AGING BLUNTS EFFECTS OF TRIIODOTHYRONINE ON RABBIT CARDIAC MYOCYTES

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INTRODUCTION: Aging is associated with many changes in cardiac function including diminished inotropic responses to catecholamines¹. The limiting factor of inotropic response to β -adrenergic stimulation in aged myocardium might act subsequent to protein kinase activation but proximal to the Ca^{2+} -troponin interaction². It is not known whether aging affects the myocardial responses to triiodothyronine (T_3). We studied the inotropic effects of T_3 on cardiac myocytes isolated from young and old rabbits.

METHODS: This project was approved by our IACUC. Freshly isolated ventricular myocytes were prepared from hearts of young (4 months old) and old (3 years old) rabbits (N=7), using retrograde aortic perfusion with 0.1 % collagenase in low Ca^{2+} - minimal essential medium. The percent (%) shortening and maximum rate of shortening (R_{max} , $\mu\text{m}/\text{sec}$) were measured by using a video edge detector. Measurements were obtained during stimulation at 2 Hz at baseline, with serial additions of 10^{-8} , 10^{-7} and 10^{-6} M T_3 , in the absence or presence 10^{-6} M dantrolene (sarcoplasmic reticulum Ca^{2+} channel blocker) or 10^{-6} M nifedipine (sarcolemmal L-type Ca^{2+} channel blocker). ANOVA was used for statistical analysis. A value of $p < 0.05$ was accepted as significant. Data were presented as Mean $\pm$ S.E.M.

RESULTS: The basal % shortening and R_{max} were not significantly different between the young ($4.3 \pm 0.3\%$; $56 \pm 7 \mu\text{m}/\text{sec}$) and the old animals ($4.9 \pm 0.4\%$; $61 \pm 12 \mu\text{m}/\text{sec}$). Serial additions of T_3 (10^{-8} , 10^{-7} & 10^{-6} M) increased % shortening and R_{max} in the young animals but had no significant effects in the old animals. At the concentrations of 10^{-7} and 10^{-6} M T_3 , the changes in % shortening (Fig 1) and R_{max} of the basal values were significantly different between the two groups. Both dantrolene and nifedipine blocked the inotropic effects of T_3 in the young animals.

DISCUSSION: The data showed that aging greatly decreased myocardial sensitivity to acute T_3 stimulation. The positive inotropic effects of T_3 were blocked by L-type and SR calcium channel blockers in young animals. This suggests that aging might decrease the sensitivities of myocardial L-type and SR calcium channels to T_3 .

REFERENCES: 1. Circ Res 36:262-9, 1975. 2. Am J Physiol 239:H501-8, 1980