

increase in the inner membrane marker, succinic dehydrogenase, or in malic dehydrogenase, which is found both on the inner membrane and in the space between inner and outer membranes. No increases could be found in the activity of any other enzyme studied, including fumarase in the mitochondrial matrix and the microsomal enzyme DPN-nucleocidase. Lactate dehydrogenase was also unaffected.

The effect of adrenalectomy on the mitochondrion appears to be restricted to those enzymes in the outer membrane. Furthermore intact mitochondria are not essential. If the hearts are homogenized in distilled water there is an increase in MAO activity. But the further increase as a result of adrenalectomy is the same as that produced in Chappell-Perry medium.

It appears that the effects produced in the heart mitochondria after adrenalectomy of the rat and those produced by extraction of the tissue in hypotonic media are exerted at different sites in the mitochondrial membrane.

L.D.C. is a British Council Scholar.

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#### Changes in catechol-O-methyl transferase activity in the rat submaxillary gland after surgical and pharmacological procedures

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Monoamine oxidase (MAO) in the sympathetically innervated submaxillary gland has an intra- and extraneuronal localization (Iversen, Glowinski & Axelrod, 1966; Almgren, Andén, Jonason, Norberg & Olson, 1966). Jonason (1969) suggested, from indirect evidence, that catechol-O-methyl transferase (COMT) was localized outside the adrenergic nerves in the gland. To obtain information on the localization of COMT in the submaxillary gland the activity of the enzyme was measured in post-ganglionically sympathectomized and ligated glands and after reserpine and desipramine.

The excretory duct of one of the submaxillary glands was ligated in six rats and the superior cervical ganglion removed on one side of another nine. Five rats were ligated and post-ganglionically sympathectomized on the same side. Fourteen days later the glands were removed; MAO (Snyder & Hendley, 1968) and COMT activities (Broch & Guldberg, 1970) were determined in whole gland homogenates with the unoperated side acting as control. Small pieces of the glands were processed for fluorescence histochemistry of monoamines. Other rats were treated with reserpine (5 mg/kg intraperitoneally). Desipramine (25 mg/kg) was given subcutaneously three times at intervals of 8 hours. The rats were killed 24 h after the onset of drug administration.

Control glands showed a network of fluorescent adrenergic fibres around the acinar cells. In the atrophied gland the acinar cells were reduced in volume but the adrenergic fibres were unaffected. In sympathectomized glands there were no fluorescent

adrenergic fibres. Ligation reduced the MAO activity, expressed per weight of tissue, by  $67\% \pm 4$  (mean of the percentage decrease  $\pm$  s.e. of mean) —  $P < 0.005$  — while the reduction after post-ganglionic sympathectomy was only  $26\% \pm 8$  ( $P < 0.05$ ). COMT was unaffected by ligation when expressed as activity per weight of tissue; expressed as activity per gland there was a reduction of  $60\% \pm 4$  ( $P < 0.001$ ). Post-ganglionic sympathectomy reduced the COMT activity per weight of tissue by  $32\% \pm 5$  ( $P < 0.01$ ). 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  $28\% \pm 3$  ( $n=5$ ,  $P < 0.05$ ) and  $76\% \pm 6$  ( $n=5$ ,  $P < 0.001$ ) respectively. The corresponding results for 18 and 24 h after drug administration were for MAO  $44\% \pm 6$  ( $n=5$ ,  $P < 0.01$ ) and  $45\% \pm 3$  ( $n=5$ ,  $P < 0.01$ ) and for COMT  $76\% \pm 4$  ( $n=4$ ,  $P < 0.001$ ) and  $56\% \pm 7$  ( $n=4$ ,  $P < 0.002$ ). 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.

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#### 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,