THE SIGNIFICANCE OF THE RECURRENT COLLATERAL IN THE STRUCTURAL ORGANIZATION OF NERVOUS CENTERS

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(Presented by Active Member AMN SSSR V. V. Parin)
Translated from Byulleten' Eksperimental'noi Biologii i Meditsiny, Vol. 53, No. 2, pp. 106-110, February, 1962
Original article submitted July 18, 1960

It is known from descriptive neuromorphology that the axons of neurones, which may be described as "the exit elements" of the nervous centers, give off return collaterals.

This feature is characteristic of motoneurones of the spinal cord, of the pyramidal cells of the cerebral cortex, of the Purkinje cells of the cerebellum, the mitral cells of the olfactory bulbs [16], and of the pyramidal cells of Ammon's horn [3, 16] etc.

Recently, Szentagothai [18] has described recurrent collaterals in axons of the cells of Clarke's column.

The recurrent collateral has attracted attention because of physiological investigations which have shown that it exerts an inhibitory effect when the parent axon is stimulated. The time characteristic of the antidromic inhibition of spinal motoneurones indicates that the antidromic impulses spread along the recurrent collateral, reach an internuncial neurone, which then brings about inhibition of the mononeurone through a synaptic connection [17, 10]. In similar experiments in which the optic nerve was stimulated, antidromic inhibition of the retinal ganglion cells [12] has been obtained, and has supported the suggestion by Polyak [15] that the axons of the ganglion cells may give off recurrent collaterals. The recurrent collaterals of the axons of pyramidal cells are directly related to the antidromic inhibition of the corresponding neurones as observed in experiments on the isolated pyramidal tracts [19]. Finally, some investigators have proposed that among the nerve fibers inhibiting the neurones of the cochlear nucleus there are some which have recurrent collaterals from the axons.

It can be seen therefore that as regards the function of the recurrent collateral, little more has been done than to define the problem, and its solution has acquired special significance, because we are here concerned with a general phenomenon involved in the structural and functional organization of the nervous system.

The object of the present investigation has been to study the site and mode of termination of the recurrent collaterals of axons of certain neurones, using the methods of experimental neuromorphology.

METHOD

We applied the method of retrograde degeneration, whose essential feature is that when an axon is divided, or damaged in some other way, degenerative changes which may proceed as far as complete necrosis invade the corresponding nerve cell [3].

We induced the retrograde degeneration of the neurones, and consequently also of their collaterals and synaptic endings by dividing them, or by applying pressure by means of a ligature to the appropriate nerve trunks.

The following types of experiment were carried out: 1) ligation of the ventral roots of the spinal cord; 2) intracranial division and application of a ligature (intraorbitally) to the optic nerve; 3) division of the olfactory tract, to produce retrograde degeneration of the mitral cells of the olfactory lobes; 4) division and ligation of the vagus nerve (above the nodose ganglion).

The experiments were carried out on cats and white rats. The animals were killed 12-36 days after the operation. The material was impregnated with silver (using the method of Campos, Cajahl, or Gliss), which revealed normal and degenerating nervous structures. Sections 5-30 μ thick were cut on a freezing microtome, stained by the method of Cajahl and Campos, and were then embedded in paraffin and stained by the method of Cajahl and Gliss.

RESULTS

In cats, retrograde degeneration of the spinal motoneurones was induced by placing a ligature on the ventral roots approximal to the spinal ganglia. Next, in order to eliminate any possible stimulating effect of the ligature on the posterior roots, ligatures were placed on both ventral and dorsal roots. The experiments lasted long enough for complete degeneration and disappearance of the branches of the fibers of the posterior roots and of their synaptic terminations in the spinal cord.

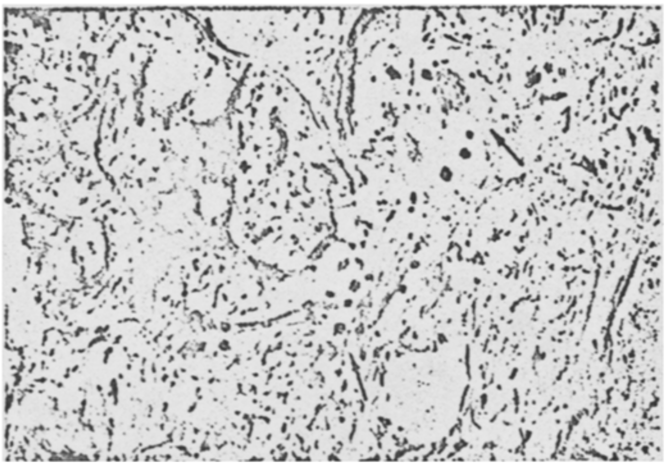

Fig. 1. Degeneration of the synaptic endings on internuncial neurones of the spinal cord (21 days after application of a ligature to the ventral root). Silver impregnations. Micrograph. Magnification: objective 40×, ocular 7×.

