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Neural mechanisms of sexual behavior in the male rat: Emphasis on ejaculation-related circuits

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ABSTRACT

Sexual behavior of the male rat can be described as a 'sequence': a series of behavioral transitions eventually leading to a consummatory act: ejaculation. A 'funnel-model' is presented to describe the behavioral progression during the sexual sequence.
The ejaculation itself is extensively controlled by the 'spinal ejaculation generator', consisting of several elements with afferent sources of genitosensory information, with ascending projection fibers to inform the brainstem and forebrain as well as with descending afferent fibers providing the supraspinal control mechanisms with the opportunity to restrict ejaculations to the optimal moments and circumstances.
The messages ascending from the spinal cord reach several interconnected thalamic, hypothalamic and limbic brain areas and are integrated with olfactory information. These brain areas play a role in mechanisms like 'sexual satiety' or a temporary interruption of sexual activities (post-ejaculatory interval), but the exact facilitatory and inhibitory mechanisms involved have not been elucidated yet. In the 'downward' mechanisms controlling the spinal 'release' of an ejaculation, the medial preoptic nucleus plays an important role in cooperation with a number of brainstem areas. This nucleus is also explicitly involved in the rewarding experiences coming with an ejaculation.
Finally, the role of several neurotransmitters and-peptides on male sexual behavior are discussed shortly, because sometimes they show remarkable effects on specific aspects of the behavioral sequence. We conclude that, despite our increased knowledge about the brain mechanisms involved in the control of ejaculation, we are still far away from a complete understanding and quite a few questions remain to be resolved.

1. Introduction

Sexual behavior of the male rat can be described as a series of behavioral elements eventually cumulating to ejaculation. Before performance of this act, the male has to determine that the environment is save and that a female is available in the proper estrous condition, through a series of successive behavioral elements to provide the male with exactly this kind of information (Veening, 1975, 1992; Pfaus et al., 1999). In Fig. 1, this phase is indicated as Phase 1, 'scanning- or initiation-phase'. In this phase, the male is scanning the environment, combined with some sniffing and some undirected locomotory activities. The presence of an alarm pheromone, for instance, released by other males, has an inhibitory effect on male sexual activities (Kobayashi et al., 2013a).

During the appetitive or precopulatory phase, the male rat displays active exploratory behaviors of the environment and female (Pfaus and Wilkins, 1995) (approaching, following and sniffing the female) including specifically the investigation of the female's anogenital region, presumably to obtain the necessary olfactory information for initiation of the copulatory phase. If the female is in the estrous condition, she will, meanwhile, start performance of proceptive behaviors (including darting, hopping, and ear-wiggling) (Whishaw and Kolb, 1985; Pfaff, 1999; Pfaus et al., 1999) potentially to focus the male's attention and leading to the first mounting attempt. In Fig. 1, this phase has been indicated as Phase 2, the precopulatory phase. For other behavioral sequences this phase has been coined as appetitive — or procurement phase.

The occurrence of a mount can be considered as the transition from the appetitive or precopulatory phase into the consummatory or copulatory phase In Fig. 1: Phase 3. A series of successive mounts and intromissions, each typically followed by short bouts of genital grooming, eventually leads to the ejaculation, followed by an extended bout of genital grooming and a refractory period of sexual inactivity, i.e. the post-ejaculatory interval (PEI), typically lasting a few minutes. During PEI the male is still aware of his environment, and for that reason PEI has been included in Phase 1, in Fig. 1. The introduction of a male intruder (Veening, 1975) would, for instance, lead to an immediate

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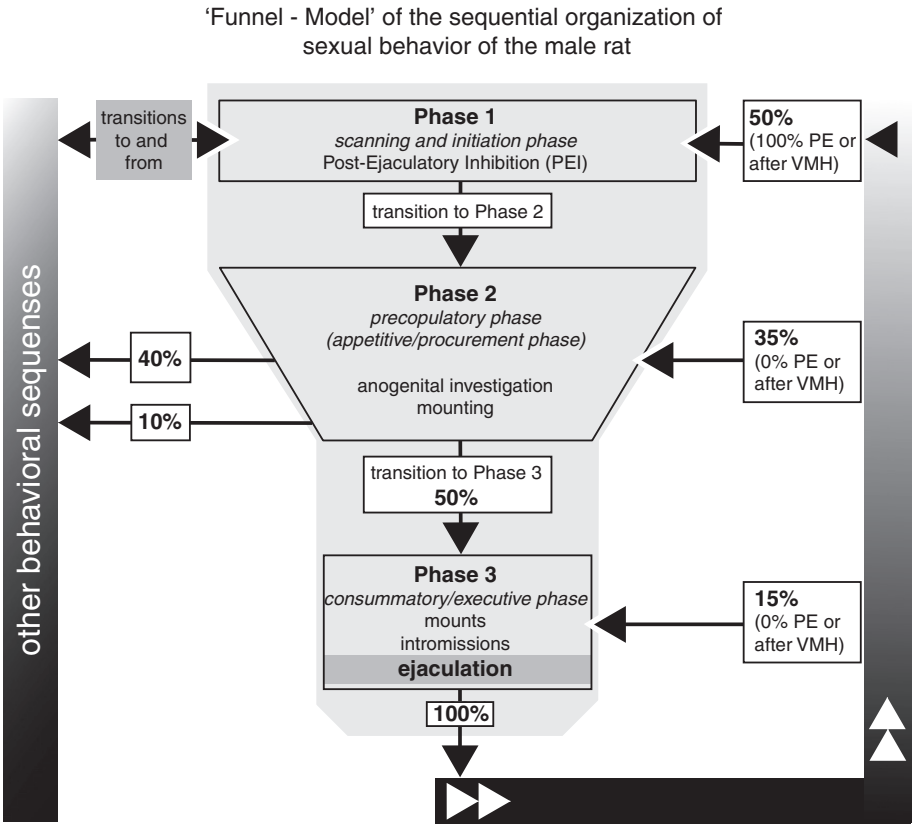

