Entry of Sodium-24 in Isolated Rabbit Atria

Acetylcholine has been shown to increase potassium permeability in myocardial tissues[1-3]. Its effect on transport of sodium, however, is inconclusive. Earlier flux studies[3,4] and, more recently, microelectrode studies[5-7] suggest that acetylcholine (ACh) may have an effect on entry of sodium during the rising phase of the action potential. This communication deals with the effect of ACh on the rate of net entry of sodium-24 in isolated rabbit atria under different stimulus frequencies. The results presented may explain some of the findings of other investigators working on the effect of ACh, using the microelectrode technique.

Isolated left atria attached to platinum–iridium electrodes were equilibrated 30–60 min. in a Ringer–bicarbonate medium which was continuously oxygenated. At the end of this time the control atria were placed in a modified Ringer's solution containing 1/4 normal potassium (1·35 mM) and tracer amounts of sodium-24. Treated atria were placed in identical medium containing ACh 80 μgm./ml. The net entry of sodium-24 was determined over an additional 30-min. interval. During this period of time the atria were stimulated at varying frequencies with a 2–10-V. pulse of 0·5 m.sec. duration. The atria were then homogenized in distilled water and evaporated samples of the homogenate were counted in a Beta scintillator. All experiments were carried out at 30° C. The data are expressed as a rate of net entry of sodium-24 in c.p.m./gm./30-min. interval.

Fig. 1 summarizes the results obtained. Each point represents the mean of 6–8 experiments. Rate of net entry of sodium-24 is plotted as a function of stimulus frequency. ACh almost doubled the rate of entry of sodium in quiescent atria. Stimulating the atria at 180 and 400 cycles/min. caused a sharp increase in net entry of sodium-24 in control atria and to a lesser extent in ACh-treated atria. Over the frequency-range of 180–400 cycles/min., ACh had no significant effect on sodium entry. At frequencies above 400 cycles/min. the rate of sodium entry dropped markedly in control preparations but continued to increase in ACh-treated atria, approaching a maximum at 1,200 cycles/min.

These experiments indicate that ACh affects the rate of net entry of sodium in quiescent and electrically driven atrial preparations. The increase in sodium entry in quiescent atria may be due to the hyperpolarization which ACh produces with the concomitant increase in net efflux of potassium[8,9]. The lack of a significant effect of ACh over the range of 180–400 is difficult to explain; however, the effect of ACh at higher frequencies suggests a direct effect of the agent on the sodium carrier system. That the sharp drop in rates of entry in control preparations at frequencies of about 400 cycles/min. is due to a change in the conduction process and not to a change in the rate of firing of individual cells is evident from the following studies: using rabbit atria Vaughn Williams[7] demonstrated that as the stimulus frequency increased (150–250 cycles/min.) conduction velocity decreased. At frequencies above 250 cycles/min. conduction velocity fell sharply. He also showed that ACh increased conduction velocity. A property intimately related to conduction velocity is the rate of rise of the transmembrane action potential. Johnson and McKinnon[5] observed in ventricular strips that as the stimulus frequency increased, the rate of rise of the action potential decreased. This effect was most

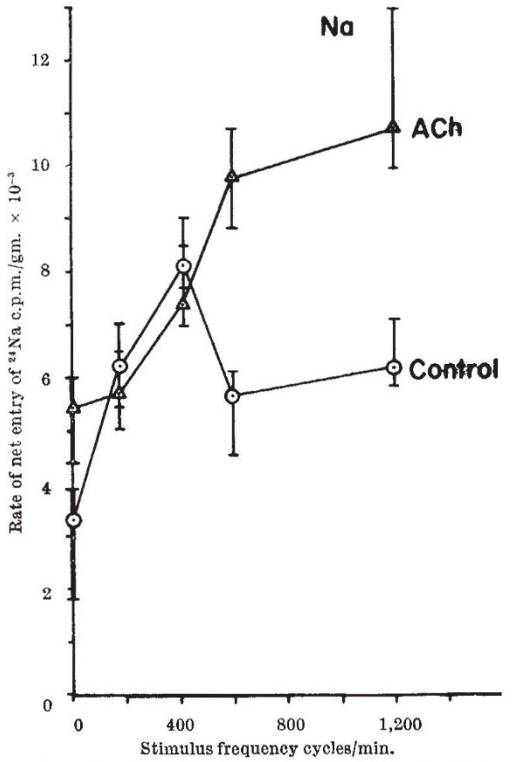

Fig. 1. Entry of sodium-24 in isolated left atria of rabbits as a function of stimulus frequency. Vertical bars represent ranges obtained

marked at frequencies greater than 600 cycles/min. Quinidine, a drug known to depress conduction, decreases the rate of rise of the action potential[6,10] and depresses the rate of net entry of sodium-24[11,12]. The effects of quinidine can be reversed by ACh[6]. Finally, it has been shown by Klein and Holland[13] that the maximum following frequency of single atrial cells was of the order of 800 cycles/min., and in ACh-treated preparations the maximum following frequency was in excess of 1,200/min. The gross maximum following frequency was found to range from 350–400 cycles/min. and in ACh-treated atria the range was 500–700 cycles/min.

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