FUNCTIONAL PROPERTIES OF ISOLATED SPINAL CORD GRAFTS IN LARVAL AMPHIBIANS.

"fibers from central neurones of spinal grey can connect directly with skin & serve afferent function"

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Attempt to demonstrate Resonance phenomena failed here.

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Functional Properties of Isolated Spinal Cord Grafts in Larval Amphibians.*

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The thesis that the operation of the central nervous system can be satisfactorily explained in terms of fixed neurone arrangements, rests largely on the interpretation of the structural organization of the central gray, as it presents itself in the normal animal. If the central nervous system really owes its fundamental functional manifestations to the minute details of its neurone architecture, any major disorganization of the latter should thoroughly derange the former. Accordingly, a study of the functional capacities of a central nervous system whose anatomical connections have been thrown into confusion promises information of crucial interest. Such a condition can be produced by transplantation.

Fragments of spinal cord, including several segments, excised from larval salamanders *(Amblystoma punctatum)* were grafted into the gelatinous connective tissue of the dorsal fin fold. Hosts and donors were of identical age (ca 2 cm in length) and had been in full functional activity for many weeks. In 7 of the 14 animals thus operated a limb was grafted at some distance anteriorly or posteriorly to the cord graft. All grafts became quickly vascularized and well incorporated.

Histological study revealed 3 main changes in the grafted cord fragments: (1) varying degrees of reduction of the gray matter; (2) considerable deformation and disorganization of the surviving portion; (3) outgrowth of bundles of nerve fibers into the surroundings.

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The outgrowing nerve fibers form connections with skin, trunk muscles, and in the presence of a grafted limb, also with the latter. The cables connecting cord and limb grafts are always much stronger than other bundles. This fact, highly significant for the interpretation of normal nerve development, suggests that the first pioneering fibers to become attached to the limb thereby acquire some faculty—a kind of "stickiness", as it were—converting them into a preferential contact pathway for later fibers. Arrived inside the limb, the fibers form abundant and typical connections with muscles and skin.

Within a few weeks of the transplantation these isolated cord-limb complexes begin to exhibit functional activity, in which 3 successive phases can roughly be identified: an early phase of "spontaneous" activity; a later phase of responsivity to stimuli applied to the grafted center; a final phase of true reflex responsivity.

The first phase is characterized by intermittent or almost incessant twitching of the limb muscles. The twitches usually appear in spells, starting with irregular fibrillations and gradually building up to violent convulsions. A single fit may last for several minutes. At the peak of activity, the contractions are remarkably well synchronized, the limb executing strong periodic beats, sometimes at fairly regular intervals of the order of one to several seconds. The seizures appear no matter whether the animal is at rest or in motion, but are usually more intense following a period of host activity.

During the following weeks the spontaneous bursts become scarcer, with longer periods of inactivity separating the individual fits. During this phase reactions can, however, often be evoked by lightly pressing against the cord graft; the response follows the stimulus with a latency of sometimes more than a second and consists of anything from a single jerk to a seizure of several minutes' duration.

A few weeks later true reflex responses can usually be obtained by tactile stimulation (with cotton fibers) of the skin in the vicinity of the cord graft. In the course of time the stimulogenous area increases. The reflex response consists of a vigorous indiscriminate contraction of all limb muscles with no sign of coördination. The form of the response is essentially constant for a given case, but its size and temporal characteristics vary with the strength and mode of application of the stimulus, as well as with the condition of the host body. While a weak localized stimulus may yield a single twitch, an increase in the strength of the (mechanical) stimulus or spatial summation (stroking) or temporal summation (repetitive touch) all produce a repetitive response, with the after-discharge sometimes lasting for several seconds. Moreover, the excitability of the preparation fluctuates with the condition of the host body: prolonged host activity is invariably followed by a marked increase in the reflex excitability of the cord graft. This host influence on graft excitability is a humoral effect, since direct nerve connections between the central nervous system of the host and the cord graft are lacking.

In cases in which the grafted cord had innervated trunk muscles, the latter showed reactions similar to the ones described for the limb grafts. The contractions of the segmental muscles were always directed towards the site of the cord graft as the center of innervation. As in the limb cases, irregular fibrillations as well as synchronized beats were observed; in a few instances, slow, tonic, contractions were also noted.

The reactions described in the preceding are positively neurogenic manifestations of the isolated cord-limb graft complex itself. As a crucial check against the possible intrusion of host innervation, the host cord was pithed in several specimens, and finally the portion of the back containing the grafted units was completely excised and tested in isolation. Even so, the preparations exhibited the same functional activities as before. In fact, their excitability was even markedly increased.

These observations demonstrate that a fragment of spinal cord, after undergoing a major involution, is still in possession of certain functional properties which, accordingly, can be regarded as the fundamental dynamic properties of a nerve center deprived of its finer structural differentiation. Thus far the following have been observed in our preparations: Spontaneous firing (later subsiding); long latency; synchronization of discharges; after-discharge; repetitive action; reflexivity; spatial summation; temporal summation; fluctuating excitability; fatigue.

The details of the microscopical examination of the grafts will be reported later. The most surprising fact is the presence of abundant sensory fibers, serving as afferent pathways in the described reflexes, despite the fact that only pure spinal cord without primary afferent neurones had been transplanted. Apparently, fiber processes of the spinal gray have connected directly with the skin and become afferent in function, with a concomitant reversal of the sense of their synaptic transmission. The structural disorganization of the gray has presumably weakened the original polarity and irreciprocity of synaptic relations.