Does DPI [(3,4-dihydroxy-phenylamino)-2-imidazoline] act at dopamine receptors on cortical neurones?

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Single cortical neurones can respond both with excitation and depression to noradrenaline and dopamine applied by microelectrophoresis (Bevan, Bradshaw & Szabadi, 1977; Bevan, Bradshaw, Pun, Slater & Szabadi, 1978). At least three different receptors seem to be involved in mediating these responses: the excitatory responses to the catecholamines are mediated by both α-adrenoceptors and excitatory dopamine receptors, whereas the depressant responses to noradrenaline are mediated by β-adrenoceptors (Bevan *et al.*, 1977; 1978). It is not clear, however, whether the depressant responses to dopamine are mediated by β-adrenoceptors, by inhibitory dopamine receptors, or by both.

The imidazoline derivative DPI [(3,4-dihydroxy-phenylamino)-2-imidazoline] has been reported to be a specific agonist at inhibitory dopamine receptors on molluscan neurones (Struyker Boudier, Teppema, Cools & van Rossum, 1975). On the basis of behavioural experiments, Cools, Struyker Boudier & van Rossum (1976) suggested that DPI may also stimulate inhibitory dopamine receptors in the mammalian CNS. In the present experiments, we have compared the effects of DPI with those of dopamine and the α-adrenoceptor agonist phenylephrine on cortical neurones.

Single spontaneously active 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.*, 1977; 1978).

The agonist effects of DPI and dopamine were compared on 135 cells which responded to both drugs. Dopamine excited 113 cells, and depressed 21 cells, whereas DPI excited 134 cells, and depressed only one cell. In the case of excitatory responses, dopamine appeared to be less potent than DPI, both in terms of the intensity of the ejecting current required to evoke equivalent responses, and in terms of the magnitude of the responses evoked by identical ejecting currents (t test: $P<0.001$, in both cases). The effects of haloperidol were tested on 11 cells excited by both dopamine and DPI. Acetylcholine was used as a control agonist. On 10 cells, responses to dopamine were reversibly antagonized, while responses to DPI and acetylcholine were unaffected. On the remaining cell, responses to dopamine and DPI were equally antagonized, while the response to acetylcholine was unaffected.

The effects of DPI and phenylephrine were compared on 74 cells. Each cell was excited by both drugs. The effects of phenoxybenzamine were tested on 8 cells excited by both DPI and phenylephrine. On all these cells, phenoxybenzamine equally antagonized the responses to DPI and phenylephrine, while excitatory responses to acetylcholine were unaffected.

Our results show that DPI is a potent excitant of cortical neurones. The effects of the antagonists suggest that the excitatory responses to DPI are not mediated by dopamine receptors, but rather by α-adrenoceptors. This suggestion is supported by recent evidence that DPI stimulates α-adrenoceptors in vascular smooth muscle (Ruffolo, Miller & Patil, 1978).

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