adrenergic fibres. Ligation reduced the MAO activity, expressed per weight of tissue, by 67%±4 (mean of the percentage decrease±S.E. of mean)—$P<0.005$—while the reduction after post-ganglionic sympathectomy was only 26%±8 ($P<0.05$). COMT was unaffected by ligation when expressed as activity per weight of tissue; expressed as activity per gland there was a reduction of 60%±4 ($P<0.001$). Post-ganglionic sympathectomy reduced the COMT activity per weight of tissue by 32%±5 ($P<0.01$). Glands from rats that had been post-ganglionically sympathectomized and ligated showed very low COMT activities.

There was an absence of specific fluorescence in the submaxillary gland 18 and 24 h after reserpine. Desipramine had no effect on the intensity of the fluorescence of the noradrenergic fibres. Six hours after reserpine administration there was a reduction in the activities of MAO and COMT of 28%±3 ($n=5$, $P<0.05$) and 76%±6 ($n=5$, $P<0.001$) respectively. The corresponding results for 18 and 24 h after drug administration were for MAO 44%±6 ($n=5$, $P<0.01$) and 45%±3 ($n=5$, $P<0.01$) and for COMT 76%±4 ($n=4$, $P<0.001$) and 56%±7 ($n=4$, $P<0.002$). Desipramine caused a small, but not significant, reduction in the MAO activity with no effect on COMT.

The present results are compatible with the supposed extraneuronal location of COMT but it appears that the maintenance of enzyme activity is, in part, dependent on an intact sympathetic nerve supply. The sympathetic transmitter, noradrenaline, as a substrate for COMT may have a role in determining the activity of the enzyme.

REFERENCES

ALMGREN, O., ANDÉN, N-E., JONASON, J., NORBERG, K-A. & OLSON, L. (1966). Cellular localization of monoamine oxidase in rat salivary gland. *Acta physiol. scand.*, **67**, 21–26.

BROCH, O. J., JUN. & GULDBERG, H. C. (1970). A fluorometric method for the determination of COMT activity in brain. *Acta pharmac. tox.*, **28**, Suppl. 1, 22.

IVERSEN, L. L., GLOWINSKI, J. & AXELROD, J. (1966). The physiologic disposition and metabolism norepinephrine in immunosympathectomized animals. *J. Pharmac. exp. Ther.*, **151**, 273–284.

JONASON, J. (1969). Metabolism of dopamine and noradrenalin in normal, atrophied and post-ganglionically sympathectomized rat salivary glands *in vitro*. *Acta physiol. scand.*, **76**, 299–311.

SNYDER, S. H. & HENDLEY, E. H. (1968). A simple and sensitive fluorescence assay for monoamine oxidase and diamine oxidase. *J. Pharmac. exp. Ther.*, **163**, 386–392.

Effect of tricyclic antidepressants on monoamine responses of single cortical neurones

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The antidepressant activity of the imipramine-like drugs has been attributed to their action in blocking central reuptake mechanisms for monoamines. The presumed potentiation of neuronal responses to noradrenaline (NA) and 5-hydroxytryptamine (5HT) has never been demonstrated directly in the central nervous system.

Spontaneously active neocortical cells (eighty-three) were studied in the cat anaesthetized with halothane; thirty-eight were excited and eight depressed by iontophoretically applied 5HT, and thirty-one excited and six depressed by iontophoretically applied NA. The predominance of excitatory responses confirms earlier observations (Roberts & Straughan, 1967; Johnson, Roberts, Sobieszek & Straughan, 1969). Desipramine and imipramine did not affect the majority of cells when applied with iontophoretic currents of 25–50 nA for 15–30 seconds. Higher currents or longer periods of application were directly depressant and were not used.

The monoamine responses were compared before and after iontophoretic application of the antidepressant. Imipramine was used with 5HT, and desipramine with NA,

because imipramine is a more potent blocker of 5HT uptake, while desipramine is more effective on NA uptake mechanisms (Ross & Renyi, 1969). Potentiation of the monoamine response was observed in forty-seven of the eighty-three cells studied, reaching a maximum about 10 min after application of the anti-depressant. This effect occurred most frequently with iontophoretic currents of 25 nA applied for 15 seconds. Antagonism of the amine response was observed in forty-five cells, usually after antidepressant applied at 50 nA for 30 seconds. The antagonism was immediate, and recovery was complete within 10 minutes. In many cells both effects were seen, the antagonism preceding the potentiation. Excitatory and depressant responses to the monoamines were affected in the same way. The interactions between desipramine and NA were similar to those between imipramine and 5HT.

The specificity of the effects of imipramine and desipramine was investigated in thirty-five cells excited by acetylcholine; seventeen responses were potentiated and eighteen antagonized. The latencies and durations of effects and the currents used to apply the antidepressants were similar to those with the monoamines.

Thus antidepressants can potentiate monoamine responses in the central nervous system, but antagonism also was seen requiring slightly larger currents to apply the antidepressant. Although antagonism of both NA (Callingham, 1967) and 5HT (Domenjoz & Theobald, 1959) occurs in peripheral systems, little importance has been ascribed to it in explanation of the central actions of the antidepressants. The similarity between the effects of antidepressants on responses to acetylcholine and to monoamines suggests that cholinergic systems might be involved, and that the study of antidepressant drugs should not be restricted to an examination of their actions on monoamine systems.

We are indebted to the Schizophrenia Research Fund and the Scottish Home and Health Department for financial support. C. M. B. is a S.R.C. Scholar.

REFERENCES

CALLINGHAM, B. A. (1967). The effects of imipramine and related compounds on the uptake of noradrenaline into sympathetic nerve endings. In: *Proceedings of the First International Symposium on Antidepressant Drugs*. ed. Garattini, S. & Dukes, M. N. G., pp. 149–157. Amsterdam: Excerpta Medica Foundation.

DOMENJOZ, R. & THEOBALD, W. (1959). Zur Pharmakologie des Tofranil. *Arch. int. Pharmacodyn.*, **120**, 450–489.

JOHNSON, E. S., ROBERTS, M. H. T., SOBIESZEK, A. & STRAUGHAN, D. W. (1969). Noradrenaline sensitive cells in cat cerebral cortex. *Int. J. Neuropharmac.*, **8**, 549–566.

ROBERTS, M. H. T. & STRAUGHAN, D. W. (1967). Excitation and depression of cortical neurones by 5-hydroxytryptamine. *J. Physiol., Lond.*, **193**, 269–294.

ROSS, S. B. & RENYI, A. L. (1969). Inhibition of the uptake of tritiated 5-hydroxytryptamine in brain tissue. *Eur. J. Pharmac.*, **7**, 270–277.

Actions of 3,4-dimethoxyphenylethylamine in relation to the effects of catecholamines on brainstem neurones

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In 1952 Osmond & Smythies suggested that disordered catecholamine metabolism might lead to the production of psychotomimetic compounds in schizophrenia, and in 1962 Friedhoff and Van Winkle found methoxy-derivatives in the urine of some schizophrenic patients. One of these compounds is 3,4-dimethoxyphenylethylamine (DMPE) which has been identified with the 'pink spot' although this remains a