Slow Conduction in the Atrioventricular Node of the Cat: A Possible Explanation

Delay of atrioventricular (AV) conduction is mainly due to slow conduction of excitation through the AV nodal region[1,2]. Slow conduction is attributable to physiological properties such as the low amplitude and the slow rate of rise of the action potential as well as to structural complexity[3–7]. Since Purkinje fibres with a low resting potential have a slow rate of rise, repolarization by the flow of electrical current restores a normal rate of rise of the action potential[8]. The question may thus be asked whether the cells of the AV node, when hyperpolarized, behave in a similar way.

Cats weighing 1.0–1.5 kg were anesthetized by i.p. injection of sodium pentobarbital (Nembutal, 20 mg/kg). The specimen comparising SA node, atria, AV node, His bundle and a small section of the ventricle was placed in a 50 ml chamber and oxygenated Ringer-Krebs solution (36 °C) was perfused at a flow rate of 10–15 ml/min. Intracellular microelectrodes (approximately 40 megohms) and a high input impedance negative-capacitance preamplifier were employed differentially to measure the membrane potential. A CR circuit with a time constant of 15 μsec was coupled in parallel with a DC amplifier in order to compute the maximum rate of the action potentials. The driving stimulus electrode was applied on the right atrium. The resting potential was changed by applying electrical current by means of a suction electrode (outside diameter, 500 μm; inside diameter, 400 μm). Although it was considered that constant current was applied by this method, the abolute amount of current passing through the membrane was unknown[9,10]. The distance between the recording electrode and the outer wall of the current applying electrode was approximately 0.2 mm. The localization of the AV nodal region was determined according to the criteria described by other authors on the basis of the anatomical localization, configuration of action potentials and extent of delay of conduction[4]. However, the subdivisions employed in the rabbit heart[11] could not be well differentiated in the cat heart.

Figure 1, A^1 is the action potential obtained during the control resting potential (−62 mV). 2 action potentials of Figures 1, A^2, 1, A^3 and 1, A^4 were obtained at resting potentials of −66, −76 and −85 mV, respectively, by applying hyperpolarizing current of various intensities. When the membrane was hyperpolarized, the amplitude and the maximum rate of rise of the action potential increased and a notch at the rising phase disappeared. The action potential was shortened.

In the example shown in Figure 1, B^1, at the control resting potential of −55 mV, the amplitude of the response was less than 10 mV and the maximum rate of rise of depolarization was less than 1 V/sec. This kind of potential change was observed in preparation which for some reason showed a conduction block. When the membrane was hyperpolarizad, the amplitude and the maximum rate of rise of the action potential increased (Figure 1, B^2, 1, B^3 and 1, B^4). The relationship between the resting potential and the amplitude of action potential in 5 experiments from 5 different cat hearts is shown in Figure 2, A. The amplitude of the action potentials increased linearly as

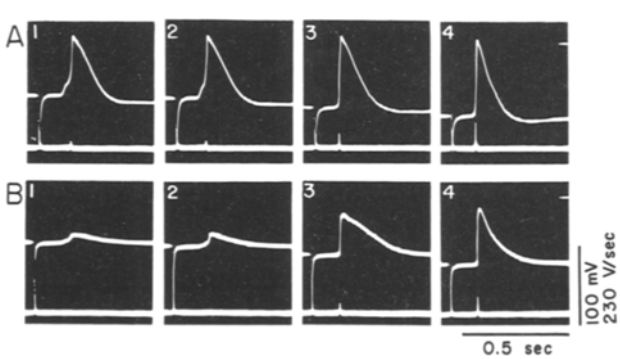

Fig. 1. Effect of hyperpolarization on the AV nodal action potential. In both A) and B), upper tracings are the action potentials and lower tracings are the first derivative of the action potential indicating the maximum rate of rise of depolarization. Horizontal bar in the fourth frame indicates zero potential. A) shows 4 action potentials taken from the same cell at 4 different resting potentials. Action potentials shown in B) were also recorded from the AV nodal fibre close to the site of the conduction block. Action potentials in A, 1) and B, 1) were obtained at the control resting potential. When the membrane was hyperpolarized, the amplitude and the maximum rate of rise of action potential increased (2, 3, 3 in A) and B)).

