CHANGES IN MONO- AND POLYSYNAPTIC SPINAL REFLEXES IN THE PRESENCE OF A PERIPHERAL INFLAMMATORY PROCESS

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A fruitful method of investigation of the activity of the spinal centers so to study the mono- and polysynaptic reflexes, as first suggested by Lloyd. This method has already been used to investigate the state of the spinal centers after deafferentation [8], degeneration of divided peripheral nerves [1, 9, 10], tenotomy [3, 4, 14], and poisoning with tetanus toxin [2, 6, 17], strichnine, and curare [5, 15, 16]. In the present investigation this method was used for the investigation of the spinal centers in one of the commonest of pathological processes – inflammation.

EXPERIMENTAL METHODS

Experiments were carried out on unanesthetized spinal cats. The spinal cord was divided at the level $C_7 - Th_1$ under ether anesthesia. After division of the spinal cord laminectomy was performed in the lumbosacral region. The ventral roots $L_5 - S_1$ were dissected out intradurally on both sides and divided. The ventral roots $L_7 - S_1$ were used for recording the mono- and polysynaptic responses. Test stimuli were applied to the central segments of the divided nerves to both heads of the gastrocnemius muscle (medial and lateral) and of the nerve to the antagonist muscle – the common peroneal nerve. A current of supermaximal strength for group 1 fibers was used. To prevent drying of the nerves and to create stable temperature conditions, the nerves were immersed in saturated mineral oil heated to 37-39°. The nerves were stimulated with single rectangular pulses of current from a stimulator manufactured by the Japanese firm San'ei. A twin-beam oscilloscope made by the same firm was used to record the responses.

An inflammatory process was set up in one of the hind limbs of the cat by injection of 0.2 ml turpentine beneath the skin of the foot 2-16 days before the experiment. Preliminary experiments demonstrated that in normal conditions the responses from the two sides were symmetrical (Fig. 1). After injury to one limb this symmetry was considerably disturbed in most experiments.

EXPERIMENTAL RESULTS

Altogether 36 experiments were performed, in which the nerves supplying the extensor muscles (nerves to gastrocnemius) were stimulated, and 26 in which the nerves supplying the flexor muscles and the skin of the foot (common peroneal nerves) were stimulated.

When both nerves were stimulated with current of supermaximal strength for group 1 fibers the character of the changes in the monosynaptic reflexes was dependent on the time elapsing after injection of the turpentine. During the first 2-3 days after injection of turpentine no regular changes in the monosynaptic reflexes in the injured limb to stimulation of the nerve to the gastrocnemius muscle or of the common peroneal nerve could be observed.

Between 4 and 11 days after the injection of turpentine, during stimulation of the nerve to the gastrocnemius (23 experiments) the amplitude of the monosynaptic reflexes fell considerably in all the experiments (Fig. 2A). In some cases monosynaptic reflexes were not recorded in the injured limb during stimulation with a current supermaximal for the monosynaptic reflexes of the uninjured limb. They could be detected only by prolonged tetanization of the nerve. The thresholds of excitation of the motor neurons of the gastrocnemius muscle of the injured limb were much higher than those of the uninjured limb. On the other hand, during stimulation of the common

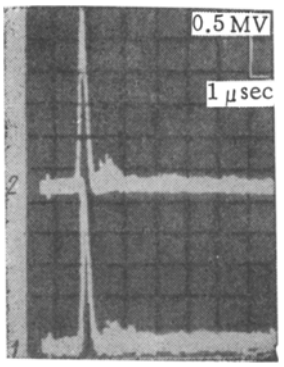

Fig. 1. Responses under normal conditions. Stimulation of 1) central segment of divided nerve supplying extensor muscles: 2) central segment of divided nerve supplying flexor muscles. The central segment of the divided ventral root 7 was used for recording.

peroneal nerve at these same periods (20 experiments), the amplitude of the monosynaptic reflexes of the motor neurons of the flexor muscles was increased in 17 experiments (Fig. 2B) and decreased in three.

After 12-16 days the symmetry of the responses of the injured and uninjured limbs was completely restored during stimulation of both the nerve to gastocnemius and the common peroneal nerve. Hence, the asymmetry of the monosynaptic responses of the injured and uninjured limbs during stimulation of nerves supplying the extensor and flexor muscles was most marked 4-11 days after the injection of turpentine. The changes observed during stimulation of the nerve to gastrocnemius and of the common peroneal nerve were, as a rule, antagonistic in character.

