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Potentiation and antagonism of neuronal responses to monoamines by methysergide and sotalol

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It has been reported that methysergide can antagonize responses of single cortical neurones to 5-hydroxytryptamine (Roberts & Straughan, 1967). Sotalol has been found to be an effective antagonist of noradrenaline on cortical neurones (Johnson, Roberts, Sobieszek & Straughan, 1969). We wish to report some further experiments which show that responses to monoamines can also be potentiated by methysergide and sotalol.

Spontaneously active neurones were studied in the somatosensory cortex of the halothane-anaesthetized cat. All the drugs were applied by microelectrophoresis. All the cells included in this study responded with excitation to noradrenaline, 5-hydroxytryptamine and mescaline. Repeated responses to noradrenaline, 5-hydroxytryptamine and mescaline were compared before, during and after a prolonged application of methysergide or sotalol.

The effect of methysergide was studied on 20 cells. On 15 of these cells, responses to the monoamines were reduced in the presence of methysergide. On five cells, potentiation of the effects of the monoamines was also seen. This potentiation was only observed when methysergide was applied with low ejecting currents and was always superseded by antagonism when the intensity of the ejecting current was increased. Similar results were obtained with sotalol. On 14 cells antagonism alone was seen; on three cells potentiation was also observed. Responses to noradrenaline, 5-hydroxytryptamine and mescaline were affected similarly in the presence of methysergide and sotalol; responses to acetylcholine did not change.

The dual action of methysergide and sotalol on responses to the monoamines can be interpreted in terms of two independent mechanisms: a lower concentration of methysergide or sotalol may affect a more sensitive 'potentiating' mechanism only, whereas a higher concentration may activate an 'antagonistic' mechanism as well.

A similar dual action on responses to the monoamines has been observed with the tricyclic antidepressants (Bradshaw, Roberts & Szabadi, 1973). In the case of the antidepressants, potentiation might be explained in terms of uptake blockade, while antagonism may be due to the blockade of post-synaptic receptors. However, this explanation is less plausible in the case of methysergide and sotalol, since methysergide has little uptake blocking activity (Born, Juengjaroen & Michal, 1972). Moreover, mescaline has only a very low affinity for uptake mechanisms in the periphery (Iversen, 1967).

Another possibility is that potentiation of excitatory responses to the monoamines results from the blockade of masked inhibitory receptors. Excitatory and inhibitory monoamine receptors have been found to co-exist on some invertebrate neurones (Gerschenfeld, 1973). It has been suggested that this may also be the case on some mammalian central neurones (Szabadi & Bradshaw, 1973).

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