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Reproductive behavior in female rats

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Abstract
Reproductive physiology and sexual behavior in rats play crucial roles in understanding their reproductive capabilities and mating dynamics. Female rats exhibit mating behavior during estrus, involving mounting, intromission, and ejaculation. Lordosis, the arched-back posture, is a characteristic behavior evaluated using the lordosis quotient (LQ). Video recording enables accurate assessment of lordosis, and female rats actively participate in mating through proactive behaviors and vocalizations. In natural settings, females display a range of mating behaviors, indicating their motivation and preferences. Serotonergic drugs' effects on lordosis are complex and influenced by 5-HT receptor activation. Female rats modulate the mating pace through pacing behavior, optimizing vaginal-cervical stimulation for successful pregnancy. In laboratory settings, females regulate their mating rate through approach and avoidance behaviors. Pacing is measured by the exit ratio and interintromission interval, which increase as sexual stimuli intensify. Pacing reflects the female's ability to discern sexual cues and execute appropriate motor responses. Understanding reproductive physiology and sexual behavior in female rats provides insights into their reproductive capabilities, mating dynamics, and the impact of serotonergic drugs. Pacing behavior plays a vital role in optimizing reproductive outcomes, highlighting the nuanced nature of sexual behavior in rats. Controlled sexual interactions can elicit positive effects and conditioning, further emphasizing the importance of studying sexual behavior in female rats.

Keywords: *Female rats, lordosis, pacing, reproduction, sexual behavior*

1. Introduction

Rats are an important model organism that provides many advantages compared to mice. They serve as valuable tools for modeling human diseases such as cardiovascular diseases, cancer, cognitive and memory studies, reproductive mechanisms, and diabetes. Rats have a physiology that closely resembles that of humans, and their larger size is particularly beneficial for conducting surgical procedures and assessing the impact of drug applications. By utilizing rats in research, a deeper understanding of human diseases can be gained, leading to the development of improved treatment approaches.[1]

Rats have become increasingly favored in comparison to other rodents in recent years. They offer substantial advantages as models for investigating various physiological phenomena, such as learning and memory, and provide valuable insights into the functioning of human physiological systems. Additionally, rat behavior, particularly in the realm of social and sexual behaviors, holds considerable significance in comprehending human behavior patterns. Therefore, studying rat behavior, especially in relation to sexual behavior, holds significant promise for further advancements in our understanding.[2,3]

Rodents exhibit a range of social behaviors that are primarily associated with reproduction. These behaviors encompass tasks such as defending their territories, seeking potential mates, engaging in mating rituals, and caring for their offspring. The ultimate objective of sexual behavior in rodents is successful reproduction. It is noteworthy that sexual behaviors can vary between male and female rodents, and the intricate regulation of these behaviors involves the serotonin system within the brain. Serotonin, a neurotransmitter, is distributed across various brain regions that have an impact on sexual behavior. Certain serotonin receptors are known to facilitate sexual behavior, whereas others act as inhibitors.[4–6] Through the application of serotonergic drugs and genetic manipulations, researchers have made significant strides in unraveling the pivotal role of the serotonin system in the modulation of sexual behavior.[6]

Rats, being creatures that are predominantly active at night while also engaging in behaviors such as movement and feeding during the day, possess a circadian rhythm that holds significant implications for comprehending their behaviors and considering it in laboratory settings. This factor notably plays a pivotal role in determining the timing and interpretation of outcomes concerning various behavioral measurements. To illustrate, let us delve into the tail flick test, a widely employed assessment of pain threshold in rats. This evaluation entails applying a stimulus to the rat's tail and gauging the duration of the subsequent tail flick response, which serves as an indicator of the rat's sensitivity to pain. Intriguingly, it has been observed that female rats exhibit shorter tail flick response durations specifically during the mid-dark period, as well as during the estrus and metestrus phases. Such hormonal fluctuations hold the potential to exert an influence over the behavioral responses exhibited by female rats, consequently imparting an impact upon the outcomes derived from experimental procedures.[7–9]

The primary focus of this comprehensive review is to delve into the intricate realm of reproductive behaviors

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observed in rats. By shedding light on these behaviors, we aim to enhance our understanding of the complex mechanisms underlying rat reproduction. Moreover, this review will not only explore the various facets of rat reproductive behavior but also delve into the associated physiological and behavioral aspects that contribute to successful reproduction in this fascinating species.

