

References

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Effects of testosterone and ethinyloestradiol on the synthesis and uptake of noradrenaline and 5-hydroxytryptamine in rat hindbrain: evidence for a presynaptic regulation of monoamine synthesis?

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The participation of brain monoamines in the regulation of pituitary secretory activity is well

established (Ganong, 1975) and the feedback control of plasma levels of gonadal steroids is dependent upon the ability of oestrogens, progestogens and androgens to affect central catecholamine and 5-hydroxytryptamine (5-HT) metabolism. Some of the actions of injected hormones on monoamine metabolism are presumably identical to those of endogenous hormones, with the caveat that there may be additional dose-dependent effects. Studies of the effects of hormones on defined neuronal processes may, therefore, provide some information on the physiological regulation of monoaminergic function as opposed to the pharmacological changes produced by foreign drugs.

The effects of testosterone (10 mg/kg s.c.) and

Table 1 Effects of testosterone (T) and ethinyloestradiol (EO) on the uptake and synthesis of noradrenaline (NA) and 5-HT in two hind-brain regions of male rats

Treatment	5-HT (n moles/g \pm s.e. mean)		NA (n moles/g \pm s.e. mean)	
	Midbrain	Pons/medulla	Midbrain	Pons/medulla
None	4.48 \pm 0.17	3.68 \pm 0.07	7.30 \pm 0.48	4.94 \pm 0.44
Testosterone (T)	3.59 \pm 0.19	3.24 \pm 0.23	6.49 \pm 0.33	4.54 \pm 0.31
Phenelzine (P)	4.79 \pm 0.18	4.24 \pm 0.27	8.90 \pm 0.52	6.23 \pm 0.25
P + T	8.16 \pm 0.09	6.85 \pm 0.29	11.07 \pm 0.95	6.66 \pm 0.60
% age change due to T	+120%	+96%	+49%	+20%
None	5.64 \pm 0.41	5.23 \pm 0.19	6.11 \pm 0.44	4.07 \pm 0.13
Ethinyloestradiol (EO)	5.49 \pm 0.23	5.91 \pm 0.26	5.67 \pm 0.22	4.72 \pm 0.30
Phenelzine (P)	6.87 \pm 0.38	5.83 \pm 0.14	6.80 \pm 0.18	5.12 \pm 0.22
P + EO	8.12 \pm 0.47	7.48 \pm 0.46	7.04 \pm 0.34	5.28 \pm 0.25
% age change due to EO	+26%	+15%	+13%	+14%
None	8.94 \pm 0.80	6.22 \pm 0.33	2.82 \pm 0.13	2.54 \pm 0.20
Testosterone (T)	6.18 \pm 0.38	4.59 \pm 0.27	2.41 \pm 0.27	3.19 \pm 0.42
H75/12	6.18 \pm 0.42	4.24 \pm 0.16		
H77/77			2.06 \pm 0.40	2.35 \pm 0.14
T + H75/12 or H77/77	6.18 \pm 0.42	3.88 \pm 0.07	3.90 \pm 0.39	2.45 \pm 0.28
% age change	-31%	-16%	-14%	0
None	6.76 \pm 0.60	4.74 \pm 0.40	5.03 \pm 0.24	3.83 \pm 0.36
Ethinyloestradiol (EO)	5.53 \pm 0.20	3.60 \pm 0.20	5.75 \pm 0.33	4.12 \pm 0.16
H75/12	6.07 \pm 0.17	3.95 \pm 0.17		
H77/77			4.88 \pm 0.33	3.77 \pm 0.21
EO + H75/12 or H77/77	5.79 \pm 0.29	4.03 \pm 0.11	5.39 \pm 0.20	3.83 \pm 0.29
% age change	-15%	-24%	0	0

Each value is the mean of determinations from 5 rats. The % age changes shown are statistically significant (Student's *t* test) at least the *P* < 0.05 level.

ethinyloestradiol (100 µg/kg s.c.) on the rates of depletion of noradrenaline and 5-HT following 4- α -dimethyl-*m*-tyramine (H77/77) or 4-methyl- α -ethyl-*m*-tyramine (H75/12) respectively (2×12.5 mg/kg) have been determined as a measure of the effects of the hormones on the reuptake of monoamines by the neuronal pumps (Carlsson, Corrodi, Fuxe & Hokfelt, 1969a, b). An indication of the effects of the hormones on monoamine synthesis has been obtained by examining the accumulation of noradrenaline and 5-HT 4 h after 100 mg/kg (i.p.) phenelzine (Neff & Costa, 1968). The results of these determinations are shown in Table 1. The dissection and analytical techniques followed the method of Fludder and Tonge (1975).

Carlsson *et al.* (1969a, b) suggest that the depletions caused by the substituted *m*-tyramines are due to the displacement of monoamines because of the high affinity for the concentrating mechanisms. The data presented in Table 1 therefore suggest that both testosterone and ethinyloestradiol cause decreases in the uptake of noradrenaline and 5-HT and may thereby increase effective concentrations in the two brain areas shown here. The fact that testosterone and ethinyloestradiol have similar effects is consonant with the proposition that androgens may be aromatized to oestrogenic compounds in the brain before exerting some of their actions (Naftolin, Ryan & Petro, 1972).

It is apparent from the results presented in Table 1 that decreased amine uptake is accompanied by

increased amine synthesis, suggesting that either steroid effects on the two processes are unrelated, or that synthesis may be regulated by presynaptic intraneuronal levels of free noradrenaline and 5-HT.

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