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Are there α-adrenoceptors in the young chick atria?

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1 The effect of noradrenaline and isoprenaline were studied in the 15-day old chick atria. Noradrenaline increased both the rate and force of atrial contractions whilst isoprenaline only slightly increased force at very high concentrations.

2 The increase in force after noradrenaline and isoprenaline was reduced by phentolamine, an α-adrenoceptor antagonist. The β-antagonist, propranolol and the cardioselective β_1-adrenoceptor antagonist, atenolol, did not reduce the positive inotropy. Noradrenaline-induced positive chronotropy was, however, resistant to both α- and β-adrenoceptor blockade.

3 It is concluded that the force of contraction of the chick atria may be α-adrenoceptor-mediated whilst the rate seems to be mediated by a mechanism sensitive to noradrenaline but insensitive to α- and β-adrenoceptor blockade.

Introduction

Catecholamine receptors mediating positive chronotropic and inotropic responses in the mammalian myocardium are known to be β_1-adrenoceptors. Recently, a positive inotropic response to phenylephrine has been observed in the rabbit, cat, man and the guinea-pig (Schumann, 1980). Benfey (1980) showed that phenylephrine has a positive chronotropic action on the isolated atria of some mammals although this was resistant to α-adrenoceptor blockade. In a series of studies involving the chick, it has been consistently observed that isoprenaline does not influence the contraction of the atria to any appreciable extent. The present paper investigates the phentolamine-sensitive and propranolol-resistant positive inotropic actions of noradrenaline in the chick atria.

Methods

Fifteen-day old chicks were killed by exsanguination. The thorax was cut open to expose the heart. The heart was removed and kept moist in Ringer-Locke solution and the pericardium was dissected away. Threads were tied to the top of each atrium, ventricular tissues were carefully removed and the atria cleaned of adhering connective tissue. The spontaneously active right atrium was attached to the tissue holder in a 10 ml organ bath to drive the electrically-quiescent left atrium which was attached to the transducer. Contractions were recorded on a Ugo Basile microdynamometer recorder. The bath contained modified Ringer-Locke solution of the following composition (mmol l^{-1}): NaCl 154, KCl 5.4, $CaCl_2$ 1.8, $NaHCO_3$ 6.0, $MgCl_2$ 0.5 and glucose 5.5. The bath was kept at 30°C and bubbled with pure oxygen. The tissue was equilibrated for 60 min with a solution change every 10 min. A resting tension of 800 mg was applied to the tissue. Results are expressed as means ± s.e.mean of at least 5 observations and the difference between means was accepted as significant after Student's *t* test analysis if $P < 0.05$.

Noradrenaline (Sigma), and isoprenaline bitartrate (Sigma) were dissolved in 0.9% w/v NaCl solution plus an equivalent amount of sodium metabisulphite to stabilize the solution. Phentolamine hydrochloride (Ciba-Geigy), propranolol hydrochloride (Sigma), atenolol hydrochloride (ICI), and cocaine hydrochloride (Krakowski, Poland) were dissolved in freshly distilled water. Drug concentrations refer to the base.

Results

Atria from 15-day old chicks contracted rhythmically as soon as they were set up. These rhythmic beats stabilized to a steady height after 10 min. Noradrenaline (10^{-7}–10^{-5} M) produced concentration-related increases in both the force and the rate of contractions of the atria (Figure 1). The $-\log EC_{50}$ of noradrenaline was 6.6 ± 0.11. Maximum response