2. Reproductive physiology and pregnancy

Puberty, a significant milestone marking the initiation of sexual maturity, signifies the ability of young, fertile offspring to engage in reproduction. In the realm of rats, the onset of puberty is often observed earlier in females than in males and can exhibit variability contingent upon factors such as strain or stock. Typically, the transition to puberty in rats occurs within the range of 2 to 3 months, although studies have reported variations spanning from 40 to 72 days. It is noteworthy that the emergence of estrus, a precursor to attaining complete reproductive competence, is discernible at approximately 35 to 36 days of age in Wistar rats.[7,10–13]

In rats, the estrous cycle, which governs reproductive activity, lasts typically for 4 to 5 days and occurs continuously throughout the year, unaffected by seasonal changes in laboratory conditions. This cyclical process encompasses four distinct stages: estrus, metestrus, diestrus, and proestrus, each occupying roughly equal periods within a 4-day cycle. However, occasional variations may result in 6-day cycles, wherein either diestrus or proestrus is prolonged. Notably, prepubertal rats may exhibit a uterine appearance suggestive of fluid accumulation during the proestrus phase, necessitating differentiation from hydrometra. Ovulation, the release of mature eggs, generally takes place approximately 8 to 11 hours following the initiation of estrus, commonly occurring from midnight until 2 a.m., although this timeframe can be subject to modification based on the light-dark cycle. It is important to highlight that eggs remain viable for approximately 10 to 12 hours, during which they maintain their capacity for fertilization.[7,13–15]

Following fertilization, the intricate process of blastocyst implantation into the endometrium takes place within a period of approximately 5 to 7 days, ensuring a successful attachment. This pivotal event necessitates a specific time frame of around 12 to 24 hours for its completion, highlighting its intricate nature.[14,16] Moving forward, the momentous occasion of birth typically occurs 21 to 23 days subsequent to mating; however, it is noteworthy that occasional early deliveries, as early as 19 days, can transpire. As a result, the characterization of pregnant rats with precise mating times as “timed pregnancies” grants researchers the invaluable opportunity to meticulously monitor and comprehend the different stages of gestation. This comprehensive understanding holds significant importance, as it allows for the thorough examination of pregnant rats in research settings, leading to a more accurate interpretation of the resultant findings.[7,13]

The typical gestation period for rats usually ranges from 21 to 23 days, although it can be extended by an additional 8 to 22 days in cases involving factors like blastocyst diapause and delayed implantation, particularly observed in lactating rats. Detecting the presence of developing fetuses becomes easier through manual examination after the 12th day of pregnancy. Around the 13th day of pregnancy, noticeable signs of abdominal enlargement start to appear, while mammary gland development becomes observable around the 14th day. It is crucial to maintain a serene and stress-free environment for female rats both before and after birth to prevent instances of maternal cannibalism. Although females enter a fertile estrus period after giving birth, conscious breeding during this time is generally avoided due to potential complications that may arise with the offspring. Estrus cycles typically resume within 2 to 4 days after the weaning of the pups, marking the beginning of a new reproductive cycle.[7,17]

