TTX-like effects of adrenaline on the sodium current in isolated mammalian myocardium

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The effects of adrenaline on action potentials were measured in guinea pig papillary muscles using conventional microelectrode technique. Adrenaline was used in the concentration range from 0.01 to 1 µM, TTX from 0.1 to 20 µM. Maximum rate of rise ($\dot{V}max$) and membrane potential (V) were measured during stepwise depolarization through K_o-increase. The obtained curves ($\dot{V}max$ versus V) were S-shaped and could be fitted by the equation $\dot{V}max = \dot{V}s/(1 + \exp((Vh - V)/s))$. $\dot{V}s$ is the saturation value of $\dot{V}max$, Vh the membrane potential at $\dot{V}max$ one half of $\dot{V}s$ and V the membrane potential. A concentration of 2 µM TTX diminished $\dot{V}max$ in a potential dependent manner (1). From normal resting potentials (-95 mV) down to about -65 mV the reduction of $\dot{V}max$ was not more than about 10 %. At lower potentials the inhibitory effect increased significantly and at about -55 mV a block of the Na-dependent part of the rising phase was seen. Accordingly the corresponding differentiation signal lost its first peak, which is known to depend on the fast Na-current (2). The ensuing second peak, correlated to the Ca-current, remained essentially unchanged. In similar experiments the effects of adrenaline were studied. At normal membrane potential and 0.1 µM adrenaline $\dot{V}max$ was unchanged or reduced by less than 5 % (3). At lower resting potential the reduction of $\dot{V}max$ was more pronounced (about 40 % at -55 mV). Under identical conditions a 80 - 100 % inhibition was found with TTX in a 20 fold higher concentration.

Similar to findings with TTX the curve of $\dot{V}max$ versus membrane potential obtained during the influence of adrenaline, was steeper and shifted to more positive membrane potentials by about 2.5 mV at Vh.

The inhibitory effects of adrenaline were also found after inactivation of the slow Ca-current through D-600 (1 µg/ml) indicating, that the depression of $\dot{V}max$ is not an indirect effect of either Ca-ion movement, Ca-accumulation or Ca-dependent contraction. The ß-receptor blocker pindolol (1 µg/ml) diminished the depressant effects of adrenaline at -55 mV membrane potential. These results show pronounced inhibitory effects of adrenaline on the partially inactivated fast sodium system. They may indicate influences of the ß-adrenergic system on the fast Na-current which are indipendent of the simultaneous and cAMP mediated stimulation of the Ca-current.

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