

SCA 36 INOTROPIC EFFECTS OF TRIIODOTHYRONINE ON CARDIAC MYOCYTES ISOLATED FROM YOUNG AND OLD RABBITS

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Introduction: Aging is associated with many changes in cardiac function. One important change is the diminished inotropic response of aged myocardium to catecholamines(1). It has been suggested that the limiting factor of inotropic response to beta-adrenergic stimulation in aged myocardium might act subsequent to protein kinase activation but proximal to the Ca^{2+} -troponin interaction(2). It is not known whether aging affects the myocardial inotropic responses to triiodothyronine (T₃). We studied the inotropic effects of T₃ on shortening of isolated cardiac myocytes isolated from young and old rabbits.

Methods: Freshly isolated ventricular myocytes were prepared from hearts of young (4 months of age) and old (3 years of age) New Zealand white rabbits (n=7), using retrograde aortic perfusion with 0.1% collagenase in low- Ca^{2+} minimal essential medium (MEM). The percent (%) shortening and maximum rate of shortening (R_{max}, $\mu\text{m}/\text{sec}$) were measured by 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 T₃, 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 measurements of myocyte % shortening and R_{max} were not significantly different between young ($4.3 \pm 0.3\%$; $56 \pm 7 \mu\text{m}/\text{sec}$) and old animals ($4.4 \pm 0.3\%$; $58 \pm 8 \mu\text{m}/\text{sec}$). Serial additions of T₃ (10^{-8} , 10^{-7} 10^{-6} M) increased myocyte % shortening and R_{max} in both young and old animals. At the concentration of 10^{-6} M T₃, the increases of myocyte % shortening and R_{max} above the basal values were slightly lower in the old animals ($25 \pm 6\%$; $30 \pm 10\%$) than those in the young animals ($36 \pm 7\%$; $42 \pm 10\%$) (Fig 1, 2). Both dantrolene and nifedipine blocked the inotropic effects of T₃ in young and old animals. These blocking effects were not different between the two groups.

Discussion: The data showed that T₃ increased inotropic responses in young and old ventricular myocytes in a dose-dependent manner. However, aging appears to blunt the myocardial inotropic responses to T₃. The inotropic effects of T₃ were blocked by L-type or SR calcium channel blockers in the young and old animals. This

suggests that T₃ may act on both calcium channels to produce the inotropic effects and that aging does not seem to affect the myocardial sensitivities to the calcium channel blockers.

Reference: (1). *Circ Res* 36:262-9, 1975. (2). *Am J Physiol* 239:H501-8, 1980.

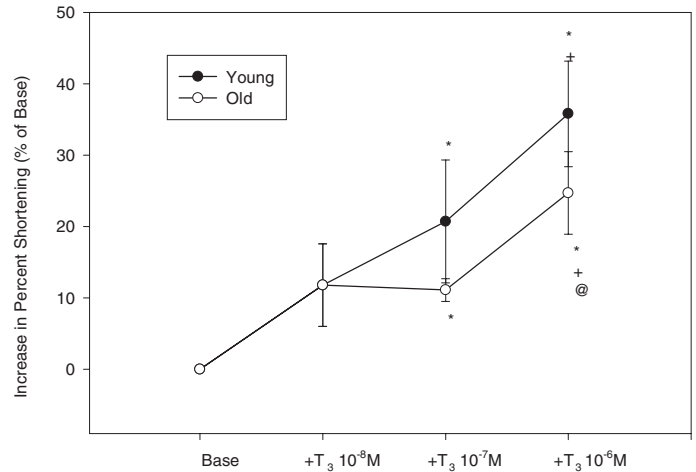


Fig. 1. The effects of T₃ on Percent Shortening in Young and Old rabbit cardiac myocytes.

* Significantly different from Base. + Significantly different from T₃ 10⁻⁸M.

@ Significantly different from T₃ 10⁻⁷M.

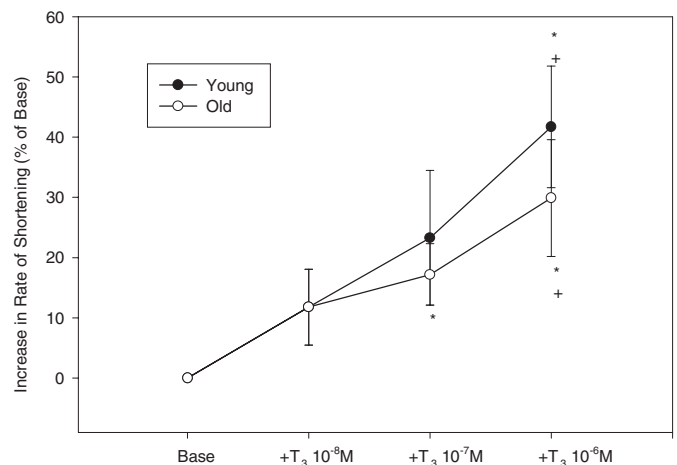


Fig. 2. The effects of T₃ on Rate of Shortening in Young and Old rabbit cardiac myocytes.

* Significantly different from Base. + Significantly different from T₃ 10⁻⁸M.