Fig. 1. This figure presents the 'funnel-model' of sexual behavior in the male rat. It is based on a wider range of behavioral experiments, including feeding behavior and territorial aggression, combined with the effects of electrical stimulation of the ventromedial hypothalamic nucleus (VMH), in the male rat (Thesis, Veening, 1975, Groningen University). The sequential analysis of all behavioral transitions showed that the possibility to choose for another transition than the regularly preferred one, is gradually decreasing during the progression of the behavioral sequence: the 'funnel-model'. This implies that during the male sexual sequence, in the initiation phase many transitions are possible leading to or away from sexual activities, but after mounting at least 50% of the transitions will be followed by an intromission, and after a few intromissions the chance to ejaculate will grow to virtually 100%. Even if a disturbing factor like electrical stimulation of the VMH was applied immediately preceding the occurrence of an ejaculation, ejaculation was not inhibited but males completed ejaculation, (or 'took a last bite' when hungry, or finished the fighting in a territorial confrontation) before returning to Phase 1 (initiation phase or PEI), which change was normally the immediate effect of the inhibitory VMH-stimulation. In Phase 2, the animal explores the conspecific animal, to determine if it is a male intruder, an anestrous or an estrous female, to initiate the appropriate behavioral sequence. The arrows to the left of Phase 2 (40%, early, and 10%, later) illustrate the decreasing probability that the animal will depart from the ongoing sequence. The arrows at the right side indicate the chances before ejaculation that a male will proceed immediately back into Phase 3 (for the next intromission) or into Phase 2 (to start another series of precopulatory activities). After ejaculation, the male will always (100%) return into the PEI-phase (Phase 1) before starting either a new sex sequence, or a different one, for instance if the animal is also very hungry. If the VMH is stimulated during ejaculation, the male will always immediately return to Phase 1. Abbreviations: PE: post-ejaculation; PEI: post-ejaculatory-interval VMH: electrical stimulation of the ventromedial hypothalamic nucleus.

appropriate action. Otherwise and if undisturbed, after a few minutes the male starts actively approaching the female again, followed by the next copulatory sequence and ejaculation. Following as much as 5–8 copulatory series (Pattij et al., 2005; Snoeren et al., 2013a), or an additional few copulatory sequences with the introduction of an unfamiliar female (the Coolidge-effect; Snoeren et al., 2011; Veeneman et al., 2011; Snoeren et al., 2013a), males eventually reach sexual satiety and sexual behavior may be inhibited for several days (for review see Phillips-Farfan and Fernandez-Guasti, 2009).

The transitions between the successive behavioral elements are important (Stavy and Herbert, 1989; Hlinak, 1990a,b). A specific transition-analysis provides us with additional information about the normal structure of a behavioral sequence, as performed under the chosen experimental conditions (Veening, 1975; Spruijt and Gispen, 1984), but also clearly shows the effects of external factors, like receiving intermittent intracranial brain stimulation randomly at different points in the sexual sequence (Veening, 1975, 1992) or of an intracranial infusion of a neuropeptide in a specific brain area (Stavy and Herbert, 1989).

A transition analysis on sexual behavior of the male rat revealed that specific behavioral transitions occurred much more frequently than would be expected when all transitions were chosen completely randomly. These 'preferred' transitions were clearly different under different conditions, when the males were provided with food, after a fasting period, or when accompanied with an estrous female or a male intruder (Veening, 1975, 1992). Apparently, the behavioral sequences are modified when the males are in different 'behavioral states', like feeding, mating or territorial aggression.

In addition, the effects of disturbing factors on the progression of behavior in a specific sequence can be studied in detail. Thus, the application of an intermittent intracranial stimulation of the ventromedial hypothalamic nucleus (VMH) of the male rat at different moments during the progression of the behavioral sequence had a characteristic effect, observed in each of the sequences studied (feeding, sex and aggression). The effect of the VMH-stimulation was clearly disruptive, but the behavioral effects were much stronger in the early phase of every sequence than at the end, for instance when the male was on the verge of an ejaculation. These findings are depicted in the proposed 'Funnel-Model' of the sequential organization of male sexual behavior (see Fig. 1). It shows that in the precopulatory phase, the normal sequence is easily interrupted, even after the first mount has occurred (arrows to the left indicate the chance of disturbing the 'regular sequence'). If the distracting stimulation starts in the consummatory phase, it is much more difficult to interrupt the regular sequence. If the VMH-stimulation started just before ejaculation, ejaculation itself was not disrupted and behavioral changes were observed only after ejaculation (Veening, 1975, 1992). In fact, all female-directed activities were postponed to at least the end of the intracranial stimulation