

tributed to methodological artefacts such as poor mixing. Rather, the *in vitro* state may in some way be responsible for producing enhancement of simple sugar absorption in the alloxan diabetic rat, which does not occur *in vivo*.

Zusammenfassung. Leerdarm- und Krummdarm-Aufsaugung von D-Galaktose und Wasser wurde mit einer Pumpendurchströmung *in vivo* bei normalen und Alloxan-diabetischen Ratten geprüft. 24 Stunden Fasten erhöhte die Aufnahmefähigkeit normaler Ratten, ergab

aber keinen Unterschied zwischen normalen Ratten beim Fasten und solchen, die mit Alloxan für 24, 48 und 72 Stunden diabetisch wurden.

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The Adrenergically Mediated Coordination of Contraction in Isolated Cell Groups from Rat Ventricular Myocardium

After the classification of adrenergic receptors into α - and β -types¹, it has become established that adrenergic receptors of myocardium are entirely of the β -type^{2,3}. However, GOVIER et al.⁴ found that the positive inotropic effect can be brought out also by α -adrenergic stimulation of the guinea-pig heart. Recently, techniques have been developed for isolating myocardial cells from adult mammals so that single cells are able to contract rhythmically⁵⁻⁷. In the present work the technique of BLOOM⁵ was used to study the role of adrenergic receptors in the coordination of contractions of isolated myocardial cells from the rat heart.

Sprague-Dawley rats of both sexes were used; they were 35–37 days old (Experimental Series I) and 7–17 days old (Series II). The latter age group was chosen after the observation that myocardial cells from younger animals functioned more regularly in the experimental conditions. The animals were killed by decapitation; the ventricles were dissected free from the atria and homogenized for 10 sec in a blender at 50,000 rpm in 10 ml of ice-cold homogenizing medium (HM) made according to BLOOM⁵. A sample of one cell group at a time was transferred from the homogenate into fresh HM on a depression slide. Into this HM, the substances to be studied had been added in concentrations given in the Tables. Adrenaline (A) and noradrenaline (NA) were used as stimulators of both α - and β -adrenergic receptors and phenylephrine (PhE) to stimulate primarily the α -receptors⁸. Further,

propranolol (Pr) was used as β - and phenoxybenzamine (PBz) as α -receptor antagonist⁹. Experimental Series I was carried out in order to find out how the rhythm of cell contractions was changed during incubation. The average time intervals between successive contractions are shown in Figure 1 and it will be seen that the frequency of the contractions decreased linearly during the period of incubation ($p < 0.025$). Single cells of a cell group usually contracted in an uncoordinated manner, i.e. each cell according to its own rhythm. In some cases, however, the action of the cell group became coordinated so that one cell served as a pacemaker, which started the waves of contractions (Figure 2). As this coordination of contractions seemed to occur more often after an addition of NA, Experimental Series II was carried out in order to study the role of adrenergic receptors in this phenomenon.

Table I shows the effects of various adrenergic agonists, A, NA, and PhE and antagonists, Pr and PBz on the coordination. A, NA and PhE increased the initiation of coordination when compared with the numbers of coordinations in HM ($p < 0.001$, KENDALL's τ -test for 2×2 contingency table). This indicates that adrenergic stimulation induces the initiation of coordination. Pr did not induce the coordination, neither did PBz. To study further the types of adrenergic receptors involved, experiments were performed in which the α - and β -receptors were first blocked with PBz and Pr, respectively, and then stimulated with PhE. The results are in Table II.

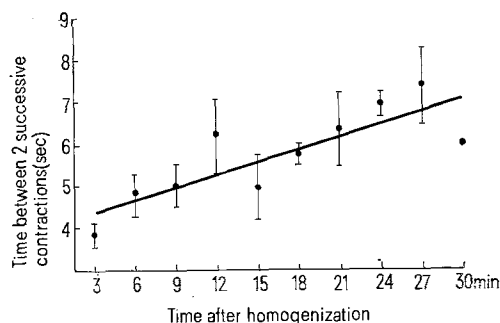


Fig. 1. Changes in the frequency of the uncoordinated contractions of myocardial cells during the incubation in homogenate medium. Abscisse: Time in min after homogenization. Ordinate: Time in sec between 2 successive contractions. Coefficient of regression is 0.049. Vertical bars indicate \pm S.E.M.

