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Muscle Androgen Binding in Female Rats Treated with Testosterone

The myotropic and growth promoting effects of androgens are well documented (8) Thus, the administration of testosterone, trembolone or stanozolol to female rats produces an anabolic response (1, 9, 10). Nevertheless, the mode of action of these steroids in the muscle cell has been difficult to elucidate, mainly for technical reasons.

It is now recognized that testosterone and other synthetic anabolic agents may directly act through an androgen receptor, which has been detected in skeletal muscle from male and female rats (4, 7, 11). Furthermore, it has been postulated that the anabolic actions of androgens may occur because glucocorticoid effects are antagonized (13). In that context, an experiment was undertaken to investigate the influence of testosterone injected to female rats on the binding capacity (Bmax) and apparent ligand affinity (Kd) of their androgen receptors in an attempt to determine some of the possible factors concerned with the regulation of androgen action in muscle.

Intact female rats (eight per group) weighing about 135 g were injected subcutaneously with testosterone (1 mg/kg/day) or placebo (maize oil) for 7 days. The receptor assay was performed as previously described (14). The cytosol, obtained from pools of gastrocnemius, soleus and plantaris muscles from both legs, was incubated for 20-24 h at 0° C with 1, 2, 6, 7 [^{3}H]-testosterone within a wide range of concentrations (0.4 to 12 nm). The calculation of binding data was carried out according to the method of Scatchard. The statistical differences between groups were evaluated by the Students's «t» test.

Testosterone at the assayed dose stimulated the growth rates of intact female rats ($p < 0.01$) as previously reported (9). Also, statistically significant differences were found in gastrocnemius muscle weights between the control group and the steroid-treated animals ($p < 0.05$). Interestingly, on a relative weight basis, an increase in musculature has been recently reported in heifers following trembolone administration (3).

It is generally assumed that steroid hormone actions involve their combination with cytosolic-receptor molecules and a subsequent translocation of the steroid-receptor complex into the nucleus, where it binds to genetic material and elicits a biological response. However, recent evidence strongly suggests a variable distribution of cytoplasmic and nuclear loci for estrogens and glucocorticoids, whereas no data are firmly available for the androgen receptor (7).

No differences in the dissociation constants (Kd; nM) were seen between the experimental groups. Muscle hypertrophy was accompanied by a decrease in cytosol [^{3}H] testosterone receptor concentration ($p < 0.05$), when expressed in fentomoles per gram of tissue (Table). The reduction in receptor numbers is most likely due to a migration of the testosterone receptor complex to the nucleus as shown before with trembolone (14), although a process of desensitization is not discarded. The

Table I. *Body weight, daily gain, muscle weight and receptor characterization in female rats treated with testosterone (1 mg/kg/day) for 7 days.*
The results (Mean ± S.D.) were statistically evaluated by the Student's «t» test (n=8). N.S., non significant.

		Control	Testosterone	
Final body weight	(g)	151.7±7.5	162.5±11.7	$p < 0.05$
Daily weight gain	(g/d)	2.5±0.4	4.0±0.9	$p < 0.01$
Gastrocnemius weights	(g)	2.50±0.12	2.89±0.10	$p < 0.05$
Dissociation constant	(nM)	0.51±0.22	0.45±0.18	N.S.
Binding capacity	(fmol/g)	87±8	71±13	$p < 0.05$

significance of this adaptative response would be considered as a consequence of the steroid-hormone receptor interaction in target tissues as reported for glucocorticoids (2) and with adrenoceptors (6, 12). Summing up, our results indicate that the testosterone treatment to female rats reduces the binding capacity without apparent changes in the receptor affinity, which has been previously found under other hormonal manipulations (5, 13).

Key words: Androgen receptor, Testosterone, Female rat.

Palabras clave: Receptor androgénico, Testosterona, Ratas hembra.

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