The most effective experiments were those in which a ligature was applied to the first cervical segment, which in cats can be reached without opening the vertebral canal.

The results of these experiments showed that 12-36 days after application of the ligature, a large number of motoneurones are to be found in various stages of degeneration ranging from ectopia of the nucleus, through various degrees of vacuolization, to complete destruction of a proportion of the neurones.

In these preparations, there were also degenerative changes of the synaptic terminations of some of the internuncial neurones lying among the motoneurones.

In some cases, the internuncial neurones showing degenerative changes lay in the immediate neighborhood of the degenerating motoneurones (Fig. 1). It is important to note that in these cases the main mass of the synaptic endings on the cell bodies of the motoneurones show no changes which could be regarded as degenerative. In one of the preparations we were also able to observe direct contact of an outgrowth of an internuncial neurone with the body of a motoneurone.

In cross and tangential sections of cat retinae examined 15-18-20 days after a ligature had been applied to the optic nerve, retrograde degeneration could be seen in some of the ganglion cells; N. G. Feldman observed similar changes [7] after intraorbital division of the optic nerve on rabbits and dogs. In the internal granular layer, fine degenerating nerve fibers could be seen, some of which ended on the bodies and outgrowths of the amacrine cells as fine terminal threads.

As has been pointed out previously [5], results obtained in experiments in which the ligature is applied to the optic nerve give convincing evidence that the axons of the ganglion cells give off return collaterals.

According to the results we obtained, the latter form synaptic connection with the amacrine cells of the retina.

Thus, all the evidence is that the effect of antidromic inhibition of the ganglion cells, as observed by Granit [12], is brought about by structures resembling those which are affected by antidromic stimulation of motoneurones.

The retrograde degeneration of the mitral cells of the olfactory bulb in white rats was produced by complete or partial unilateral division of the olfactory tract at the point where it leaves the olfactory bulb.

At a time 16-18 days after division by frontal and sagittal sections of the olfactory bulbs, a large number of mitral cells could be found in various stages of degeneration. There were also degenerating fine nerve fibers in the granular layer of the bulbs. In many cases it could be seen that these fibers terminated as homogenous intensely stained swellings on the bodies of small neurones lying at the base of the layer of mitral cells (Fig. 2). In some preparations, fragments of degenerating terminal threads were also found in the olfactory glomeruli.

Thus, in these experiments we obtained evidence that in this region, the return collaterals of the axons of neurones which are "exit elements" (mitral cells) enter into synaptic contact with the internuncial neurones.

It is pertinent to enquire whether axons of neurones such as those of the vagal motor nucleus, which represent "exit elements" also have return collaterals.

To find the answer we used material obtained in experiments in which a ligature had been applied to the vagus nerve above the nodose ganglion.

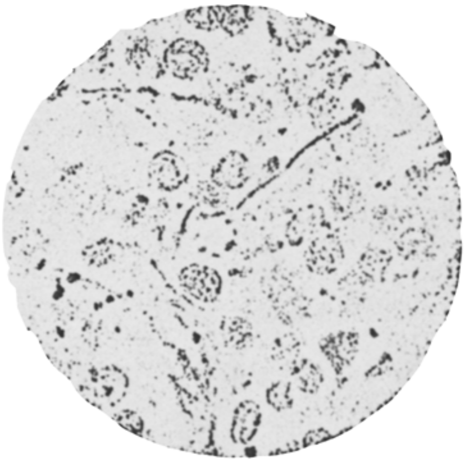

Fig. 2. Degeneration of the synaptic endings on the cells of the granular layer of an olfactory bulb (18 days after division of the olfactory tract). Silver impregnations. Micrograph. Magnification: objective 40 ×, ocular 7 ×.

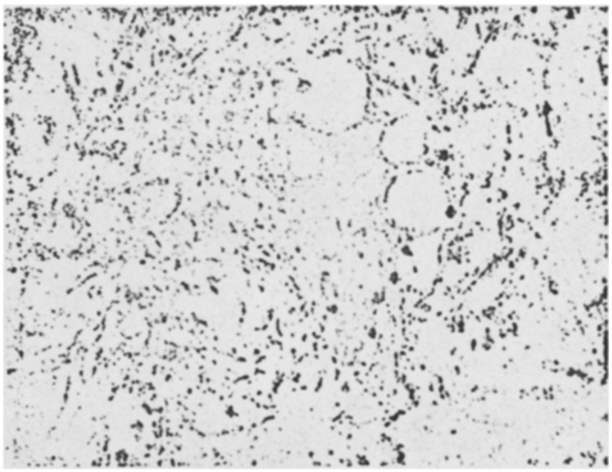

Fig. 3. Degeneration of synaptic endings on neurones of the medulla (28 days after division of the vagus nerve above the nodose ganglion). Silver impregnations. Micrograph. Magnification: objective 40 ×, ocular 7 ×.

