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Age-dependent changes of β_2-adrenoceptor function in the rabbit heart

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It has been suggested that β_2-adrenoceptor (β_2AR) stimulation is the main mechanism by which sinoatrial heart rate is increased in adult New Zealand white rabbits (Barbuti et al. 2007). We have studied the age-dependent function of sinoatrial and ventricular β_2ARs in mixed breed Chinchilla and California rabbits. Spontaneously beating right atria (RA), left atrial trabeculae (LA) and right ventricular papillary muscles (PM), were dissected from the hearts of new-born (1-3 days), juvenile (1-2 months) and adult (1-2.5 years) rabbits. PM and LA were paced at 1Hz. The tissues were pretreated 90 min with phenoxybenzamine (5μM) to block α-adrenoceptors and neuronal uptake of adrenaline as previously described (Kaumann et al. 2009). β_2ARs were activated with adrenaline in the presence of the β_1AR-selective antagonist CGP20712A (300nM) and maximum stimulation of β_1AR+β_2AR assessed with isoprenaline (200μM). Fractional values (f) of the maximum effects of adrenaline through each β_1AR and β_2AR, $f_1+f_2=1$, and pD_2s were estimated from concentration-effect curves (Table 1). High adrenaline concentrations surmounted the blockade of β_1AR by CGP20712A. CGP20712A-resistant chronotropic and inotropic effects of adrenaline, blockable by the β_2AR antagonist ICI118551 (25-50nM), were detected in RA and PM respectively, but not in LA of the 3 age groups.

Table 1

f_2 (x100) and pD_2 values of adrenaline for the sinoatrial node in right atria (RA) and right ventricular papillary muscles (PM). Data are mean±S.E.M. n = number of rabbits.

	Newborn				Juveniles				Adults			
	RA	n	**PM**	n	**RA**	n	**PM**	n	**RA**	n	**PM**	n
f_2	55±12	8	41±12	10	8.3±2.9	10	8.3±2.4	15	14.1±4.0	10	9.8±2.8	12
pD_2	7.47±0.16		7.67±0.14		7.43±0.24		7.79±0.20		7.26±0.13		7.57±0.24	

Conclusions: Adrenaline increases sinoatrial beating rate and ventricular force similarly through β_1ARs and β_2ARs in new-born rabbit hearts but the contribution of β_2ARs decays markedly in juvenile and adult rabbit hearts.The inotropic effects of adrenaline on rabbit left atria are entirely mediated through β_1ARs, regardless of age.

Barbuti A, Terragni B, Brioschi C, DiFrancesco D (2007) J Mol Cell Cardiol 42:71-78.

Kaumann AJ, Galindo-Tovar A, Escudero E, Vargas ML (2009) Naunyn-Schmiedeberg´s Arch Pharmacol 380:421-430.