MECHANISM OF STIMULANT EFFECT OF ACETYLCHOLINE IN ISOLATED FROG HEART

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Summary: The mechanism of stimulant effect of acetylcholine has been investigated in atropinised isolated frog heart. The effect is reproducible and is not blocked by hexamethonium but is blocked by dichloroisoprenaline. It persists after reserpine treatment and is increased after noradrenaline injection in such hearts. The mechanism of this effect thus appears to be a dual one, being partly mediated through the release of noradrenaline.

Key Words: acetylcholine atropine hexamethonium dichloroisoprenaline nicotine cardiac stimulant effect

INTRODUCTION

Isolated rabbit auricles brought to a standstill by quinidine, start contracting again when exposed to small concentrations of acetylcholine (2). Similarly, in atropinised frog heart, acetylcholine produces tachycardia which is blocked by ganglion blocking agents (3,6). The cardiac stimulant effect of acetylcholine in atropinised preparations has been attributed to sympathetic ganglionic stimulation or a direct release of noradrenaline from the sympathetic nerve endings (5). However, although the parasympathetic ganglia are known to exist in the frog heart, the presence of sympathetic ganglia or similar tissue is uncertain (4). In the present paper, the mechanism of the stimulant effect of acetylcholine has been studied in frog heart.

MATERIALS AND METHODS

Isolated frog heart was set up according to the technique of Bulbring (1) and was perfused with frog Ringer solution. The contractions were recorded with Starling heart lever. The drugs used were: acetylcholine (1×10^{-7} to 1×10^{-5} g); atropine sulphate (1×10^{-6} g); nicotine (5×10^{-6} g) and reserpine (0.5 *mg*/100 *g im* for 2 days).

RESULTS AND DISCUSSION

Acetylcholine alone caused cardiac inhibition in all the 12 preparations tested. After atropine perfusion acetylcholine caused cardiac stimulation (Fig. 1) in 7 preparations while in the remaining 5 preparations cardiac stimulation was not produced even after increasing the concentrations of atropine and acetylcholine. The cardiac stimulant effect was reprodu-

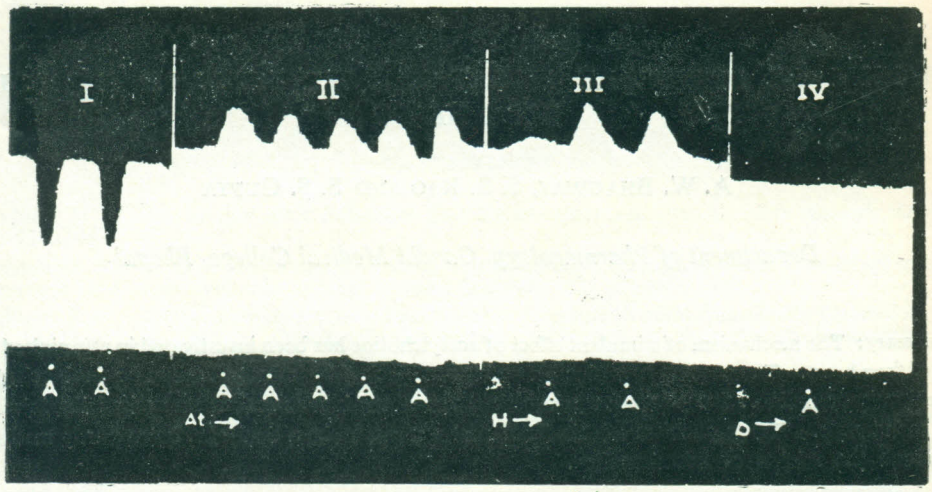

Fig. 1 : Effect of acetylcholine (A at dots) (I) before, (II) after atropine perfusion (At 1 x 10^{-6} g), (III)after atropine and hexamethonium perfusion (H 1 x 10^{-6} g) and (IV) after DCI perfusion (D 1 x 10^{-6} g). Atropine perfusion continued during IV.

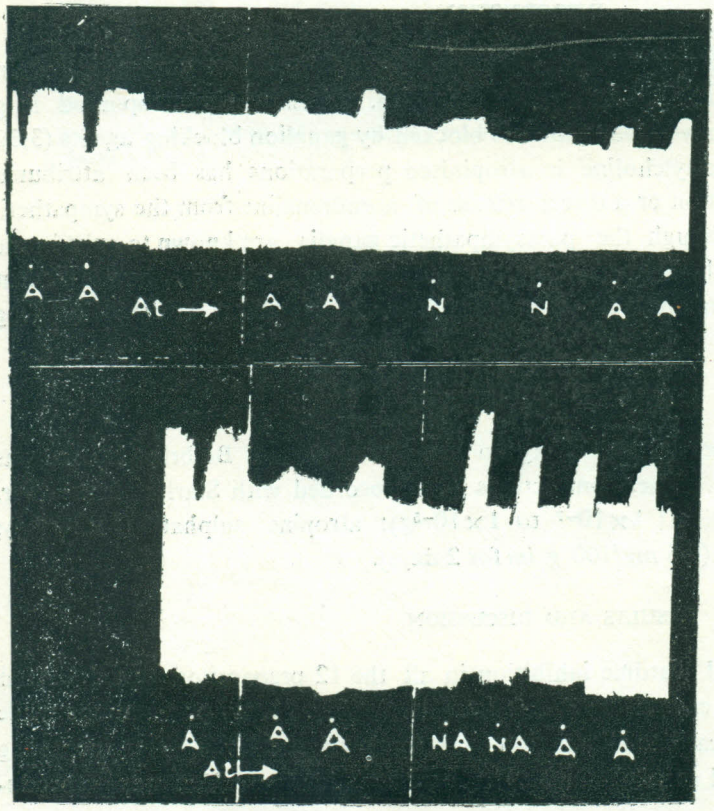

Fig. 2 : Effect of acetylcholine (A at dots) and nicotine (N at dots) in perfused heart of frog treated with reserpine (0.5 mg 100 g im for 2 days). After atropine perfusion (1x10^{-6} g). Upper record shows the effects before the administration of noradrenaline and lower record shows the increase in cardiac stimulant effect of acetylcholine after prior administration of noradrenaline (NA at dots)

cible after repeated administration of acetylcholine and was not blocked by hexamethonium perfusion but was blocked by DCI in all the 7 preparations (Fig. 1). In hearts treated with reserpine the cardiac stimulant effect of acetylcholine though less than in non-reserpinised hearts could be elicited in all the preparations (3 experiments) tested. The cardiac stimulant effect of nicotine was reduced or absent in these preparations. In these hearts the stimulant effect of acetylcholine increased after prior treatment with noradrenaline (Fig. 2).

The experiments indicate that the stimulant effect of acetylcholine in atropinised heart is partly mediated through the release of noradrenaline and could not be due to stimulation of ganglion like structure. Further, the absence of tachyphylaxis after repeated administration of acetylcholine in atropinised hearts and the persistence of small but significant effect after reserpine treatment suggest that the release of noradrenaline may not be the only mechanism involved in this effect.

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