GILLESPIE, J.S. (1972). The rat anococcygeus muscle and its response to nerve stimulation and to some drugs. *Br. J. Pharmac.*, 45, 404-416.

KOKETSU, K. (1958). Action of tetraethylammonium chloride on neuromuscular transmission in frogs. *Amer. J. Physiol.*, 193, 213-218.

TASAKI, I. & HAGIWARA, S. (1957). Demonstration of two stable potential states in the squid giant axon under tetraethylammonium chloride. *J. Gen. Physiol.*, 40, 859-885.

THOENEN, H., HAEFELY, W. & STAEHELIN, H. (1967). Potentiation by tetraethylammonium of the response of the cat spleen to post-ganglionic sympathetic nerve stimulation. *J. Pharmac. exp. Ther.*, 157, 532-540.

## Comparison of the effects of mescaline, noradrenaline and 5-hydroxytryptamine on single cortical neurones

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Previously we have reported that single cortical neurones can respond either with excitation or with depression to microelectrophoretic application of mescaline, and that these responses can be antagonized by the β-adrenoceptor antagonist, sotalol, and the 5-hydroxytryptamine antagonist, methysergide (Bradshaw, Roberts & Szabadi, 1971). In the present communication we report the results of some further studies in which we attempted to identify the receptor at which mescaline acts on cortical neurones.

Single spontaneously active neurones were studied in the somatosensory cortex of cats anaesthetized with halothane. Drugs were applied from 5-barrelled micropipettes by microelectrophoresis.

Of 199 cells yielding consistent responses to mescaline, 159 were excited, 34 were depressed, and 6 responded in a biphasic fashion (depression followed by excitation). Responses to mescaline were compared with responses to noradrenaline and 5-hydroxytryptamine on 66 cells. Fifty-one of these cells responded in the same direction to all three agonists. The remaining 15 cells responded in the same direction to noradrenaline and mescaline and in the opposite direction to 5-hydroxytryptamine. When responses to mescaline were compared with responses to noradrenaline and 5-hydroxytryptamine using a range of ejecting current intensities mescaline appeared to be less potent than the other amines.

Desensitization to the excitatory effects of mescaline was observed on 12 cells. Following desensitization to mescaline, neurones were found to be less sensitive to noradrenaline. This cross-desensitization was usually not specific, however, since responses to acetylcholine were also reduced.

The effect of mescaline on responses to noradrenaline and 5-hydroxytryptamine was also studied on 5 cells which did not respond to mescaline. The simultaneous application of mescaline resulted in antagonism of excitatory responses to noradrenaline and 5-hydroxytryptamine.

We have investigated the effects of sotalol (17 cells) and methysergide (20 cells) on responses to mescaline. We have found that sotalol and methysergide reversibly antagonized responses to mescaline. This antagonism was specific inasmuch as responses to acetylcholine were not affected. However, neither antagonist was able to discriminate between the actions of mescaline, noradreanline and 5-hydroxytryptamine.

These results suggest that mescaline may act at receptors similar to those activated by noradrenaline and 5-hydroxytryptamine on cortical neurones. However, although the correlation studies suggest that mescaline acts at noradrenaline receptors, it is not clear from the antagonist studies using sotalol and methysergide whether noradrenaline and 5-hydroxytryptamine act at the same or at different receptor sites. The apparently lower potency of mescaline might be due to a lower transport number of mescaline. However the observation that on some cells mescaline had very little agonistic effect yet was able to antagonize responses to noradrenaline and 5-hydroxytryptamine suggests that the lower potency of mescaline might be due to a lower intrinsic activity of this drug.

### Reference

BRADSHAW, C.M., ROBERTS, M.H.T. & SZABADI, E. (1971). The effect of mescaline on single cortical neurones. *Br. J. Pharmac.*, 43, 871-873.