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Tricyclic antidepressants and monoamines: the relationship between uptake blockade and potentiation of neuronal responses

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It has previously been reported that the tricyclic antidepressants imipramine and desipramine can potentiate the responses of single brain cells to micro-electrophoretically applied monoamines (Bradshaw, Roberts & Szabadi, 1974). The potentiating effect of the antidepressants is generally ascribed to the efficacy of these drugs in blocking the uptake of monoamines into nervous tissue (Schildkraut, 1965). In order to investigate this hypothesis we have examined whether the tricyclic antidepressants can potentiate neuronal responses to the monamines in situations where uptake mechanisms are unlikely to be involved.

Single spontaneously active neurones were studied in the cerebral cortex and corpus striatum of the halothane-anaesthetized rat. All the drugs were applied by microelectrophoresis. Repeated responses to monoamines were compared following a brief application of an antidepressant (desipramine or iprindole).

1. It has been reported that iprindole is ineffective in blocking the uptake of noradrenaline (NA), 5-hydroxytryptamine (5-HT) and dopamine (DA) into brain tissue (Ross, Renyi & Ögren, 1971). We have found, however, that responses of single neurones to NA, 5-HT and DA can be potentiated by iprindole (18 cells in the cerebral cortex, 6 cells in the corpus striatum).

2. Although desipramine is a powerful inhibitor of NA uptake, its effects on the uptake of DA are very weak (Shore, 1972). We have found that responses of single striatal neurones to DA are potentiated by desipramine (7 cells).

3. In previous experiments we have found that cortical neurones can respond to microelectrophoretic application of mescaline, and that these responses are pharmacologically similar to those evoked by NA and 5-HT (Bevan, Bradshaw, Roberts & Szabadi, 1974). It has been reported that mescaline has an extremely low affinity for NA uptake mechanisms in the periphery (Iversen, 1967). Nevertheless, we have found that responses of cortical neurones to mescaline can be potentiated by desipramine (10 cells).

These findings indicate that uptake blockade cannot fully explain the potentiating effects of the tricyclic antidepressants on neuronal responses to the monoamines. An alternative explanation could be that the potentiation seen in our experiments is due to a post-synaptic effect of the antidepressants (Bradshaw, Roberts & Szabadi, 1974).

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