

# AUTORADIOGRAPHIC DEMONSTRATION OF CHANGES IN $\alpha$ -ADRENOCEPTOR AND MUSCARINIC CHOLINERGIC RECEPTOR DENSITY IN ISCHAEMIC RAT HEART

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$\alpha$ -adrenergic and muscarinic cholinergic agonists and antagonists have direct actions on the heart.  $\alpha_1$ -adrenergic and muscarinic cholinergic receptors have been identified in membrane preparations of cardiac muscle (Guicheney & Meyer, 1981; Nedoma *et al*, 1986). A variable distribution of these receptor types has been described using *in vitro* autoradiography (Dashwood & Spyer, 1986). Recently we have shown that coronary artery ligation-induced ischaemia produces a striking depletion in muscarinic cholinergic receptor density in cardiac muscle. In the present study we have examined the effects of coronary artery ligation on  $\alpha_1$ - and  $\alpha_2$ -adrenoceptor density as well as muscarinic cholinergic receptor density in the rat heart.

Male Sprague-Dawley rats were anaesthetised with sodium pentobarbitone (60 mg kg<sup>-1</sup> i.p.) and prepared for coronary artery ligation by the method described by Clark *et al* (1980). Occlusion was maintained for 30 minutes after which the heart was excised, frozen rapidly and stored until analysis. 20  $\mu$ M frozen serial sections were cut through the hearts, thaw mounted on gelatinised microscope slides and used for autoradiography. Sections were incubated in 1 nM [<sup>3</sup>H]QNB, 2 nM [<sup>3</sup>H]rauwolscine and 5 nM [<sup>3</sup>H]prazosin in order to identify muscarinic cholinergic,  $\alpha_2$ - and  $\alpha_1$ -receptors respectively. Paired sections were incubated in the presence of 1  $\mu$ M carbachol, yohimbine and phentolamine in order to establish the degree of non-specific binding.

Variable receptor distributions across the heart were apparent. There was a striking depletion of muscarinic cholinergic receptors at areas of ischaemia accompanied by a depletion of  $\alpha_1$ - or  $\alpha_2$ -adrenoceptors. Interestingly a 30 minute coronary artery occlusion had a more pronounced effect on muscarinic receptors than either  $\alpha_1$ - or  $\alpha_2$ -adrenoceptors. The ischaemic area was verified using the periodic acid Schiff method to stain for glycogen. These ischaemia-induced receptor changes may account, in part, for the changes in sensitivity of ischaemic tissue to drugs and putative transmitters.

The support of the British Heart Foundation is gratefully acknowledged.

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