The changes in the polysynaptic reflexes investigated by stimulation of the same nerves were much less regular than the changes in the monosynaptic responses. Here, too, the most uniform changes were observed 4-11 days after injury to the limb. During stimulation of the nerve to gastrocnemius the polysynaptic reflexes were reduced in amplitude in 15 and 25 experiments (see Fig. 2A), unchanged in 7, and increased in three. During stimulation of the common peroneal nerve the polysynaptic reflexes were increased by comparison with the uninjured limb in 13 of 20 experiments (see Fig. 2B), unchanged in 4, and decreased in three. Hence the changes in the polysynaptic reflexes during stimulation of the nerve to gastrocnemius and of the common peroneal nerve were not so clearly defined as the changes in the monosynaptic reflexes.

Besides the amplitude of the mono- and polysynaptic reflexes, the posttetanic potentiation of the monosynaptic reflexes during stimulation of the same nerves was also studied. The homonymous nerves of the injured and uninjured limbs were tetanized with a current of the same strength as that used to investigate the amplitude of the monosynaptic responses, with a frequency of 400 pulses/sec, for a period of 10 sec.

The duration of the posttetanic potentiation of the motor neurons of the extensor muscles was shortened in 19 of 23 experiments to a slight degree (its normal duration is 2-4 min). In the injured limb the duration of the posttetanic potentiation was 0.5-1.0 min shorter than in the uninjured limb. The amplitude of the monosynaptic responses before and after tetanization remained smaller in the injured than in the uninjured limb.

Different results were obtained during tetanic stimulation of the common peroneal nerve: a slight increase in the duration of posttetanic potentiation (between limits of 1.0 and 1.5 min) was observed in 7 of 14 experiments; its duration remained unchanged in 6 experiments, and decreased in one. The amplitude of the monosynaptic reflexes before and after tetanization remained greater than in the uninjured limb in most experiments. Thus the duration of posttetanic potentiation after tetanization of the nerve to gastrocnemius in most cases was slightly shortened, whereas after tetanization of the common peroneal nerve it was slightly longer than its duration in the uninjured limb.

Hence, the investigation of the mono- and polysynaptic reflexes of the centers for the extensor and flexor muscles of the limb showed that in most cases an inflammatory process in the limb causes a decrease in the amplitude of the mono- and polysynaptic reflexes during stimulation of the nerves to the extensor muscles and an increase in their amplitude during stimulation of the flexor muscles.

When these changes are analyzed attention must be paid, firstly, to the constant flow of impulses traveling from the focus of injury to the spinal centers. As several writers have shown [7, 18], impulses from a focus of injured tissue spread along AS and C fibers. Experiments in our laboratory have shown that impulses from an inflammatory focus developing at the site of an injury also travel along the same fibers. These fibers correspond to the group III and IV fibers in Lloyd's classification. Impulses spreading along fibers of groups II, III, and IV are known to travel to the motor neurons of the flexor muscles regardless of whether the afferent nerve fibers of the flexor or extensor muscles are stimulated. The discharge under these circumstances always has a facilitating effect on the motor neurons of the flexor muscles and an inhibitory effect on the motor neurons of the extensor muscles.

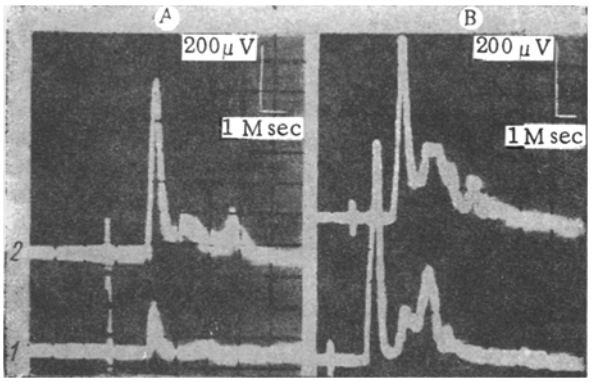

Fig. 2. Mono- and polysynaptic reflexes of left (1) and right (2) injured limbs. Mono- and polysynaptic reflexes from the nerve to the gastrocnemius (A1) and the common peroneal nerve (B1) of the injured limbs, compared to the normal ones (A_2 and B_2, respectively).

