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Evidence for the presence of monoamine oxidase in sympathetic nerve endings

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RECENT studies have emphasized the role of monoamine oxidase (MAO) activity in sympathetic nervous function.[1] It is thought that MAO activity is responsible for the catabolism of a portion of norepinephrine which is released intraneuronally and then leaves the nerve in the form of inactive metabolites. An important supposition for this point of view is the presence of MAO in sympathetic nerves in the region of the nerve endings. In attempting to establish a role for MAO in the inactivation of neurohumors at sympathetic nerve endings, several workers have measured MAO activity in such tissues of the cat as the nictitating membrane, iris, and blood vessels, after sympathetic denervation.[2, 3] No consistent reduction in MAO activity after sympathetic denervation could be demonstrated. If MAO is present extraneurally as well as intraneurally, it is possible that in the tissues examined in these studies the proportion of neural to extraneural MAO was so small that even a complete loss of the neural enzyme after denervation would not be reflected in measurements performed on the whole tissue.

A considerable portion of the total mass of the pineal gland is composed of sympathetic nerve endings.[4] Accordingly, studies were undertaken to examine the effect of sympathetic denervation on MAO activity in the rat pineal gland, and our results show that there is a 50% reduction in the MAO activity of this organ. Sympathetic denervation of the submaxillary gland results in a smaller but significant decrease in MAO activity.

Sprague-Dawley female rats (160–180 g) were maintained under diurnal lighting conditions with 12 hr of light (7 a.m.–7 p.m.) and 12 hr of darkness, unless otherwise specified, and were killed between 10 a.m. and noon. Bilateral or unilateral superior cervical ganglionectomy was performed under ether anesthesia. Groups of rats were blinded by bilateral orbital enucleation performed under light pentobarbital (Nembutal) anesthesia. MAO activity of innervated and denervated tissues was measured by a method previously described[5] between 7 and 30 days after operation.

Seven days after bilateral superior cervical ganglionectomy, there was about a 50% decrease in MAO activity of rat pineal glands as compared to sham-operated controls (Table 1). Enzyme activity remained depressed for at least 30 days after the operation.

TABLE 1. EFFECT OF SUPERIOR CERVICAL GANGLIONECTOMY ON PINEAL MONOAMINE OXIDASE OF RATS IN DIURNAL LIGHTING

	No. of rats	Pineal weight (mg)	MAO activity*
Sham operated	10	1·12 ± 0·14	1·01 ± 0·06
Ganglionectomized (7 days)	7	1·03 ± 0·12	0·53 ± 0·02†
Ganglionectomized (30 days)	10	0·98 ± 0·08	0·58 ± 0·05†

* MAO activity in all tables is expressed as mμmoles ^{14}C-indole acetic acid formed from ^{14}C-tryptamine per mg pineal in 1 hr ± standard error of the mean.

† Differs from control $P<0·001$.

It has been previously shown that exposure to light both continuously and under diurnal conditions affects the activity of at least two enzymes in the pineal gland, the melatonin synthesizing enzyme, hydroxyindole-O-methyl transferase[6] and 5-hydroxytryptophan decarboxylase.[7] Sympathetic denervation of the pineal gland alters the activity of these enzymes presumably by interfering with the anatomic pathway that mediates the effects of light on the pineal gland.[8, 9] To examine whether the reduction in pineal MAO activity after sympathetic denervation was related in any way to effects of light exposure, the following experiment was designed. Groups of rats were subjected respectively to bilateral superior cervical ganglionectomy, bilateral orbital enucleation, or to sham operation. One day after operation, the rats were placed in constant light or constant darkness, except for a 25-W red light bulb which was used while the cages were cleaned, in rooms equipped with double-door light baffles and air conditioning. Animals were killed after 30 days in the constant light or dark

TABLE 2. EFFECT OF SUPERIOR CERVICAL GANGLIONECTOMY ON PINEAL MONOAMINE OXIDASE OF RATS IN CONSTANT LIGHT OR DARKNESS

	MAO Activity	
Group*	Light	Darkness
Sham operated	1·04 ± 0·05	1·10 ± 0·16
Ganglionectomized	0·60 ± 0·09†	0·58 ± 0·08‡
Blinded	1·18 ± 0·09	0·90 ± 0·11

* Each group contained from 8 to 10 rats.

† Differs from control $P<0·001$.

‡ $P<0·01$.

environment and their pineal glands were assayed for monoamine oxidase activity (Table 2). In confirmation of earlier findings,[6] exposure to continuous light or darkness had no effect on pineal MAO activity. Blinding also had no discernible effect. However, there was a highly significant decrease in the pineal MAO activity of ganglionectomized rats whether kept in constant light or constant dark environment.

In other experiments the effects of sympathetic denervation on MAO activity in salivary glands was examined. Rats were subjected to unilateral superior cervical ganglionectomy, and both submaxillary glands were removed and assayed for monoamine oxidase activity 7 days after ganglionectomy (Table 3). There was a 28% decrease of enzyme activity in denervated glands as compared with the contralateral innervated glands. Similar findings have been obtained by Pöch.[10]

TABLE 3. EFFECT OF SUPERIOR CERVICAL GANGLIONECTOMY ON SALIVARY GLAND MONOAMINE OXIDASE ACTIVITY

Group	No. of rats	MAO Activity
Innervated side	7	4·67 ± 0·23
Denervated side	7	3·32 ± 0·35*

* $P < 0.01$.

The decrease in MAO activity after sympathetic denervation of tissues suggests that MAO is localized in sympathetic nerve endings. The marked effect of denervation on this enzyme activity in the pineal gland is in accordance with the high concentration of sympathetic nerve endings in this organ. These data are consistent with theories which hold that deamination of a portion of endogenous catecholamines can occur within the sympathetic nerves under normal conditions and especially after release by certain drugs, such as reserpine and guanethidine.[1] Catecholamines so released would then enter the circulation as deaminated and, consequently, inactive metabolic products.

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Comments on "7-hydroxychlorpromazine in the urines of schizophrenics receiving chlorpromazine"*

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IT WAS reported by Fishman and Goldenberg[1] early in 1963 that chlorpromazine is hydroxylated by man and animals at the 7-position to yield a family of closely related derivatives. These metabolites

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