Parturition in rats usually occurs, on average, with a litter size ranging from 6 to 12 pups. However, it’s important to note that this number can vary depending on the specific rat breed and the age of the mother. Newborn rat pups are classified as altricial, which means they are born hairless, blind, deaf, and entirely reliant on their mothers for survival. The developmental journey of these pups encompasses several significant milestones. For example, their external ears typically open up within a span of approximately 2.5 to 3.5 days, while their incisor teeth start to emerge around 6 to 8 days after birth. It takes approximately 7 to 10 days for them to develop a complete coat of fur. The opening of their eyes generally occurs around 14 to 17 days, and they begin to consume solid food around the two-week mark. In laboratory environments, it is common practice to separate the rat pups from their mothers and introduce them to independent living and self-feeding when they reach around 20 to 21 days of age, at which point they have attained a sufficient level of maturity.[14,17,18]

3. Sexual behavior

In female rats, mating behavior unfolds during the critical period of estrus, marking their peak sexual receptivity. Estrus typically initiates in the evening of proestrus, shortly after the lights are dimmed, and extends until the early hours of the morning. The intricate dance of mating involves a sequence of interactions between the male and female counterparts, encompassing mounting, intromission, and culminating in ejaculation. These distinct interactions can be discerned and characterized under diverse experimental settings, each displaying unique features and qualities. During mounting, the male grasps the female’s sides with precision, employing his forepaws to gently stroke and caress her. When the female is receptive, this mounting action triggers a reflexive response known as lordosis, where her back arches gracefully, and her tail elevates in anticipation. Successful intromission occurs when the male’s penis adeptly penetrates the female’s vagina during mounting, symbolizing successful entry. The mating process is characterized by a series of repeated intromissions, building up to the grand finale of ejaculation, which entails the release of seminal fluid containing vital spermatozoa.[15,19]

3.1. Lordosis and preceptive behaviors

Lordosis, a characteristic behavior observed in female rats during mating, is commonly evaluated using a parameter known as the lordosis quotient (LQ). The LQ represents the percentage of time the female rat displays the lordosis posture when mounted by a male. It is calculated by dividing the number of instances the female exhibits lordosis by the total number of male contacts

and multiplying the result by 100. The LQ serves as a valuable tool for assessing the sexual receptivity of female rats, providing insights into their level of receptiveness. While some researchers opt for a qualitative assessment of lordosis intensity, the prevailing approach involves the use of LQ, which enables a more comprehensive and quantitative analysis of female mating behaviors. This method allows researchers to gain a deeper understanding of the intricate aspects of female rat sexual behavior and facilitates the interpretation of experimental findings.[15]

To accurately determine the lordosis quotient (LQ), it is crucial to engage in meticulous observation of the female rat's posture. Video recording of behavioral interactions emerges as the preferred and most effective method, as it allows for repeated playback and in-depth analysis, including the option for slow-motion examination if required. When assuming the lordotic posture, characterized by a distinctive arching of the back and often accompanied by a raised head, the female rat exhibits a clear indication of sexual receptivity. It is noteworthy that instances of lordosis can persist even after mounting, intromission, or ejaculation, often followed by a transient period of immobility. Additionally, the experimenter can elicit lordosis by gently stimulating the lateral regions of the female rat's hind legs with their index and thumb, facilitating a controlled response. Typically, sexually receptive females demonstrate an LQ that approaches or even reaches 100%, signifying a high level of sexual receptivity. However, researchers commonly establish operational criteria, defining sexual receptivity as an LQ surpassing 50%, allowing for consistent evaluation and comparison across studies.[15]

While lordosis initially appears as a reflexive response, female rats actively participate in the mating process, demonstrating their proactive engagement. Through a repertoire of behaviors including purposeful approaches, conspicuous presentations, lively hops, swift movements, and animated ear wiggling, female rats effectively communicate their sexual interest and eagerly seek out sexual interactions with males. These proactive behaviors serve as insightful indicators of the female rat's sexual initiative and unwavering motivation. Furthermore, female rats emit alluring ultrasonic vocalizations, enchanting the attention of males throughout this intricate process. It is important to note that these behaviors, meticulously observed in controlled laboratory settings, may exhibit some variation contingent upon the specific contextual factors surrounding the mating environment. Notably, the aforementioned behaviors tend to prominently manifest when rats are paired within relatively compact test cages. Such remarkable behaviors not only underscore the active role played by female rats during the mating process but also accentuate their profound motivation and fervent involvement.[15,19]

