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SEX STEROIDS, CARDIAC ^{3}H-NOREPINEPHRINE, AND TISSUE MONOAMINE OXIDASE LEVELS IN THE RAT

RICHARD J. WURTMAN and JULIUS AXELROD

Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Md., U.S.A.

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Abstract—Rat hepatic monoamine oxidase (MAO) activity is greater in male than in female animals. This difference can be reversed by chronic administration of an opposite sex steroid. When the MAO activity of rat heart is 90 per cent inhibited, the rate of disappearance of ^{3}H-catecholamine from this tissue is reduced; 50 per cent inhibition has no effect on this rate. Since sex differences in MAO activity are less than 50 per cent, these differences are probably of little physiologic significance.

MONOAMINE OXIDASE (MAO) activities in the adult rat heart[1] and liver[2] have been shown to be related to sex, males having significantly more enzyme activity per unit weight of tissue[2] or tissue protein.[1] This prompted a study on the effects of castration or administration of sex steroids on MAO levels in rat tissue. It is demonstrated that the MAO activity of rat liver is changed when a sex steroid associated with the opposite sex is administered, but it is not altered with castration.

Little information is available on what level of MAO inhibition is required to alter those function *in vivo* with which MAO is associated. It will be shown that in the heart, the reduced MAO level of female rats, measured *in vitro*, does not appear to be related to the activity of this enzyme *in vivo*.

METHODS

Groups of six or seven male and female Sprague-Dawley rats weighing about 100 g were surgically gonadectomized under pentobarbital anesthesia. In other similar groups, estradiol pellets (25 mg) were implanted subcutaneously in males, and testosterone pellets (25 mg) in females. Control animals were subjected to a sham operation. After five weeks, all rats had gained 110–160 g except the males treated with estradiol, which had gained only 60 g. Female rats subjected to gonadectomy or testosterone administration were found to have small uteri and an absence of vaginal estrus. Male rats given estradiol had atrophic testes and depressed body weight; those subjected to castration had infantile vas deferens and seminal vesicles. Animals were killed by neck fracture, the presence of pellet material was verified, and liver was homogenized in chilled istonic KCl and assayed for MAO as described.[3]

To study the relation between cardiac MAO activity and ^{3}H-catecholamine levels, mature rats weighing 200 g were given 0, 1, or 10 mg of JB 516 (β-phenylisopropylhydrazine)/kg intramuscularly 18 hr before receiving 10 μc of DL-^{3}H-norepinephrine hydrochloride/100 g (New England Nuclear Co., 13·5 mc/μmole) intravenously. Forty-eight hours after receiving the catecholamine, the rats were killed by neck

fracture. Aliquots of cardiac ventricle were assayed for MAO activity and ^{3}H-norepinephrine, by methods previously described.[3, 4]

RESULTS AND DISCUSSION

The MAO activities of the hearts and livers of female rats were 70–73 per cent of those of males (Tables 1 and 2). Castration did not alter hepatic MAO activity in

TABLE 1. EFFECT OF SEX HORMONES ON HEPATIC MAO ACTIVITY

Treatment	MAO Activity*
Female	
1. Untreated	4·86 ± 1·26
2. Castrated	4·54 ± 0·56
3. Testosterone	7·10 ± 1·20
Male	
4. Untreated	6·88 ± 1·00
5. Castrated	7·36 ± 1·41
6. Estradiol	4·36 ± 0·64

* Expressed as μmoles C^{14}-indoleacetic acid formed from ^{14}C-tryptamine per gram tissue per hour. Groups 3, 4, and 5 differ significantly from groups 1, 2, and 6 ($P < 0·01$).

TABLE 2. RELATIONSHIP BETWEEN MAO ACTIVITY AND ^{3}H-NOREPINEPHRINE CONTENT IN RAT HEART

Six to ten rats were given 0, 1, or 10 mg JB 516/kg i.m. 18 hr before receiving 10 μc ^{3}H-norepinephrine/100 g. They were killed 48 hr later, and cardiac MAO activity and ^{3}H-norepinephrine were determined. MAO activity is expressed as μmoles ^{14}C-indoleacetic acid formed from ^{14}C-tryptamine per gram tissue per hour. Data are given as mean ± standard error.

	MAO activity	^{3}H-norepinephrine cpm/g heart
Male	0·75 ± 0·08	3,200 ± 1,000
Female	0·56 ± 0·04*	3,400 ± 400
Male + JB 516 (1 mg/kg)	0·39 ± 0·04†	3,800 ± 1,200
Male + JB 516 (10 mg/kg)	0·07 ± 0·02‡	8,000 ± 700†

* $P < 0·05$.
† $P < 0·01$.
‡ $< 0·001$.

either sex, but testosterone raised female enzyme levels to those of untreated male rats, while estradiol lowered male levels to those of untreated females (Table 1). These results suggest that hepatic MAO activity in the adult rat depends upon which sex hormone was last present before MAO activity was measured.

It has previously been shown that MAO inhibition has no effect on the free and easily releasable ^{3}H-norepinephrine in the heart.[5] However, once the catecholamine is firmly bound, MAO inhibition reduces the rate at which ^{3}H-norepinephrine leaves the heart.[5, 6] In hearts of female rats, although MAO activity was only 73 per cent that of males, there was no difference in the amount of ^{3}H-catecholamine retained for 48 hr (Table 2). The inhibition of up to about 50 per cent of MAO activity by JB 516

also produced no effect on cardiac ^{3}H-norepinephrine levels. When MAO was more than 90 per cent inhibited, a marked elevation of ^{3}H-norepinephrine in the heart was observed. To produce observable changes in cardiac ^{3}H-catecholamine metabolism, it appears that more than 50 per cent of MAO activity must be inhibited. This suggests that sex differences in MAO levels may not be relevant, a conclusion that is consistent with the observation[2] that changes of 30–40 per cent in MAO activity produced by altered thyroid status did not produce corresponding changes in the fraction of deaminated ^{3}H-catecholamine found in the heart.

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