réponse E.M.G. du triceps est remplacée par celle du biceps et la sensation de flexion réapparaît. Ainsi les effets perceptifs et électromyographiques lors de la fermeture des yeux ou lors de la vision de l'environnement semblent équivalents (figure 2). Il apparaît sur les enregistrements une très légère activité E.M.G. dans le biceps au moment du développement maximum des activités tricipitales liée à des diffusions des signaux électrophysiologiques (contrôle effectué pendant une activation volontaire du triceps).

Discussion. Nos résultats semblent indiquer que, selon le contexte perceptif, la vibration du tendon d'un muscle est susceptible de mettre en activité soit les motoneurones homonymes, soit les motoneurones des muscles antagonistes. En effet, la perception par le sujet de l'immobilité de son avant-bras (yeux ouverts), c'est-à-dire la perception d'une position définie et stable de celui-ci, confère aux afférences d'origine fusoriale des propriétés excitatrices sur le noyau moteur du muscle vibré. A l'inverse, la perception par le sujet d'une sensation illusoire de mouvement, lorsqu'il a les yeux fermés ou lorsqu'il regarde l'environnement, confère aux mêmes afférences des propriétés excitatrices sur le noyau moteur du muscle antagoniste.

Nos résultats diffèrent de ceux de Goodwin et al.[9] qui obtiennent toujours chez leurs sujets (yeux fermés) des réponses de type T.V.R. dans les muscles vibrés. L'obtention, soit d'une T.V.R., soit d'une réponse des muscles antagonistes, nous semble devoir être liée aux conditions expérimentales différentes impliquant l'activité ou la passivité des muscles concernés. En effet, dans les expériences de Goodwin et al.[9], les sujets maintiennent activement (contre les forces de gravité) l'avant-bras dans un plan vertical.

Dans les limites de nos conditions expérimentales, nos résultats suggèrent la prééminence des informations visuelles sur les informations proprioceptives fusoriales. En effet, si nous prenons par exemple le cas d'une vibration du triceps, les informations fusoriales évoquées par la vibration sont sensiblement analogues à celles qui peuvent naître de l'étirement du triceps lors d'une flexion, et sont probablement codées comme telles puisqu'elles entraînent, chez le sujet yeux fermés et bras immobilisés, la perception d'un mouvement illusoire de flexion. Par contre, dès que le sujet regarde son avant-bras, les informations visuelles – indiquant que l'avant-bras est immobile et non en train d'exécuter un mouvement de flexion – deviennent prééminentes et suffisent à faire disparaître la réaction E.M.G. du biceps c'est-à-dire la réaction de flexion.

En résumé, les effets moteurs des afférences d'origine fusoriale semblent dépendre du contexte perceptif dans lequel elles sont évoquées, et suggèrent un remodelage fonctionnel de la connectivité neuronique au niveau spinal. L'hypothèse d'un tel remodelage s'appuie d'ailleurs sur des résultats neurophysiologiques, puisqu'il semblerait que les afférences fusoriales issues d'un muscle, puissent activer les motoneurones des muscles antagonistes[12–15].

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Opposite effects of β-adrenoceptor stimulation and 8-bromo-cyclic AMP on potassium efflux in mammalian heart muscle

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Summary. β-adrenoceptor stimulation by isoprenaline increases the potassium efflux in beating guinea-pig atria. This effect is not mimicked by 8-bromo-cyclic AMP, a cyclic AMP analogue which exerts a positive inotropic effect in this preparation.

