swim as aptly and coordinately as normal animals (P. Weiss, unpublished). This merely amplifies von Holst’s (1935) results with de-afferented fishes.

An essential lack of dependence of the motor patterns upon the sensory influx seems thus established beyond question. On the other hand, chronically de-afferented limbs by and by develop a certain disturbance which presents a problem of its own. Weeks or months after the operation, during which time the limbs have been in well-coordinated use, some sort of tonic rigidity begins to appear which increasingly interferes with the normal coordination (Chase, Gray; l. c.). No interpretation of this late effect of de-afferentation has thus far been offered other than the circumlocution that somehow sensory integrity was necessary for permanent motor integrity. On the basis of my own experience with the phenomenon, I would submit that the motor patterns are not really destroyed, even in the long run, but merely prevented from manifestation by an excessively strong tonic background. By way of hypothesis, one may point to the fact that, according to Moldaver (1936), the loss of sensory influx causes a hypersensitivity of the segmental motor centers, laying them open to abusive bombardment, which in due time might very well result in chronic hyperactivity of the motor cells themselves.

If the cause of this phenomenon is uncertain in the adult, it is no less so in the larva, where it has also been observed. Of course, the fact that de-afferented limbs of adults retain their basic coordination, does not yet exclude a more pertinent participation of the sensory system in the first origin of coordination during development. This does not seem very likely in view of the fact that the onset of motility in amphibian larva antedates the differentiation of sensory fibres (Coghill, 1929). However, it is understandable that
more direct experimental efforts had to be made to decide the matter.

Detwiler and Van Dyke (1934), Du Shane (1938) and Chase (1940), all working with urodeles, obtained larvae devoid of sensory ganglia by removing dorsal parts of the embryo containing the neural crest, which includes the formative cells for the ganglia. Limb function in such animals was impaired in varying degrees, mainly owing to the prevalence of an excessive extensor and adductor tone, similar to the one developing in de-afferented adult limbs. Although the spinal cords of most of these animals were also defective, some of the authors adduce circumstantial evidence that the motor disturbances were correlated with the sensory rather than with the spinal damage. The hypertonicity may again be explicable, as above, by the chronic lack of the normal depressing effect of the sensory influx upon the motor cord. Then, locomotor patterns, even if present, would remain blocked by the excessive tone. Since no attempts have been made to reduce the hypertonicity through drugs or operations, this angle of the problem remains wide open. Surely, the constructive rôle of sensory control has not been proved by these defect experiments. In fact, recent experiments carried out on a more favorable material, have definitely disproved it.

While urodeles grow limbs so early that in order to de-afferent them, one must operate on very young stages, the anuran tadpole develops its hind legs not until shortly before metamorphosis, when the spinal ganglia are already fully formed and easily accessible to clean extirpation. De-afferentation at this stage does not, therefore, involve the hazards of embryonic operations. Tadpoles of Rana catesbiana operated in this way developed limbs permanently devoid of sensory innervation, with motor innervation from a cord which had not suffered by the operation. When these limbs became functional during metamorphosis, they displayed fully coordinated motility in swimming, jumping, righting, turning. Some specimens did show paralytic disturbances which are the subject of further study. But the majority functioned well without having ever been under sensory control. It is obvious, therefore, that sensory innervation is no prerequisite for the development of coordinated limb function, and that the lack of motility sometimes observed to be associated with sensory defects should be attributed to secondary suppression of the performance, rather than to a primary failure of the formation, of the motor patterns.

In conclusion, therefore, all evidence points to the fact that the basic patterns of motor coordination are products of self-differentiation of the centers, and that the sensory influx, however
important in other respects, plays no constructive part in their making.