Neuronal responses to adrenoceptor agonists in the cerebral cortex: evidence for excitatory α-adrenoceptors and inhibitory β-adrenoceptors

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Single cortical neurones are sensitive to noradrenaline (NA) applied by microelectrophoresis; both excitatory and depressant responses have been described (Krnjević & Phillis, 1963; Johnson, Roberts, Sobieszek & Straughan, 1969; Bevan, Bradshaw, Roberts & Szabadi, 1974). In the present study we have compared the effects of NA with those of other α- and β-adrenoceptor agonists on cortical neurones.

Spontaneously active single neurones were studied in the somatosensory cortex of the halothane-anaesthetized rat. All the drugs were applied by microelectrophoresis. Our techniques have been described elsewhere (Bevan *et al.*, 1974).

Out of 194 cells giving consistent responses to NA, 128 (66%) were excited and 66 (34%) were depressed by the drugs. Out of 93 cells responding to isoprenaline (IPNA), 26 (28%) were excited, and 67 (72%) were depressed. IPNA was applied with increasing ejecting currents (0–100 nA) to 22 cells which were depressed when IPNA was applied with lower ejecting currents; on 14 cells the depression was reversed into an excitation as the intensity of the ejecting current was increased. Phenylephrine was studied on 23 cells; 22 of these cells gave consistent excitatory responses, one cell did not respond. Salbutamol was studied on 11 cells excited by phenylephrine; all these cells were depressed by salbutamol.

Excitatory responses to NA were reversibly antagonized by phentolamine (10 cells), phenoxybenzamine (5 cells), and propranolol (4 cells). Excitatory responses to IPNA could be antagonized by phenoxybenzamine (5 cells); on one of these cells a depressant response was revealed after the abolition of the excitation. Excitatory responses to IPNA were reversibly antagonized by sotalol on two cells. Excitatory responses to phenylephrine were reversibly antagonized by phenoxybenzamine (7 cells); on two of these cells the depressant response to IPNA, and on one cell the depressant response to salbutamol, was not affected by phenoxybenzamine. Acetylcholine (ACh) was used as a control agonist in each of the antagonism studies: responses to ACh were not affected.

Depressant responses to IPNA could be antagonized by sotalol (10 cells). On two of these cells an excitation was revealed after the abolition of the depressant response. Responses to ACh were not affected.

These results indicate that the same cortical neurone may respond both with excitation and depression to adrenoceptor agonists; the excitatory responses may be mediated by α- and the depressant responses by β-adrenoceptors. The ability of the β-adrenoceptor antagonists (propranolol, sotalol) to antagonize excitatory responses (see also Johnson *et al.*, 1969) could reflect the α-adrenoceptor blocking properties of these drugs at somewhat higher concentrations than are required for β-adrenoceptor blockade (Gulati, Gokhale, Parikh, Udwadia & Krishnamurty, 1969). Indeed, lower doses of sotalol often potentiate nueronal excitatory responses to NA, whereas higher doses have an antagonistic effect (Bevan *et al.*, 1974).

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