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The action of atropin, quinin, quinidin, and Ouabain on the fibrillation of the skeletal muscles.

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The fibrillary contractions of the skeletal muscles of the cat, following the systemic administration of physostigmin, were studied on thirty-three animals. Tracings of the fascicular movements of the pectoralis major muscle were analyzed, and changes in the action current of the pectoralis major, and of the adductor muscles of the hind leg were recorded, according to the method of Forbes and Thacher.[1]

Evidence was presented in a previous communication[2] that the quantitative antagonism between physostigmin and atropin varies in different structures of the body. The antagonism of atropin is complete in the secretory system. It is of interest that atropin sulphate in intravenous doses of 2.5 to 5.0 mg. per kilogram of body weight, prevents or abolishes fibrillation of the skeletal muscles, when the latter is induced by intravenous injection of 0.3 to 0.5 mg. per kilogram of body weight of physostigmin salicylate. These produce marked generalized fibrillation in control animals. Massive doses of atropin do not prevent fibrillation induced by larger doses of physostigmin.

In the case of the skeletal muscles we are dealing, therefore, with a double antagonism, which, above a certain ratio, is complete in favor of the action of physostigmin. The experiments demonstrate a simultaneous drug antagonism with reversed results in different structures of the same animal.

The experiments with atropin suggest that the skeletal muscles contain certain nerve structures, which are parasympathetic in their pharmacological behavior. (Similar observations on the skeletal muscles of man were made recently by Weiss and Kennedy.[3]) Atropin prevents generalized convulsions due to physostigmin.

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[1] Forbes, A., and Thacher, C., *Am. J. Physiol.*, 1920, lii, 409.

[2] Weiss, Soma, *J. Pharm. and Exp. Therap.*, in press.

[3] Weiss, S., and Kennedy, F., *Arch. Neur. and Psych.*, 1924, xi, 543.

Quinin and quinidin prevent or suppress fibrillation induced by physostigmin, the muscular effect of which is not prevented by atropin. The minimal dose of quinidin is smaller than that of quinin, but they are equally effective when the activity is expressed in percentage of the fatal dose. Definite effect was noted on the electromyogram after the intravenous administration of doses as small as 15 per cent of the fatal dose of quinin or quinidin. Neither physostigmin nor atropin has any effect on the clonic convulsions induced by quinin or quinidin.

Voluntary movements of the muscles are maintained after inhibition of the fibrillation with quinin or quinidin, an observation different from that found in the curare-physostigmin antagonism.[4] The quinin and quinidin antagonism is effective before these drugs exert marked stimulating (convulsive dose about sixty per cent of the fatal dose) or depressing effect on the central nervous system.

Quinin and quinidin do not check the effect of physostigmin on the secretory system.

These experiments suggest that quinin and quinidin have a direct action on certain structures in the skeletal muscle substance peripheral to the motor end-plate.

Ouabain, a typical digitalis body, does not influence the fibrillation. This finding is in harmony with the recognized effect of the digitalis bodies on auricular fibrillation, and with the findings of Hatcher and Weiss,[5] that the toxicity of the digitalis and of the quinin group on the cardiac musculature are independent of each other, and that there is no synergism between the two groups.

It is hoped that this study may serve as an additional evidence for the similar physiological and pharmacological behavior of the skeletal and cardiac muscles. The possible therapeautic application of quinin and quinidin in certain tremors requires further study.

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[4] Pal, J., *Centralbl. Physiol.*, 1900, xiv, 255.

[5] Hatcher, R. A., and Weiss, S., unpublished experiments.