In sections of the medulla oblongata, it was also possible to observe retrograde degeneration of the neurones of the vagal motor nucleus, and of the synaptic endings on small neurones lying as a rule at the periphery of the nucleus.

The similarity of the appearance observed in the spinal cord and in the medulla, in the corresponding experiments, allows us to assert that the axons of the afferent neurones of the vagus also give off return collaterals which enter into synaptic connection with the internuncial neurones.

It must however be pointed out that in the medulla, the degenerating synaptic endings were found also much more frequently on the bodies of large neurones than was the case in either the cord or the olfactory bulbs. Figure 3 illustrates this point, and shows the tendency for such synapses to occur at the part of the neurone where the axon takes origin.

The sum total of the evidence here presented leads to the conclusion that "exit elements" of the nervous centers in different parts of the nervous system are represented by a characteristic neurone circuit, as follows: neurone → return collateral of the axon → internuncial neurone → neurone, and we will refer to this arrangement as a microanatomical element of the structural organization of the central nervous system (as distinct from a histological element) [6, 7].

There is however evidence that the return collaterals of the axons of the cortical neurones may terminate either on internuncial neurones or on dendrites of the parent neurone. Here we must not neglect the great importance attributed to activation of the dendrites in changes of excitability of the neurones with respect to impulses reaching them directly, and in the development of neuronal inhibition [1, 2, 9]. There are indications that the return collateral of an axon terminating on its own dendrites exerts a modulating influence upon it [13].

According to Ramon and Cajahl [15], the return collateral from an axon of a pyramidal cell of the cerebral cortex may terminate on the initial segment of the axon of the same or of a closely adjacent neurone. This observation is important in connection with the theory of inhibition [11] whose morphological basis is the presence of a synaptic apparatus on the initial segment of the neurone, and has been described for the Mauthner's cells of the lower vertebrates.

In other words, the circuit representing an exit element may apparently be formed without the involvement of an internuncial neurone, a conclusion which is in line with our investigations on the vagal motor nucleus.

Here it is important to note that in all cases of the possible action of a return collateral onto a neurone (through dendrites, or through the initial segment of the axon) we are concerned with additional stimuli converging with orthodromic impulses received by the neurone in question. Therefore, the ultimate effect of the action on the neurone will in all cases be of the same kind.

There are however observations which suggest that the return collaterals exert a qualitatively different effect on neurones according to whether they terminate directly upon it, or are connected via an internuncial neurone. For example, it has been shown that antidromic impulses may enhance the excitability of adjacent motoneurones to orthodromic impulses [4, 20], and may also activate pyramidal cells [14].

Further investigations are required into the physiological significance of the neurone circuit as representing an exit element, but already we can see that it must be of significance in connection with the physiology and pathology of disturbances of reflex regulation. For example, in hypertensive desease, the extent of the dependence of vascular tone on nervous influences may be determined not only by functional disturbances of the afferent systems at the junctions at which impulses meet in the neuronal circuit, but also by functional disturbances of the exit elements of the vasomotor center, which is also represented by a neuronal circuit responsible for the nature of the efferent stimulus to the vessels.

SUMMARY

Experiments were performed on cats and albino rats to investigate the synaptic connections of recurrent collaterals of the axons of neurones representing "exit elements" of the nerve centers. The method was to cause a retrograde degeneration of the neurones, and therefore also of their axon collaterals by section of the corresponding nervous pathways.

From the results obtained it could be deduced that collaterals of the motoneurone axons of the spinal cord form synaptic connections with Renshaw cells. The axons of the ganglion cells of the retina also have collaterals which form a connection with the amacrine cells. Recurrent collaterals of the mitral cell axons of the olfactory bulbs are connected with the small cells lying at the basis of the mitral cell layer. Axons of the cells of the vagal motor nucleus also possess collaterals which form a connection with small cells of the nucleus. However, they may terminate on the cell bodies of the effector neurones. The combined evidence from these experiments and those reported in the literature lead to the conclusion that the "exit element" of a nervous center is a peculiar neurone circuit involving the recurrent collateral. Its significance is still unknown, and remains to be studied.

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