Many effects of β-adrenergic agents seem to arise from stimulation of adenylate cyclase and the subsequent increase in intracellular cyclic AMP levels[1]. It remains an open question whether cyclic AMP also mediates the effects of β-adrenoceptor stimulation on the potassium movements in heart muscle fibres. Dudel and Trautwein[2] found that strips of atrial muscle were substantially hyperpolarized by adrenaline, and Waddell[3] pointed out that adrenaline and noradrenaline increase the fluxes of potassium through the resting cell membrane. This view was reemphasized by Glitsch et al.[4], but on the other hand, adrenaline has no marked effect on the resting membrane conductance[5]. Recently, it has been shown that adrenaline increases a voltage- and time-dependent outward current (called i_x[6]) during the action potential in Purkinje fibres[7] and atrial muscle[8]. Tsien et al.[7] provided evidence for the view that cyclic AMP may mediate the effects of noradrenaline on both inward and outward plateau currents and the consequent changes in the action potential. We report here that β-adrenoceptor stimulation by isoprenaline increases the efflux of potassium in beating guinea-pig atria. This effect, however, is not mimicked by 8-bromo-cyclic AMP, a

cyclic AMP analogue that is more resistant to degradation by the phosphodiesterase activity, and exerts a strong positive inotropic effect in guinea-pig atrial muscle[9].

Materials and methods. The preparations used in this study were left atria from guinea-pigs. The mounting of the preparations has been described in detail[10]. Drugs were freshly dissolved in Tyrode solution (composition in mM: NaCl, 136.9; KCl, 5.4; $MgCl_2$, 1.05; $CaCl_2$, 1.8; NaH_2PO_4, 0.42; $NaHCO_3$, 11.9; glucose, 5.5) which was gassed with 95% O_2–5% CO_2 and kept at 35 °C. Isoprenaline in the test solutions was protected from oxidative degradation by ascorbic acid (50 mg/l) and EDTA (18.6 mg/l). In all experiments, the preparations were first loaded with ^{42}K for 90 min; then, the amount of ^{42}K released by the muscle into nonradioactive Tyrode solution was determined every 5 min by liquid scintillation spectrometry. Following a 30-min period in drug-free solution, the preparations were transferred to the corresponding test solutions for 60 min. After the efflux period of 90 min, the experiment was stopped and the residual activity in the muscle was determined. The ^{42}K content of the muscle was calculated by cumulative addition of all released amounts of radioactivity for any time for which the ^{42}K effluent from the preparation had been determined. The theoretical curves of ^{42}K extrusion were obtained from plots of log concentration against time, using the method of least squares. Correlation coefficients were greater than 0.996 in each experiment. The statistical evaluation of results was performed using Student's t-test for paired data. A P-value of less than 0.01 was considered significant.

Results and discussion. Figure 1 shows the efflux curve of ^{42}K in guinea-pig atria electrically stimulated at 2 Hz. The time constant (τ) of potassium extrusion amounted to 39.7 min under control conditions and was reduced to 34.0 in the presence of isoprenaline. The increase in the potassium efflux in response to isoprenaline is smaller than that seen with acetylcholine in rat atrial muscle[11]; it is probably not mediated by cholinergic stimulation because, in the presence of atropine, the ^{42}K efflux was enhanced by isoprenaline to the same extent as was found without atropine (τ changed from 42.0 min under control conditions to 36.0 min in the presence of isoprenaline; N = 4, not shown). The isoprenaline-induced increase in ^{42}K efflux was, however, completely abolished in the presence of propranolol (τ was 40.5 min obtained from experiments in 4 preparations; not shown) which indicates that the effect is mediated by stimulation of β-adrenergic receptors. In resting preparations, the efflux rate of ^{42}K was slower ($\tau = 50.8$ min) than in beating preparations and was not affected by isoprenaline (figure 2). This indicates that the increase in ^{42}K efflux due to isoprenaline is closely related to the action potential. These results are in agreement with the observation in calf Purkinje fibres[7] and frog atrial muscle[8] that isoprenaline increases i_x during the cardiac action potential. The increased activation of i_x may be responsible for both the shortening of the action potential and repolarization to more negative potentials, as seen in the presence of adrenaline.

It is known that β-adrenergic stimulation of the heart also increases the inflow of calcium ions during the action potential (see Reuter and Scholz[12]). If by means of this action of isoprenaline a net gain of calcium occurs during systole in the intracellular space, the effect of isoprenaline on i_x might be brought about indirectly, since it has been suggested that an increase in the intracellular calcium concentration enhances the potassium conductance in Aplysia nerve cells[13] and cardiac Purkinje fibres[14]. Evidence exists, however, that not i_x but the background current of potassium is activated by intracellular calcium[15–17]. In our experiments, the rate of ^{42}K efflux was not affected when the calcium concentration was increased from 1.8 mM to 7.2 mM (τ was 41.2 min obtained from experiments in 4 preparations; not shown). This condition clearly increases the inflow of calcium ions during the action potential[18] and enhances the force of contraction.

