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Rhythmic Activity of Single Nerve Fibers Induced by Low Calcium.

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In the course of certain experiments on the chemical excitation of nerve we have observed the development of rhythmic volleys of impulses in the individual fibers which recur at regular intervals for long periods of time. Because of the possible relation of such a phenomenon to the mechanism of rhythmic activity of the nervous system in normal and pathological states we have studied this type of response in some detail.

All of the experiments have been performed on the sciatic nerve of the frog. In order to facilitate the penetration of the solution used for stimulation the sheath of the excised nerve was removed for a length of about one cm. and here the fibers were carefully separated so as to form a large number of small bundles. The region thus treated with the solution was usually at one end, but it was equally satisfactory to do so anywhere along the course of the nerve. A single fiber was then isolated at the other end of the nerve and placed on non-polarizable electrodes leading to an amplifier and oscillograph.

Partial removal of the ionized calcium in the nerve by sodium citrate or a reduction of its concentration by bathing the fiber bundles in calcium-free Ringer's fluid initiates a continuous train of impulses from the treated end at the rate of about 100 per sec. When the nerve fiber has been brought into this condition which causes a sustained discharge of impulses we find that the substitution of normal Ringer's fluid for the citrate or the calcium-free solution ultimately transforms the discharge into a series of rhythmic volleys. The continuous discharge goes on for a time which is variable from preparation to preparation and then suddenly stops, followed after an interval of a few seconds by a burst of impulses. The activity of the nerve has now become rhythmic for succeeding volleys of impulses are discharged from the treated region.

Both the durations of the volleys and the intervals between successive volleys undergo progressive changes as the normal physicochemical conditions of the nerve are gradually restored. There is a continuous decline in the duration of the active period—or the

volley—while the intervals at first increase in duration and then decrease. After this period of transition a fairly constant state is attained which may continue for 30 min. or more, and during this time the durations of the successive volleys and intervals remain remarkably constant. Ultimately the intervals between the volleys grow longer again, and the resting condition of the nerve is reached as the interval goes to infinity.

During the period of regular and rhythmic activity the duration of the volleys may be several seconds and the intervals 10 or 15 sec., or, as has frequently occurred, each volley may continue for 1 or 2 min., and recur every 10 min. But even at these longer intervals the volleys and the periods of silence are constant to within a few percent for an hour or more.

The impulses within a volley follow a definite sequence. Whereas the original spontaneous activity consists of a train of impulses of fairly constant frequency the impulses within a burst start at a high frequency of 300 to 350 per sec., drop off to about 100 per sec., and then cease abruptly.

The character of this activity resembles in certain respects that of injured mammalian nerve fibers reported by Adrian[1] and alcohol treated crustacean fibers studied by Fessard.[2] The phenomena which we are reporting are, however, initiated by physiologically significant factors and are completely reversible so that the whole process can be stopped at will and the nerve returned to a resting condition by applying a solution containing an excess of ionized calcium. The value of such a controllable preparation of peripheral nerve tissue for the study of the fundamental mechanisms of rhythmicity will be obvious. It is not unlikely that the basis of such mechanisms and of our observations will be found in chemically induced alterations of irritability described by Lehmann[3] and by Katz.[4]

1 Adrian, E. D., *Proc. Roy Soc. (B)*, 1930, **106**, 596.

2 Fessard, A., *L'Activité Rythmique des Nerfs Isoles*, Paris, 1936.

3 Lehmann, J. E., *Am. J. Physiol.*, 1937, **118**, 613.

4 Katz, B., *J. Physiol.*, 1936, **88**, 239.