It seens that the flow of impulses constantly arriving from the focus of inflammation along the fibers of groups III and IV causes a partial depolarization of the motor neurons of the subthreshold zone of the flexor center, as a result of which a test volley, sent along the common peroneal nerve, facilitates the discharge of the motor neurons not only in the zone of discharge, but also in the subthreshold zone. The amplitude of the monosynaptic reflex of the motor neurons of the flexor muscles is increased. At the same time the flow of impulses arriving from the focus of inflammation along the fibers of groups III and IV has an inhibitory effect on the motor neurons of the extensor muscles. As a result of the partial hyperpolarization of part of the motor neurons, the zone of discharge is narrowed and the monosynaptic reflex, recorded in response to test stimulation of the nerve to gastrocnemius, is reduced in amplitude.

Probably the partial depolarization of the internuncial neurons arising as a result of the action of impulses from the focus of inflammation may explain the increase in the amplitude of the polysynaptic reflexes of the spinal centers of the flexors. In our experiments an increase in the amplitude of the polysynaptic reflexes, rather than in their duration, was observed, so that it may be supposed that this increase was due to an increase in the frequency of discharge of the internuncial neurons and to a shortening of their reflex pathways.

Besides impulses from the inflammatory focus, when the changes in the monosynaptic reflexes were analyzed it was also necessary to take into account the changes in the flow of afferent impulses arising as a result of the flexor orientation of the limb, as a result of which the group of extensor muscles was relaxed and in a state of what might be called "functional deafferentation."

The changes in the polysynaptic reflexes in our experiments were less regular than the changes in the monosynaptic responses. This may, possibly, be explained by differences in the degree of development of the inflammatory focus and in the intensity of the flexor orientation.

A problem of special interest is that of the pre- and postsynaptic origin of the inhibition of the reflexes observed in our experiments. As mentioned above, we found no appreciable changes in the posttetanic potentiation when an inflammatory focus was present in the limb. Formerly this was accepted as sufficient evidence of the postsynaptic origin of the inhibition of the reflexes. In the light of the discovery of the special form of presynaptic inhibition [11, 12, 13], resulting from depolarizing internuncial neurons, this process requires further investigation.

Attention must be directed to the fact that regular changes in the mono- and polysynaptic reflexes from the injured limb did not appear until the 3rd-4th day after injury to the limb. It is curious that in the experiments involving deafferentation, tenotomy, division of the peripheral nerves, and so on clear changes in the mono- and polysynaptic reflexes were found only at a considerable interval after the operation [3, 4, 8, 9, 14]. Evidently the changes in the synaptic connections in the neurons of the spinal centers can only develop when a certain time has elapsed after interruption of the afferent pathways.

It is interesting to compare this fact with another – namely that the disturbance of a function (the flexor orientation of the injured limb) develops extremely rapidly, during the first hour after injury to the limb. Evidently the flexor orientation of the injured limb, at least in the early stages, is the result of the complex integrative activity of the nervous system, extending beyond the limits of the spinal segment.

One of the characteristic features of the reflex reactions of pathologically changed organs in their extreme increase or decrease in magnitude. The experiments described in this paper give grounds for the belief that one cause of this phenomenon is the partial depolarization, developing under the influence of the afferent impulses from the pathologically changed organs, or on the other hand the hyperpolarization in the neurons of the corresponding centers, leading to the involvement of a larger or smaller number of neurons in the reaction.

SUMMARY

An inflammatory process developing on the extremity caused changes in the mono- and polysynaptic reflexes. Monosynaptic reflexes of the flexor centers were enhanced, those of the extensor centers – decreased. Less distinct changes were established in respect of polysynaptic reflexes. These changes may probably be explained by the fact that impulsation from the inflammatory focus spread along of fibers groups III–IV and causes a partial neuron depolarization of the flexor centers and neuron hyperpolarization of extensor centers, as a result of which the test stimulation involves a greater or lesser number of neurons in the reaction. The changes in the reflex reactions of diseased organs conditioned by this mechanism – excessive intensification or, on the contrary, marked depression.

Of special significance is the fact that regular changes in the mono- and polysynaptic reflexes occur only on the 3rd-4th day after the development of inflammation, whereas functional disturbance of the limb flexion occurs during the first hour after the injury of the paw. Late changes in the mono- and polysynaptic reflexes followed a number of other interventions: deafferentation, tenotomy etc., which also caused immediate functional disturbances.

Evidently function disturbances in these experiments, at least at the early stages, are the result of complex activity of the nervous system, going beyond the spinal segment.

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