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Sexual behavior reduces hypothalamic androgen receptor immunoreactivity

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Abstract

Male sexual behavior is regulated by limbic areas like the medial preoptic nucleus (MPN), the bed nucleus of the stria terminalis (BST), the nucleus accumbens (nAcc) and the ventromedial hypothalamic nucleus (VMN). Neurons in these brain areas are rich in androgen receptors (AR) and express FOS-immunoreactivity in response to mating. In many species sexual satiation, a state of sexual behavior inhibition, is attained after multiple ejaculations. The mechanisms underlying sexual satiation are largely unknown. In this study we show that sexual activity reduces androgen receptor immunoreactivity (AR-ir) in some of the brain areas associated with the control of male sexual behavior, but not in others. Thus, one ejaculation reduced the AR-ir in the MPN and nAcc, but not in the BST and VMN. Copulation to satiation, on the other hand, reduced AR-ir in the MPN, nAcc and VMN, and not in the BST. The AR-ir reduction observed in the MPN of sexually satiated rats was drastic when compared to that of animals ejaculating once. Serum androgen levels did not vary after one ejaculation or copulation to exhaustion. These data reveal that sexual activity reduces AR in specific brain areas and suggest the possibility that such a reduction underlies the sexual inhibition that characterizes sexual satiety.

Keywords: Androgen receptor immunoreactivity; Medial preoptic nucleus; Male sexual exhaustion; Ventromedial hypothalamic nucleus; Bed nucleus of the stria terminalis; Nucleus accumbens

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Steroid hormones play an important role in the regulation of male sexual behavior. Thus, in general, castration decreases while exogenous androgen administration restores copulation (Meisel and Sachs, 1994). Interestingly, several factors such as previous experience, photoperiod, age, and others also influence copulatory behavior without necessarily modifying the endocrine milieu (Chubb and Desjardins, 1984; Clemens et al., 1988; Miernicki et al., 1990; Phoenix and Chambers, 1986; Wallen, 2001). It is clear that steroids act on the brain to induce sexual behavior. Within the rat brain the hypothalamus has been proposed to play a dual role in the control of this behavior. On one side, several hypothalamic nuclei are directly involved in its neural control and, on the other, hypothalamic neurons that contain gonadotropin hormone realising factors (GnRH) participate in its neuroendocrine modulation. Regarding the latter function, lesions in certain hypothalamic areas produce gonadal atrophy and thereby suppress sexual behavior (Heimer and Larsson, 1966/1967) by three possible mechanisms: (a) direct lesions of the GnRH neurons continuum primarily located in the telencephalon-diencephalon limit; (b) lesions that damage the majority of the GnRH nerve fibers traversing to the median eminence; or (c) isolation of hypothalamic areas (like the mediobasal hypothalamus) that contribute to the functional integrity of the neuroendocrine network (Silverman, 1994). In contrast, extensive bilateral electrolytic lesions encompassing the medial preoptic region and the anterior part of the hypothalamus suppress male rat sexual behavior without causing gonadal atrophy. Attempts to arouse the lesioned rats by handling or by changing the stimulus female are ineffective in inducing sexual behavior; chronic testosterone treatment is similarly ineffective, further indicating that the effects of mPOA lesions are not an indirect result of an altered gonadal regulation (Paredes et al., 1993). The androgen sensitive neurons in the mPOA participate in the regulation of copulation, since implantation of testosterone into this brain area of castrated male rats restores sexual behavior, while selective blockade of androgen receptors (ARs) in this region inhibits mating (McGinnis et al., 1996). In the mPOA the sexual dimorphic nucleus or medial preoptic nucleus (MPN), particularly rich in ARs (Handa et al., 1996), specifically participates in the control of masculine sexual behavior (De Jonge et al., 1989). Besides, the mPOA, other limbic regions like the bed nucleus of the stria terminalis (BST) and the nucleus accumbens (nAcc), play an important role in the control of male sexual behavior. In general, it is considered that the BST participates in the transmission of the olfactory information necessary for copulation (Emery and Sachs, 1976). The nAcc has also been implicated in the control of copulatory behavior (Mitchell and Gratton, 1994) particularly sexual motivation (van Furth et al., 1995). Thus, elevations in dopamine release within this area coincide with preparatory sexual activity and copulation (Pfaus et al., 1990; Damsma et al., 1992; Mas et al., 1990).

Mating in male rats, as many other behavioral processes, importantly increases FOS expression (the protein product of the *c-fos* proto-oncogene) in the MPN, the BST and to a much lesser extent in the VMN (Coolen et al., 1996). Significantly increased neuronal FOS responses have also been reported to occur in the nAcc of