that receptors for catecholamines in the liver of some animals (for example, the rat and the rabbit) differ considerably from the α- and β-subtypes which have been characterized in smooth muscle and in the heart (Ellis, Kennedy, Eusebi & Vincent, 1967).

We have examined this problem in the guinea-pig, as part of a more general study of the actions of catecholamines on liver cells. The experiments were made with tissue slices of 0.3 to 0.35 mm thickness bathed in a Krebs solution in which pyruvate (2 mM) was included as substrate, in preference to glucose.

Under these conditions, the rate of glucose release was increased (to up to 3 times the resting level) by both noradrenaline and isoprenaline, as well as by amidephrine (3(2-methylamino-1-hydroxyethyl) methanesulphonanilide methanesulphonate), a substance reported to be a specific agonist for α-receptors (Dungan, Stanton & Lish, 1965). Isoprenaline was most active, producing a 60% increase in the rate of release at 6×10^{-9}M, as compared with 3×10^{-7}M for noradrenaline and 4×10^{-6}M for amidephrine.

The effect of isoprenaline on glucose release could be abolished by the β-receptor blocking agent propranolol, which at 10^{-6}M caused a 40-fold increase in the concentration of isoprenaline needed to elicit a standard response. Phentolamine (10^{-5}M) had no effect.

In contrast, the effect of amidephrine on glucose release could be antagonized by phentolamine (again at 10^{-5}M, giving a dose ratio of about 7), but not by propranolol (10^{-6}M).

Noradrenaline gave intermediate results. Thus propranolol (10^{-6}M) gave a dose ratio of only about 4, but with propranolol (10^{-6}M) plus phentolamine (10^{-5}M) the dose ratio was 20.

We conclude there are two distinct receptors through which sympathomimetic substances can increase glucose loss from the guinea-pig liver. These may correspond to the α- and β-receptors of Ahlquist's classification; however, relatively high concentrations of antagonists (particularly phentolamine) were needed to block the response.

Noradrenaline and amidephrine also increase the membrane potential of many cells within the slices, decrease tissue potassium, and slightly increase tissue sodium. These changes, and their possible relation to glycogenolysis, are under study.

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Electrophysiological effects of alpha- and beta-receptor agonists and antagonists on Purkinje fibres of sheep heart

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The isolated Purkinje bundles of the sheep heart are suitable for the study of the effects of drugs in the same cell, for they can be impaled by micro-electrodes for

a long time without change in the electrophysiological parameters of transmembrane potentials.

The effects of α- and β-receptor agonists and antagonists are as follows.

(1) Increase in spontaneous rate and in slope of pacemaker potential (SPP), and shortening of duration of action potential (DAP) were induced by noradrenaline (5×10^{-6} g/ml.) in eight out of twelve experiments; by adrenaline (5×10^{-6} g/ml.) in two out of three experiments; by isoprenaline (5×10^{-7} g/ml.) in all preparations (five). In the presence of propranolol (10^{-6} g/ml.), noradrenaline produced a decrease in rate and SPP, but a striking increase of DAP; the effects of isoprenaline were simply blocked.

(2) Decrease or no change in rate, decreased SPP and increased DAP occurred after noradrenaline (5×10^{-6} g/ml.) in some preparations (four out of twelve); these effects did not appear in the presence of phentolamine (10^{-6} g/ml.). MDP was significantly lowered and action potentials were reduced after adrenaline (5×10^{-6} g/ml.) in one out of three experiments, and after phenylephrine (10^{-6} g/ml.).

(3) Propranolol and phentolamine, when applied alone at the same concentrations and for the same period of time, had no effects by themselves on the electrophysiological parameters.

These results (see Fig. 1) support the view that both α- and β-receptors are present in Purkinje fibres of the sheep heart.

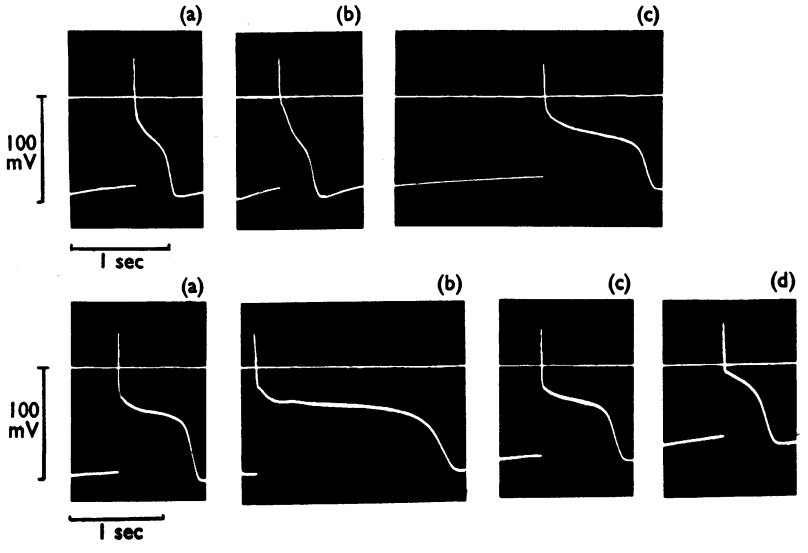

FIG. 1. Upper records: Transmembrane potentials of the same Purkinje cells; (a) control; (b) 6 min after noradrenaline 5×10^{-6} g/ml.; (c) 10 min after propranolol 10^{-6} g/ml. in the presence of noradrenaline. Lower records: Transmembrane potentials of the same Purkinje cell; (a) control; (b) 5 min after noradrenaline 5×10^{-6} g/ml.; (c) 30 min after phentolamine methanesulphonate 10^{-6} g/ml.; (d) 10 min after noradrenaline 5×10^{-6} g/ml. in the presence of phentolamine. Experiments were performed at 31° C.