The positive inotropic effect of isoprenaline can be

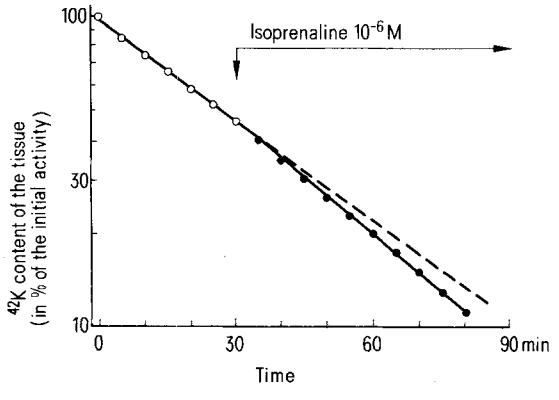

Fig. 1. Effect of isoprenaline on ^{42}K efflux in beating (2 Hz) guinea-pig left atria. ○, Control; ●, isoprenaline 10^{-6} M. Symbols represent means of 8 experiments. SE ranged from 0.60 to 1.46. Significance level for the difference between the washout curves obtained in control conditions and with isoprenaline was $p < 0.01$.

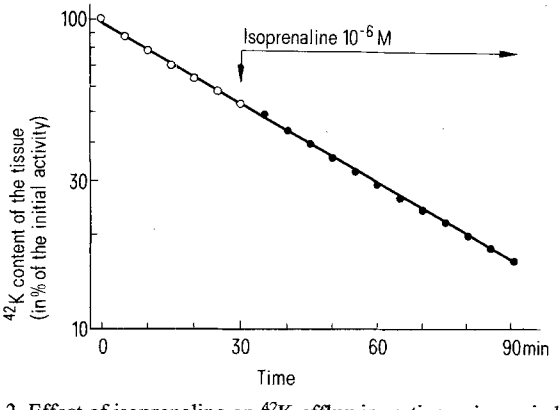

Fig. 2. Effect of isoprenaline on ^{42}K efflux in resting guinea-pig left atria. ○, Control; ●, isoprenaline 10^{-6} M. Symbols represent means of 4 experiments. $p > 0.05$.

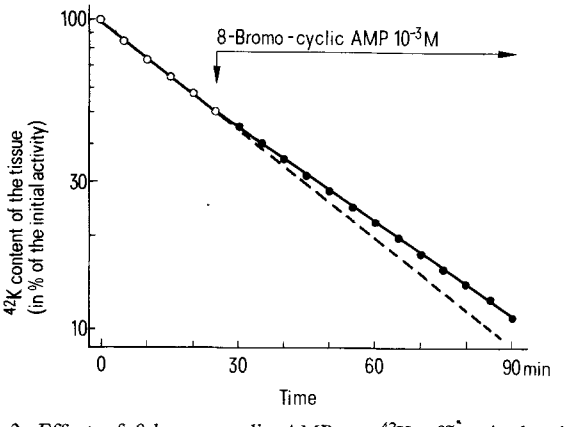

Fig. 3. Effect of 8-bromo-cyclic AMP on ^{42}K efflux in beating (2 Hz) guinea-pig left atria. ○, Control; ●, 8-bromo-cyclic AMP 10^{-3} M. Symbols represent means of 8 experiments. $p < 0.01$.

mimicked in various heart muscle preparations by the administration of cyclic AMP derivatives. In guinea-pig atria, 8-bromo-cyclic AMP in particular exerts a strong positive inotropic effect[9], whereas dibutyryl cyclic AMP is ineffective[19]. Although the effect of catecholamines on the myocardial contractile force is mimicked by 8-bromo-cyclic AMP, the efflux rate of ^{42}K was not enhanced but significantly reduced in the presence of the cyclic nucleotide (τ changed from 37.6 min under control conditions to 43.1 min in the presence of 8-bromo-cyclic AMP; figure 3). The reduction of ^{42}K efflux by 8-bromo-cyclic AMP was unexpected, but this result is in line with the observation that the action potential duration is longer in the presence of dibutyryl cyclic AMP than in the presence of noradrenaline[20]. It is also interesting that in preparations from reserpinized animals dibutyryl cyclic AMP caused inhibition of ^{42}K uptake while noradrenaline had a stimulatory effect[21].

