64 (673)

The stimulation of nerve-endings in muscle and the theory of receptive substances.

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Langley has shown that the stimulating action of nicotine upon muscle is prevented by curare and that this antagonism is exhibited also in muscles in which the nerve fibers have been removed by degeneration. This and other facts have led him to formulate the hypothesis of special receptive substances present in the muscle upon which these drugs and other chemical stimuli exert their action, and furthermore he ventures the generalization, in contradiction of the usual belief, that "in no case do chemical substances have a special action on nerve-endings."

The series of experiments here reported were made at the suggestion of Dr. J. W. Warren to test the above hypothesis. The gastrocnemius muscle of the frog was used and its reactions were studied after immersion in solutions of sodium sulphocyanide and potassium sulphocyanide. The following results were obtained.

1. *Action of potassium sulphocyanide.*—This salt was used in hypertonic solutions (2 per cent. KCNS made up in a Ringer's mixture) and in isotonic solutions (1 per cent. KCNS in water). In both cases solutions of this salt caused an immediate rapid primary contraction followed by a prolonged contracture. This effect was not removed by the action of curare nor by the degeneration of the motor nerve fibers. It was obtained also by the action of other potassium salts, *e. g.*, potassium chloride—and must be considered as an instance of the "potassium contraction" described by other authors. The potassium ions may act upon the supposed receptive substance, but evidently their effect does not depend upon the presence of the nerve terminals.

2. *Action of sodium sulphocyanide.*—This salt was used also in hypertonic and isotonic solutions as in the case of the potassium sulphocyanide. In hypertonic (2 per cent.) solutions it caused a large primary contraction followed by a condition of contracture and by frequent isolated or grouped twitches of a coördinated or

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fibrillar character. In isotonic solutions the primary contraction was lacking, but fibrillar twitches occurred, although less frequently than in the hypertonic solutions. Hypertonic solutions (2 per cent.) of sodium chloride failed to give anything more than a small increase in tone. The marked primary contraction as well as the isolated twitches observed in the hypertonic solutions of sodium sulphocyanide were entirely lacking in the muscles of curarized frogs or in frogs in which nerve degeneration had been effected by cutting out a portion of the sciatic nerve. In the latter experiments observations were made upon frogs at varying intervals from 3 to 51 days after section of the nerve. It is noteworthy that the falling out of the contraction caused by the sodium sulphocyanide was observed as early as seven days after section and at a time when a response could still be obtained from the muscle by electrical stimulation of the peripheral end of the nerve. So, also, in the case of curare it was found that the sodium sulphocyanide contraction might be abolished even when the curarization of the animal was incomplete. Two per cent. solutions of sodium sulphocyanide have no stimulating action upon the sciatic nerve when immersed in the solution.

Conclusion.—The stimulating action of sodium sulphocyanide is not simply a sodium effect. The fact that its action is abolished by curare may be explained in accordance with Langley's hypothesis of receptive substances, but the fact that its action is readily removed by de-nervating the muscle is in contradiction to the generalization made by Langley in regard to the improbability of a special action of chemical substances upon the nerve endings in muscle.

Since hypertonic solutions of the sodium sulphocyanide do not stimulate the motor fibers in the sciatic nerve, their action in stimulating the muscle can be explained only on the assumption that they stimulate the nerve endings, if one bears in mind that this stimulating action falls out after the nerve fibers in the muscle begin to degenerate, as well as after administration of curare. It is noteworthy that the stimulating effect of this sodium sulphocyanide upon the nerve-terminals disappears in the incipient stages of the degeneration following section of the motor nerves.