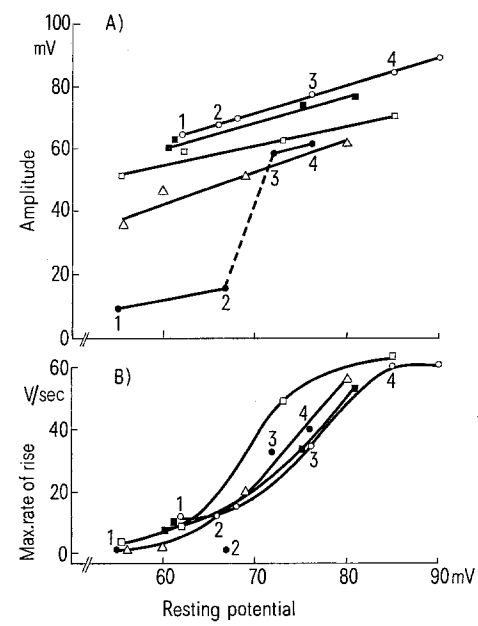

Fig. 2. A) Relationship between the resting potential and the amplitude of action potential. B) Relationship between the resting potential and the maximum rate of rise of action potential. Different symbols indicate different examples. Numerals on the original Figure shown in 1, A) and B, 1).

[1] A. M. SCHER, M. I. RODRIQUEZ, J. LIIKANE and A. C. YOUNG, Circulation Res. *7*, 54 (1959).

[2] B. F. HOFFMAN, A. PAES DE CARVALHO, W. C. MELLO and P. F. CRANEFIELD, Circulation Res. *7*, 11 (1959).

[3] K. MATSUDA, T. HOSHI and S. KAMEYAMA, Tohoku J. exp. Med. *68*, 8 (1958).

[4] B. F. HOFFMAN and P. F. CRANEFIELD, *Electrophysiology of the Heart* (McGraw-Hill, New York 1960) p., 132.

[5] B. F. HOFFMAN, *Electrical Activity of the Heart* (Elsevier, Amsterdam 1961), p. 143.

[6] T. KANNO, Jap. J. Physiol. *13*, 97 (1963).

[7] T. KANNO, Jap. J. Physiol. *20*, 417 (1970).

[8] S. WEIDMANN, J. Physiol., Lond. *127*, 213 (1955).

[9] N. SHIGETO, Am. J. Physiol. *218*, 1773 (1970).

[10] J. W. WOODBURY and A. M. GORDON, J. cell. comp. Physiol., Suppl. 2, *66*, 35 (1965).

[11] A. PAES DE CARVALHO and D. F. DE ALMEIDA, Circulation Res. *8*, 801 (1960).

the resting potential was increased in 4 experiments, except in the case shown in 1, B (solid circles in Figure 2, A). On the other hand, the relationship between the resting potencial and the maximum rate of rise of action potential showed a sigmoid curve (Figure 2, B). The upper limiting value of the maximum rate of rise of the action potentials in the cat AV nodal fibres was about 60 V/sec, in the atrial fibres 90 V/sec, and in ventricular Purkinje fibers 400 V/sec. These maximum rates were reached from resting potentials negative to −85 mV.

The maximum rate of rise of the action potential is related to the conduction velocity[12]. Measurement of the conduction time between the stimulus and the maximum rising phase of action potentials in Figure 1, A revealed a definite shortening of conduction time when the membrane was hyperpolarized.

The present results differ from those of HOFFMAN[5] who comes to the conclusion that hyperpolarization by current flow does not increase the upstroke velocity. His experiments were done with rabbit AV node and would indicate that a certain part of the node completely lacks a system capable of carrying fast Na current (so called N-region). In contrast, the present results favor the view that a fast Na-carrying system is actually present but is normally inactivated as a consequence of the very low membrane potential. Clearly, more experimentation with both the cat and rabbit AV node is necessary before the hypothesis of a species difference can be given serious consideration[13].

Zusammenfassung. Nachweis, dass bei Erhöhung des Membranpotentials im AV-Knoten der Katze eine raschere Erregungsausbreitung erzielt werden kann.

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[12] A. L. HODGKIN and B. KATZ, J. Physiol., Lond. *108*, 37 (1949).

