ADDITIONAL EVIDENCE FOR THE PRESENCE OF A_1 ADENOSINE RECEPTORS IN THE VENTRAL AORTA OF THE DOGFISH SHARK (SQUALUS ACANTHIAS)

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Our recent studies of the effects of various adenosine agonists on the vasoactivity of isolated rings from the ventral aorta of the dogfish (Evans and Weingarten, Bull. MDIBL 28: 4-5, 1989; Evans and Walton, Bull. MDIBL 29: 120-121, 1990) suggested that both A_1 (constrictory) and A_2 (dilatory) receptors may be present, as has been described for a variety of tissues (e.g., Stiles, TIPS Dec. 1986: 486-490; Williams, Neurochem. Int. 14: 249-264, 1989) including the shark rectal gland (Forrest et al., J. Clin. Invest. 72: 1163-1167, 1983; Kelley et al., J. Clin. Invest. 85: 1629-1636, 1990). However, our evidence for A_1 receptors was rather tenuous, with N^6-cyclopentyladenosine (CPA) producing only a 3% vasoconstriction above the baseline of 504 mg (Evans and Walton, op. cit., 1990), with an onset at relatively high concentrations (100 nM). CPA has a ratio of A_1 to A_2 specificity of 780, with a K_i of 0.6 nM for A_1 in rat brain membranes (Trivedi et al., J. Med. Chem. 32: 11-13, 1989). To test further the hypothesis that this vascular smooth muscle (VSM) contains A_1 receptors, we examined the effect of a more potent A_1 agonist, N^6-(2S)-[2-endo-norbornyl]adenosine ((S)-ENBA), with an A_1/A_2 ratio of 4700, and a K_i of 0.3 nM for A_1 (Trivedi et al., ibid).

The preparation and mounting of dogfish aortic VSM rings for tension measurements has already been described (Evans and Weingarten, Toxicology 61: 275-281, 1990). A 10 mM stock solution of (S)-ENBA was prepared in ethanol before dilution in elasmobranch Ringer's solution to attain the desired concentration range of 10^{-13} to 10^{-5} M. Addition of the maximal ethanol concentration (0.1%) did not itself produce any vasoactive response. Initial tension of the rings was 507 ± 24 mg (S.E., N =4).

(S)-ENBA did produce a contractile response in this preparation with an initial, significant ($p < 0.01$) response at 1 pM and an apparent EC_{50} of < 1 nM, essentially the same as its K_i in binding studies in rat brain membranes (Trivedi et al. op. cit., 1989). In addition, the maximal response (at 10 nM) was a 28% increase in tension, significantly greater than what we found for another putative A_1 agonist, CPA (see above), in this system. These results support strongly our earlier conclusion that the shark ventral aorta possesses an A_1 adenosine receptor. The role of this receptor, as well as an A_2 receptor, in the control of branchial hemodynamics in the dogfish shark remains to be determined. (Supported by NIEHS-P30-ESO3828-05 to the Center for Membrane Toxicity Studies and NSF DCB-8916413 to DHE.)