Frontiers in Neuroendocrinology 32 (2011) 146–154

Contents lists available at ScienceDirect

Frontiers in Neuroendocrinology

journal homepage: www.elsevier.com/locate/yfrne

Review

Hormones of choice: The neuroendocrinology of partner preference in animals

C.L. Henley, A.A. Nunez, L.G. Clemens *

Departments of Zoology and Psychology, and the Neuroscience Program, Michigan State University, East Lansing, MI 48824, USA

ARTICLE INFO

Article history:
Available online 4 March 2011

Keywords:
Partner preference
Development
Sex behavior
Testosterone
Estradiol
Mice
Rats
Ferrets
Sex differentiation

ABSTRACT

Partner preference behavior can be viewed as the outcome of a set of hierarchical choices made by an individual in anticipation of mating. The first choice involves approaching a conspecific verses an individual of another species. As a rule, a conspecific is picked as a mating partner, but early life experiences can alter that outcome. Within a species, an animal then has the choice between a member of the same sex or the opposite sex. The final choice is for a specific individual. This review will focus on the middle choice, the decision to mate with either a male or a female. Available data from rats, mice, and ferrets point to the importance of perinatal exposure to steroid hormones in the development of partner preferences, as well as the importance of activational effects in adulthood. However, the particular effects of this hormone exposure show species differences in both the specific steroid hormone responsible for the organization of behavior and the developmental period when it has its effect. Where these hormones have an effect in the brain is mostly unknown, but regions involved in olfaction and sexual behavior, as well as sexually dimorphic regions, seem to play a role. One limitation of the literature base is that many mate or 'partner preference studies' rely on preference for a specific stimulus (usually olfaction) but do not include an analysis of the relation, if any, that stimulus has to the choice of a particular sexual partner. A second limitation has been the almost total lack of attention to the type of behavior that is shown by the choosing animal once a 'partner' has been chosen, specifically, if the individual plays a mating role typical of its own sex or the opposite sex. Additional paradigms that address these questions are needed for better understanding of partner preferences in rodents.

1. Introduction

Intra-specific mate selection in mammals involves the choice to mate with a particular individual over others that are equally accessible. But, multiple levels of choice must be made within each mating opportunity prior to deciding on one sexual partner. The initial choice is to determine the species with which to mate. When given a choice of mating partners, it is most common for individuals to choose a conspecific over a nonconspecific. The following mating choice is the decision to mate with either a male or a female. Most individuals usually choose a partner of the opposite sex. The final mating choice is the decision to mate with one individual within the chosen sex over another.

That these are, in fact, choices is made clear by those circumstances when experience and/or genetics conspire against the grand plan. Being courted by a dozen lusty tom turkeys was the senior author's first experience in an animal behavior laboratory. As an undergraduate at Penn State University in 1959, he was invited by Ed Hale and Marty Schien [76] to observe a group of turkeys that had been hand reared. As soon as he stepped into the room, twelve adult toms abandoned their courtship of the female turkey and immediately began to court him instead, ardently searching for a way to initiate the mating process! Similar phenomena are seen in other species as well. For example, young male sheep reared by a goat will, in adulthood, prefer to mate with a female of their foster mother's, not their own species [47]; for reviews of other species see [28,36,43].

The organization of a brain system for selection of a mating partner is a critical event for every species, and it remains one of the most intriguing puzzles in reproductive neuroendocrinology. In the last 50 years it has become clear that, in addition to experience, gonadal hormones play a major role in the organization of choosing a sexual partner. Additionally, it is now well established that environmental contaminants can mimic or alter the effects of endogenous hormones [31] and thus affect reproductive functions including partner preferences [23], providing further evidence for the importance of studying the effects of hormones on the development of adult partner preference. In this review we focus on the factors that influence the choice to mate with one sex over the other. Since there are species differences among the experimental models used to study partner preferences in mammals, we discuss the data for rats, mice and ferrets in separate

* Corresponding author. Address: 203 Natural Science, Michigan State University, East Lansing, MI 48824, USA. Fax: +1 517 432 2789.
E-mail address: clemens@msu.edu (L.G. Clemens).

0091-3022/$ - see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.yfrne.2011.02.010

sections. Despite these differences, we identify general principles that provide insight into the neuroendocrinology of partner preference. Specifically, early in development hormones act on particular brain circuits and predispose an animal to a certain partner preference that emerges later in life in response to the activational effects of adult hormone levels.

2. Sexual versus social partner preference

While preference paradigms have been fruitful in understanding the role of hormone exposure in the development of affiliation preferences, these studies alone often fall short of the analyses needed to draw conclusions about whether the preference is one based on sexual motivation (i.e. sexual partner preference) versus a preference for a social consort. Sexual partner preference refers to the processes involved in selection of a *sexual* partner, but many of the partner preference studies reviewed here do not, in fact, use that end point. Only studies that allow the experimental and stimulus animals to interact, and that measure sexual behavior after the partner choice, make it possible to distinguish between sexual preference (i.e. mating with a partner) versus social preference (i.e. being near but not mating with a partner). Studies that prevent interactions between the experimental and stimulus animals or use stimuli such as odors to determine preference do not provide enough information to distinguish between the two motivational antecedents of the choice (i.e. sexual versus social). Therefore, due to the inability of most of the current paradigms to distinguish between sexual and social preference, this review will simply refer to the behavioral outcome of all studies as 'partner preference.' We recognize that investigators who study preference behavior face a dilemma in designing appropriate experiments. Thus, allowing the experimental animal to interact with the stimulus animal introduces sexual experience as a possible confounding variable. On the other hand, not allowing such interactions limits our insight into the subject's motivational state.

