

## ONTOGENY OF 5 $\alpha$ -DIHYDROTESTOSTERONE RECEPTORS IN THE HYPOTHALAMUS OF THE RAT

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There is accumulating evidence that the hypothalamus has the ability to convert testosterone to 5 $\alpha$ -dihydrotestosterone, DHT, which, as an active androgen, may play a role in the mechanism of the central action of androgen. In a previous publication we have reported high affinity and low capacity receptor proteins for DHT isolated by sucrose density gradient centrifugation from cytosols (KATO and ONOUCHI, 1973; KATO, 1975 *a, b*) and purified nuclei (KATO, 1975 *b*) from the hypothalamus of male rats at 28 or more days of age. GINSBURG *et al.* (1974) have also demonstrated the presence of DHT receptors in the rat hypothalamus using gel filtration. Moreover, receptors for testosterone in rat hypothalamus have been demonstrated by JOUAN *et al.* (1973); NAESS *et al.* (1975). Thus, a possible role of hypothalamic androgen receptors has been postulated in the mechanism of the central action of androgen. Little is known, however, about when in the course of development these hypothalamic receptors for DHT appear. Attempts have been made to isolate receptor proteins for DHT from the hypothalamus of 7-, 14- or 21-day-old male rats.

In sucrose density gradient sedimentation profiles of hypothalamic cytosols from 7-day-old rats, which were incubated *in vitro* with <sup>3</sup>H-DHT at 0°C for 1 hour, there was a small but definite peak of radioactivity of 8S. This peak was abolished by the addition of unlabelled DHT. Testosterone or androstenedione also inhibited <sup>3</sup>H-DHT binding, but cortisol in excess did not. Thus, the 8S binding components isolated from 7-day-old rat hypothalamus show some specificity for androgen. Our data on androgen, possibly DHT, binding components in the hypothalamus of 7-day-old rats are compatible with the findings of CHAMBERLAIN and ROGERS (1972) on the appearance of DHT in the neonatal rat diencephalon following injection of <sup>3</sup>H-testosterone.

In all gradients of hypothalamic cytosols at 14 days of age, a single and definite peak of radioactivity was found in the 8S region. The addition of unlabelled 5 $\alpha$ -DHT

to the incubation mixture eliminated this peak. Testosterone and androstenedione competed the  $^3\text{H}$ -DHT binding, but weaker androgen such as dehydroepiandrosterone did not. It is noteworthy that the  $5\beta$ -isomer of DHT, a biologically inactive androgen, also competed to some extent. Cortisol or diethylstilbestrol showed no competition. Thus hypothalamic cytosols from 14-day-old male rats are found to possess androgen binding components of 8S, which show specificity for  $5\alpha$ -DHT and testosterone relative to other androgens and steroids.

The hypothalamic cytosols of 21-day-old rats showed a more evident peak of radioactivity in the same region as those of 14-day-old rats; the sedimentation patterns of the former were similar to those at 28 days of age in which, as previously described, labeled DHT binds the receptors strongly. As in other age-groups, the addition of  $5\alpha$ -DHT to the incubation mixture abolished the binding of  $^3\text{H}$ -DHT to the hypothalamic components.

In summary, possible receptors for DHT in the hypothalamus appeared 7 days after birth in male rats. The concentration of receptors increased rapidly between 14 and 21 days of age, and reached a plateau at 28 days of age. These results demonstrate the development of possible DHT receptors in the hypothalamus of male rats.

When the development of possible DHT receptors in the hypothalamus of male rats is compared with that of estrogen receptors in female ones, the former seem to be easier to detect in younger animals than the latter. In this context, it is interesting to mention the early development of a negative feedback relation between testis and hypothalamo-pituitary system (YAGINUMA *et al.*, 1969; GOLDMAN *et al.*, 1971).

*Sexual Maturation, 3rd Workshop  
August 31, September 3, 1975.*

## RÉSUMÉ

### ONTOGENÈSE DES RÉCEPTEURS

#### DE LA $5\alpha$ -DIHYDROTESTOSTÉRONÉ DANS L'HYPOTHALAMUS DU RAT

Dans l'hypothalamus du Rat mâle, les récepteurs probables de la DHT apparaissent 7 jours après la naissance. Leur concentration augmente rapidement entre 14 et 21 jours et atteint un plateau à 28 jours.

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