Vascular histamine receptors in the cat

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The i.v. injection of histamine to cats elicits dose-dependent depressor responses (Dale & Laidlaw, 1910) involving both H_1- and H_2-receptors (Owen & Parsons, 1974). The depressor responses to histamine are due largely to dilatation of resistance vessels (Rocha é Silva, 1966) and so we have now investigated the role of H_1- and H_2-receptors in the vasodilator response to histamine in the blood perfused hind-limb in cats.

Experiments were performed on cats anaesthetized with pentobarbitone sodium, 60 mg kg^{-1} i.p. Systemic blood pressure was measured from the right common carotid artery. Mepyramine and metiamide were given by i.v. injection and i.v. infusion respectively. The left hind-limb was acutely denervated and perfused at constant flow with blood from the right femoral artery. Agonists were injected i.a. in 10 μl. Changes in vascular resistance were recorded as changes in perfusion pressure measured between the pump and the perfused limb.

Histamine, over the dose-range 10^{-11} to 10^{-8} mol/kg, caused dose-dependent decreases in perfusion pressure. Mepyramine (1 mg/kg) shifted the histamine dose-response curve to the right with a dose-ratio of approximately 10 and subsequent administration of 10 and 20 mg/kg mepyramine caused no further shift. When the maximal blocking effect of mepyramine had been achieved, metiamide (100 and 500 μg kg^{-1} min^{-1}) caused further dose-dependent shifts of the dose-response curve to the right with dose-ratios of approximately 60 and 320 respectively.

Metiamide alone (500 μg kg^{-1} min^{-1}) had no significant effect on the histamine dose-response curve. Administration of mepyramine (1 and 10 mg/kg) during continued infusion of metiamide, caused dose-dependent shifts of the histamine dose-response curve to the right.

Further indication that interaction with either H_1- or H_2-receptors elicits vasodilator responses has been obtained with 2-methylhistamine and 4-methylhistamine, histamine-like agonists selective for histamine H_1- and H_2-receptors respectively (Black, Duncan, Durant, Ganellin & Parsons, 1972). Both agonists elicited vasodilator responses in the hind-limb. The responses to 2-methylhistamine were reduced by mepyramine but not by metiamide, whereas the responses to 4-methylhistamine were reduced by metiamide but not by mepyramine.

The specificity of mepyramine and metiamide, as histamine antagonists, was tested by examining their effects on sub-maximal vasodilator responses elicited by intra-arterial injections of bradykinin, acetylcholine, isoprenaline and histamine. Administration of mepyramine (10 mg/kg) or metiamide (500 μg kg^{-1} min^{-1}) or both antagonists together caused no significant decrease in the responses to acetylcholine, bradykinin or isoprenaline. The responses to histamine were abolished by the combination of mepyramine and metiamide.

These experiments indicate that histamine-induced vasodilatation in the hind-limb of the cat involves both H_1- and H_2-receptors. The changes in the histamine vasodilator dose-response curves following administration of mepyramine and metiamide are very similar to the changes in the histamine depressor dose-response curves (Owen & Parsons, 1974).

References

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