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Effects of Frequency and Intensity in Stimulation of Cervical Sympathetic Nerve Fibers to Eye.**GEORGE HOLMAN BISHOP AND PETER HEINBECKER.***From the Departments of Ophthalmology and Surgery of the Washington University School of Medicine.*

Gruber¹ has shown that in the results of both afferent and efferent stimulations, in some instances essentially the same effect is produced by a high frequency and weak intensity of stimulation as by a low frequency of higher intensity, while in other instances an opposite result occurs. In afferent stimulation, spatial and temporal summation might account for the phenomena, which, however, offer more difficulty of interpretation when direct stimulation of efferent nerves show a similar effect. Dr. Gruber suggested that we attempt to correlate his findings with the analysis of fiber types which we have been carrying on by means of the oscillograph.

Results of stimulation of the cervical sympathetic were employed as criteria: dilatation of the pupil and retraction of the nictitating membrane of cat and rabbit; vasoconstriction in the conjunctiva of the cat, and in the ear of the rabbit; and pilomotor effects upon the hair between ear and eye of the cat. The nerve was stimulated posterior to the superior ganglion (mostly preganglionic fibers) and observations were made on the peripheral response in the animal, decerebrated or anesthetized, while action potentials were being recorded from the cut central end of the nerve. For the most irritable fibers giving rise to the first wave of the cervical sympathetic action potential picture, no effect can be detected from peripheral stimulation, and these fibers have previously been judged to be afferents (Bishop and Heinbecker²). The second potential component is double, and consists of the main potential of this nerve, arising from small myelinated sympathetic fibers. Stimulation of the first division of this group, giving a distinct wave in the potential picture, elicits the effect on the pupil and nictitating membrane of the eye. Stimulation of the second group elicits the pressor effect and the pilomotor effect. No effect has yet been detected from stimulation of the last group, of unmyelinated axons, and this, together with the effect of stimulation of the very short postganglionic stretch available in this nerve, is being further investigated.

¹ Gruber, C., *Am. J. Physiol.*, 1915, **36**, 299; **37**, 259.

² Bishop, G. H., and Heinbecker, P., *Am. J. Physiol.*, 1930, **94**, 170.

It can be stated at present that there is no repetition postganglionically from single stimuli preganglionically, and that the amplitudes of potential, pre- and postganglionic, are closely proportional as stimulus strength is increased. Therefore, spread and summation do not take place in this ganglion, where most if not all of the efferent fibers here concerned show a synaptic delay.

In all these effects, so far as could be judged, the same area could be affected to the same degree by weak and rapid as by strong and slow stimulation. When the action potentials were examined, however, it was found in every case that none of a given effect was produced without a strength of stimulation that excited the *most irritable fibers* of a *specific group*, as indicated by a wave in the potential record. Further, no increase of a given effect was produced at a given rate of stimulation by increasing the stimulus strength *from the maximum* to beyond the maximum of that group. The least irritable fibers of a given group may have a threshold at least 2 or 3 times that of the most irritable, the most irritable fibers of the 2 main groups here studied having a threshold ratio of about 1 to 4. Within the group concerned, a single maximum stimulus is effective for certain of the effects, but does not give the maximal response obtainable by repeated maximal stimuli. The number of fiber-stimuli rather than frequency or intensity alone thus determines the response as a whole. The fibers in the nerve responsible for each effect are thus distributed over a specific range, limited as to threshold and conduction rate.

Some peripheral mechanism appears to exist for distributing the effect of the stimulation of a few fibers over the whole area that is capable of being affected by the rest of the fibers of higher threshold in that group. This may be simply a spatial distribution in the peripheral tissue, only a few scattered muscle fibers responding to a "threshold" stimulus, but the magnitude of the total response from repeated stimulation of a few nerve fibers suggests the possibility of a peripheral summing mechanism, such as there appears to be in the heart (Heinbecker³). Conduction from one smooth-muscle fiber to another directly, upon repeated stimulation of a few fibers, or spread by way of a peripheral nerve-network, is not perhaps excluded.

³ Heinbecker, P., *Am. J. Physiol.*, 1930, **93**, 656.