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Neurohypophyseal Origin of a Humoral Factor Restoring Volume Natriuresis in Acutely Hypophysectomized Rats

It was shown in our previous paper[1] that acute hypophysectomy markedly decreased sodium and urine output during blood volume expansion, as compared to non-hypophysectomized rats. The conclusion drawn was that pituitary is involved in the humoral part of the renal mechanism of extracellular fluid volume regulation.

Attempts have been made to restore some impaired kidney functions (decreased glomerular filtration rate and renal blood flow) in chronically hypophysectomized man, dog and rat with both adenohypophyseal (ACTH, triiodothyronine, growth hormone)[2-5] and neurohypophyseal hormones (Pituitrin, Pitocin, oxytocin)[6-9]. The results have been more successful with the latter group. Thus the aim of the present study was to investigate whether a humoral substance is present in the posterior pituitary tissue that could reverse the low natriuretic response to the extracellular fluid volume expansion with saline in acutely hypophysectomized rats.

Material and methods. 15 male Wistar rats, weighing 220–250 g, were anaesthetized, surgically prepared, heparinized, injected DOCA and continuously infused with ADH and inulin-^{14}C, as described previously[1]. Following the surgical preparation, 1 h equilibration phase and the first urine-sampling period, i.v. infusion of 0.9% saline in the amount of 4% of body weight was completed in the second 20-min period. Another 3 urine samples were taken during next 60 min. The animals were divided into 3 experimental series: I. non-hypophysectomized rats; II. hypophysectomized rats; III. hypophysectomized rats with homogenate of 3 fresh neurohypophyses in 0.5 ml of 0.1% bovine albumin injected i.p. 15 min before the first urine-sampling period. Median of the weights for both kidneys in all experimental groups was 1.88 g. Chemical and radioisotopic analysis, as well as the statistical evaluation, were the same as in the previous work[1].

Results and discussion. The results are summarized in the Table. In spite of the plasma diluting effects of saline infusion, which are known to promote sodium excretion, peak sodium excretion during the extracellular fluid volume expansion in the acutely hypophysectomized rats (series II) was approximately 10 times lower than the corresponding peak for sodium excretion in the non-hypophysectomized rats (series I). The urine output and TRF_{Na} were also decreased considerably, whereas GFR showed only a slight decrease. It is thus obvious that the diluting effects of saline infusion on the sodium and urine excretion in acutely hypophysectomized rats was negligible.

However, homogenate of neurohypophyses injected i.p. in the acutely hypophysectomized rats prior to the first urine-sampling period (series III) completely restored their GFR and the ability to excrete sodium and urine immediately after the infusion of the saline load.

It is concluded on the basis of these results that the capacity to restore the impaired ability to increase renal sodium excretion during extracellular fluid volume expansion in acutely hypophysectomized rats by homogenate of neurohypophysis injected i.p. is directly related to a humoral factor present in the posterior pituitary. Homogenate from the anterior pituitary was ineffective in this respect.

As the present results show restoration to normal of the decreased GFR in the acutely hypophysectomized rats following the i.p. administration of the posterior pituitary homogenate, a posterior pituitary natriuretic factor could,

[1] B. LICHARDUS and J. PONEC, Experientia *28*, 471 (1972).
[2] R. C. DE BODO, I. L. SCHWARTZ, J. GREENBERG, M. KURTZ, D. P. EARLE and S. J. FARBER, Proc. Soc. exp. Biol. Med. *76*, 612 (1951).
[3] D. P. EARLE, S. J. FARBER, R. C. DE BODO, M. KURTZ and M. F. SIMKOFF, Am. J. Physiol. *173*, 189 (1953).
[4] P. LEES, MARY F. LOCKETT and C. N. ROBERTS, J. Physiol., Lond. *171*, 397 (1964).
[5] J. W. BAUMAN JR. and ESTELLE S. PHILLIPS, Am. J. Physiol. *218*, 1605 (1970).
[6] C. A. HANDLER and A. D. KELLER, Am. J. Physiol. *160*, 321 (1950).
[7] T. W. DEMUNBRUN, A. D. KELLER, A. H. LEVKOFF and R. M. PURSER JR., Am. J. Physiol. *179*, 429 (1954).
[8] MARY F. LOCKETT and C. N. ROBERTS, J. Physiol., Lond. *167*, 581 (1963).
[9] P. LEES and MARY F. LOCKETT, J. Physiol., Lond. *171*, 403 (1964).