One of us (H.N.) has found that the phosphodiesterase inhibitor papaverine decreases the ^{42}K efflux under the same conditions as described for 8-bromo-cyclic AMP. It remains to be established whether or not these effects are related to the intracellular accumulation of cyclic AMP.

The results show that β-adrenoceptor stimulation by isoprenaline enhances an activity-dependent potassium conductance in the heart. The augmented potassium efflux probably reflects an increase in the current called i_x during the cardiac action potential and may help to provide a shorter systole in the presence of catecholamines. This effect of catecholamines and especially of isoprenaline is not mimicked by 8-bromo-cyclic AMP. It seems possible, therefore that some of the effects of β-adrenoceptor stimulation in the heart are not mediated by the intracellular accumulation of cyclic AMP and that further pathways for the action of catecholamines must be sought.

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Circadian rhythm of β-glucuronidase[1]

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Summary. The circadian rhythm of rat liver β-glucuronidase has been studied in animals kept under highly standardized laboratory condition. A clear 24 h rhythm has been observed for this enzyme with a peak activity at 01.00 h and a trough at 13.00 h.

The circadian rhythm for the lysosomal acid phosphatase has been reported by Bhattacharya and Mayersbach[2]. Furthermore, histochemical studies using the lysosomal marker enzymes (acid phosphatase and β-glucuronidase) have established a rhythmic pattern in the shape, size and distribution of liver lysosomes[3]. These observations suggested a quantitative study of the β-glucuronidase activity of rat liver. The present communication confirms the presence of a circadian rhythm in liver β-glucuronidase activity and discusses the possible functional correlation with the body's detoxicating mechanism.

Materials and methods. Male Wistar rats of HAN breed (Institut für Versuchstierzucht, Hannover, Federal Republic of Germany) were used. For 6 weeks prior to the study, the animals were housed in a room maintained at 22 °C with 55% relative humidity. The room was illuminated artificially from 06.00 to 18.00 h and dark for the next 12-h period. Food and water were supplied ad libitum. The experiment was carried out in the month of January.

The animals were sacrificed at 3-h intervals during an uninterrupted 24-h period. The livers were removed from the animals and weighed immediately. 1 g liver tissue from each animal was homogenized in 0.9% NaCl with an 'ultra turrax' homonizer. The samples were centrifuged at 10,000 × g for 30 min and the β-glucuronidase was estimated according to the method of Fishman[4]. The unit of glucuronidase activity was expressed as nm/g liver tissue.

Results and discussion. As shown in the figure, there is a circadian rhythm in the activity of liver β-glucuronidase ($F = 0.01$). The enzyme activity remains high during the dark phase of the day and goes down after the onset of light i.e. at 07.00 h. The maximum activity ($58.66 + 6.76$) occurred at 01.00 h and the minimum ($16.84 + 2.57$) at 13.00 h. When the lowest and highest means were compared they were statistically different (0.05, t-test). The 24 h mean value was $41.73 + 17.08$. The daily rhythmic variation in the activity of acid phosphatase has been noted in several organs[5] and also in mice and rat liver respectively[2,6]. The peak activity for acid phosphatase in rat liver was observed at 19.00 h and the nadir at 13.00 h[2]. No report has so far been noted on the circadian rhythm of β-glucuronidase activity. When this enzyme activity is compared with acid phosphatase activity, it can be seen that the lowest activity for both the enzymes occurred at the same time (13.00 h) but the peak differed. The liver lysosomes are reported as heterogenous in nature[7]. It has also been reported that the