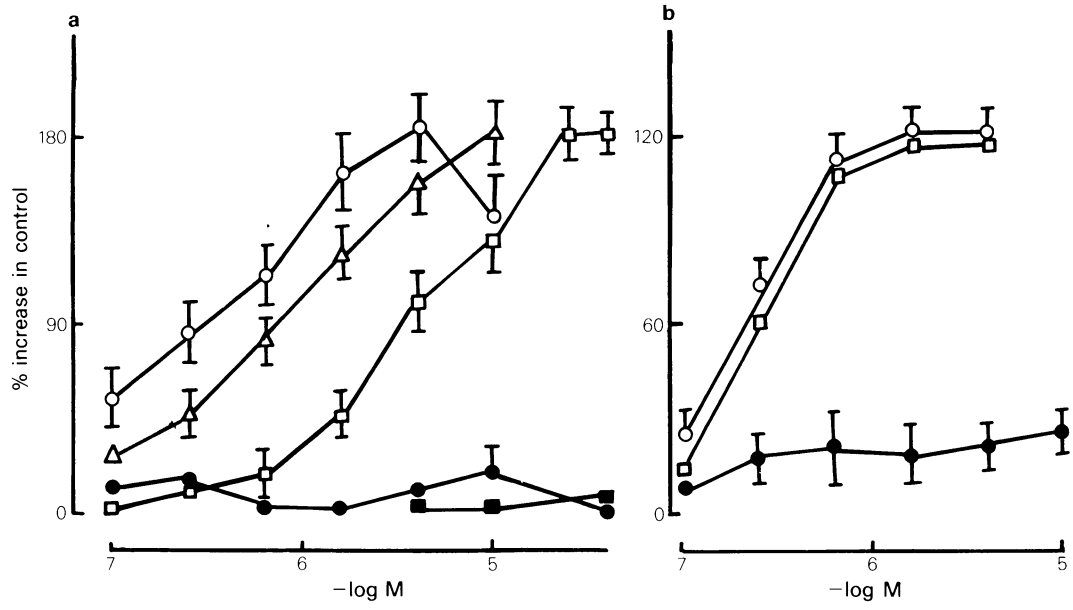

Figure 1 Concentration (− log M) versus increases in force (a) and rate (b) of atrial contractions in the 15-day old chick. Noradrenaline (○) 10^{-7}–10^{-5} M produced graded increases in the force and rate. The increase in force produced by noradrenaline was reduced by phentolamine 10^{-8} M (△) and 10^{-7} M (□). Phentolamine gave a mean pA_2 of 8.35 ± 0.11, slope of A-S plot was 0.89 ± 0.06. Isoprenaline (●) up to 10^{-5} M did not produce an appreciable effect on force and rate. The small increase in force after high concentrations of isoprenaline was abolished by phentolamine 10^{-7} M (■). Phentolamine 10^{-7} M (□) had no effect on noradrenaline-induced increase in rate (b). Each point represents the mean ± s.e.mean of 5 observations.

i.e. increase of 1 g in force, was obtained with noradrenaline 10^{-5} M. Isoprenaline (10^{-7}–10^{-5} M) did not produce an appreciable effect on the force and rate of atrial beats (Figure 1). Phentolamine (10^{-8}–10^{-7} M) produced a significant and competitive antagonism of noradrenaline-induced inotropy and gave a pA_2 value of 8.35 ± 0.11 (in the presence of cocaine). The slope of Schild's plot (Arunlakshana & Schild, 1959) was 0.89 ± 0.06 indicating competitive antagonism. The small and insignificant effect of isoprenaline on the atrial force of contractions was also abolished by phentolamine (Figure 1). Noradrenaline-induced positive chronotropy and the small effect of isoprenaline on force were resistant to β-adrenoceptor blockade with propranolol and atenolol (10^{-7}–10^{-5} M). In addition, the positive chronotropic action of noradrenaline was not blocked by phentolamine up to 10^{-6} M.

Discussion

These results suggest the presence of α-adrenoceptors and the absence of β-adrenoceptors in the chick atria. Thus, noradrenaline, but not isoprenaline, was positively chronotropic and inotropic in this tissue. The positive inotropic action of noradrenaline was reversibly blocked by phentolamine with a pA_2 value of 8.35 suggesting an α-adrenoceptor mediated effect. On the other hand, the positive chronotropic action of noradrenaline was resistant to α-adrenoceptor blockade with phentolamine and β-adrenoceptor blockade with atenolol, a β_1-adrenoceptor antagonist (Barrett, Carter, Fitzgerald, Hull & Le Count, 1973) and to propranolol. It would seem that the mechanisms involved in force generation are different from those involved in rate in the chick atria. To the best of the author's knowledge, the existence of an α-adrenoceptor mediated inotropic response in the chick has not been demonstrated before. However, in the rat ventricle, (Wenzel & Su, 1966), phenylephrine produces a positive inotropic effect which is blocked by phentolamine. More recently, Williams, Dukes & Lefkowitz (1981) demonstrated in binding studies the presence of α_1-adrenoceptors in the rat myocardium. In the pithed rat, the positive chronotropic action of phenylephrine is α_1- and β_1-adrenoceptor-mediated (Tung, Rand, Drummer & Louis, 1982). The potency of phentolamine in the present work ($pA_2 = 8.35$) is very similar to that in the rat anococcygeus muscle against noradrenaline ($pA_2 = 8.11$) and prazosin

against phenylephrine in the same tissue ($pA_2 = 8.45$) (Adenekan & Tayo, 1982). In conclusion, the present study shows that the force of atrial contraction in the 15-day old chick is mediated via α-adrenoceptors whilst the rate seems to be independent of both α- and β-adrenoceptors.

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