3. Partner preference in the rat

When adult rats (either intact or gonadectomized in adulthood and given gonadal hormone replacement) can chose between spending time with a sexually receptive female or a sexually active male, males prefer the estrous female, and females prefer the male [40,57]. This partner preference is influenced by exposure to testicular steroids early in development (organizational effects) and by the actions of gonadal hormones in adulthood (activational effects). It is convenient to divide the organizational effects of hormones on adult rat behavior into three time periods: prenatal, postnatal (the first 21 days after birth), and pubertal. Exposure to testosterone or its estrogenic metabolite during development causes both masculinization and defeminization of behavior [1,3]. Masculinization is defined as the enhancement of male-typical behavior, whereas defeminization is the suppression of female-typical responses.

3.1. Activational effects of hormones

Adult castration reduces female-directed preferences in male rats that were untreated during development, and testosterone replacement reverses the effects of castration [4,18,58,89]. Since exposure in adulthood to dihydrotestosterone (DHT), a nonaromatizable androgen, is not effective in activating a female-directed partner preference after adult castration [4], the estrogenic metabolites of testosterone are likely to mediate the activational effects of the androgen. Consistent with this view are the observations that after adult castration, estradiol administration is also able to increase the preference seen for a stimulus female [4,58]. However, providing males with the full ovarian hormonal profile of a female in estrus results in a male-directed preference; thus, castrated males exposed to both estradiol and progesterone prefer a stimulus male over a receptive female [89]. The particular effects of castration on the partner preferences of male rats are not uniform across studies. Castrated males have been shown to display a decreasing preference for the female over time [4]. However, after long term castration, males have been shown to display no preference for either stimulus animal [4,18,89], a preference for the receptive female [58], or a preference for the stimulus male [18,89].

Females that received no treatment during development display a preference for a sexually active male when tested either intact, on the day of estrus [58], or after ovariectomy and ovarian hormone replacement [24,57,58,81,89]. Without hormone replacement, rats ovariectomized as adults show either a small preference for the male [19,24] or no preference for either stimulus animal [19,58]. Exposure to testosterone in adulthood causes different behavioral outcomes depending on the length of hormone administration. When testosterone is given only at the time of testing, females ovariectomized in adulthood show a preference for the stimulus male [58]. Females exposed to short term testosterone treatment (1–4 weeks) display no preference for either stimulus [19] or a preference for the sexually active male [24,89]. Long term treatment with testosterone, however, leads to a distinct preference for the estrous female [19,81]. DHT administration has activational effects in adult females and is able to increase male-directed preference in ovariectomized animals [24], but the physiological significance of this effect of DHT is not known. Recent reports [35,60] indicate that DHT metabolites can have estrogenic effects via the estrogen receptor beta. However, there is no evidence that this estrogen receptor is involved in the activational effects of estrogens on female sexual behavior [56].

3.2. Organizational effects of prenatal hormones

There are only a few studies that examine the effects of direct prenatal manipulations on the display of adult partner preferences in the rat. Males treated on gestational days (GD) 10–19 with the anti-androgen cyproterone acetate prefer to spend time with an estrous female over a sexually active male in adulthood, both when tested intact and after adult castration and testosterone replacement [53]. These data indicate that exposure to prenatal androgens is not necessary for the organization of female-directed adult partner preference. Prenatal treatment with the aromatase inhibitor 1,4,6 androstatriene-3,17-dione (ATD) also has no effect on the adult partner preference of male rats. Males treated with ATD on GD 10–22 and tested as intact adults continue to show a preference for a stimulus female over a sexually active male that is just like that of untreated controls [20]. However, males treated with the anti-estrogen CI 628 during GD 10–19 show a reduced number of visits to the female compartment and spend less time with an estrous female compared to control males after adult castration and testosterone replacement [53]. Similarly, males exposed to CI 628 on GD 13–19, castrated in adulthood and given testosterone show no preference for a stimulus female over a stimulus male when sexually naïve at the time of testing, whereas control males show a clear preference for the female [55]. Thus in spite of the negative results associated with prenatal ATD exposure, these data indicate that prenatal endogenous estrogen plays a role in the masculinization of adult partner preference (Fig. 1A). Interestingly, the effects of prenatal treatment with CI 628 on male rat partner preference interact with both the endocrine condition of the animals and the amount of sexual experience the animals have at the time of testing. The effects of treatment with CI 628 during GD 10–19 are absent if the males are tested while intact in adulthood [53]. Similarly, animals treated with the anti-estrogen on GD 13–19