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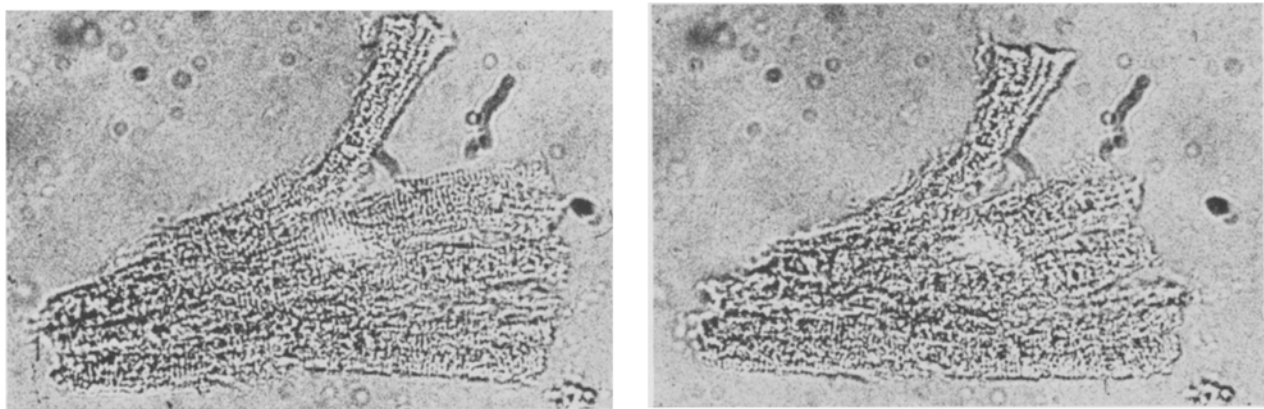


Fig. 2. A cell group in 2 different phases of a coordinated contraction. $\times 200$.

Table I. The initiation of coordination after an addition of various adrenergic agonists and antagonists into the homogenizing medium

Cases with	Homogenizing medium	Agonists			Antagonists	
		NA	A	PhE	Pr	PBz
Initiation of coordination	9	16	5	15	0	0
Non-coordination	53	10	0	14	9	9

NA (noradrenalin), A (adrenaline), PhE (phenylephrine) 10^{-6} and $10^{-7}M$ (the results with these 2 concentrations were combined as there were no differences between the effects); Pr (propranolol), PBz (phenoxybenzamine) $10^{-6}M$.

Table II. The initiation of coordination by phenylephrine (10^{-6} and $10^{-7}M$) after the addition of propranolol and phenoxybenzamine ($10^{-6}M$) into the homogenizing medium

Cases with	Pr + PhE	PBz + PhE
Initiation of coordination	3	4
Non-coordination	6	11

Abbreviations as in Table I.

After an inhibition of these receptors coordination may still be induced by PhE. The results indicate that the initiation of coordination induced by adrenergic stimulation cannot be attributed to the function of only α - or only β -receptors.

The communication between cells in the myocardium is primarily electrical. The intercalary discs are the low resistance points between the cells. Hexagonal constructions similar to those observed in the electrical synapse have been found there^{10,11}. It is not known whether the action of a transmitter or other chemical substances is connected with the function of electrical synapses. However, vesicles like those in ordinary synapses have been found also on both sides of membranes in the electrical synapses¹². The present observation that adrenergic

stimulation enhances the coordination of myocardial cell contractions, can be interpreted as improved communication between these cells. All in all, it may be assumed that similar mechanisms are involved in the transmittance of impulses through the intercalary discs of myocardial cells and through the electrical synapses.

The nature of the adrenergic receptors involved in the coordination still remains unknown. These receptors do not seem to correspond to the conventional α - or β -types but rather they resemble the receptors of nervous system, which have not been classified into these types either¹³.

Zusammenfassung. Nachweis, dass Adrenalin, Noradrenalin und Phenylephrin in vitro die Koordination der Zellkontraktionen in Herzmuskelzellgruppen von Ratten hervorrufen. Propranolol und Phenoxybenzamin hingegen konnten die koordinierende Wirkung von Phenylephrin nicht hemmen.

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