In natural settings, where rats engage in mating within larger and more intricate habitats as groups, female rats display a diverse array of mating behaviors. These behaviors encompass approaches, orientations, and even evasive maneuvers directed towards the male, which serve as clear indications of their underlying motivation. For instance, female rats may actively approach, position themselves in a specific manner, or even tactfully withdraw from the male's advances. These behaviors tend to emerge more prominently in environments that offer ample space and complexity, facilitating the full expression of their mating repertoire. In order to comprehensively evaluate these behaviors, researchers employ quantitative measures such as recording the frequency of specific actions like ear wiggling, hopping, and rapid movements through visual observation or video documentation of the sexual interactions. These established methods are widely acknowledged in the literature as reliable and effective approaches for behavioral analysis. Consequently, the existing body of research provides a thorough account of how female rats' mating behaviors manifest and are systematically assessed under more naturalistic conditions.[15,20]

In order to gain a deeper understanding of the physiological implications of serotonergic drugs on lordosis, a comprehensive analysis was conducted on the existing knowledge pertaining to changes in serotonergic activity and the density of 5-HT receptors in the female rat brain throughout the estrous cycle and in response to effective doses of gonadal steroids. Traditionally, serotonin was believed to exert primarily inhibitory effects on lordosis. However, it has been established that the impact of 5-HT can vary, encompassing both inhibitory and facilitatory influences, contingent upon the specific subtypes of central 5-HT receptors that are activated. Notably, the intricate interplay between 5-HT and lordosis is contingent on receptor subtype activation. Despite extensive research, the effects of ovarian hormones on serotonergic activity or 5-HT receptors in critical brain regions have not consistently yielded persuasive results, leading to the current understanding that there is insufficient evidence to firmly establish a significant physiological role for 5-HT in the regulation of lordosis behavior in female rats.[21]

3.2. Pacing behavior

In semi-natural settings, female rats exhibit a sophisticated range of solicitation behaviors, allowing them to intricately modulate the tempo of mating. This remarkable ability to "fine-tune" the mating process holds great importance for females, as the timing between intromissions plays a pivotal role in triggering the neuroendocrine reflex responsible for initiating the progestational state crucial for successful pregnancy. Interestingly, males and females have distinct optimal timing patterns when it comes to intromissions during mating encounters. Males generally favor a consistent and rapid series of intromissions, leading to a swift ejaculation. In contrast, females require longer intervals between intromissions to maximize the vaginal-cervical stimulation they receive during mating, optimizing their reproductive outcomes. This inherent discrepancy in timing highlights the female's remarkable control and adaptability throughout the complex mating process, underscoring their active participation in shaping the dynamics of reproductive success.[19,20,22]

In natural habitats, males and females engage in group mating to achieve their preferred mating pace. However, in laboratory settings, female rats possess the ability to regulate their mating rate in an environment characterized by both approach and avoidance behaviors towards the male. This adaptability allows them to fine-tune their mating dynamics according to their individual preferences and physiological state. By employing a combination of proximity-seeking and avoidance beha-

viors, female rats in the laboratory can actively modulate the tempo of their mating encounters. This remarkable flexibility showcases the complex interplay between innate reproductive instincts and the environmental context, providing insights into the nuanced nature of sexual behavior in female rats.[15]

Observations of paced mating behavior have directed researchers' attention toward two primary components that reflect different aspects of the interaction. These components are as follows: (1) the exit ratio, which represents the number of departures from the male after a specific mating stimulus divided by the total number of mating stimuli, and (2) the interintromission interval, which denotes the duration of avoidance from the male after a particular mating stimulus. Both measurements increase as sexual stimuli intensify (mount < intromission < ejaculation). Therefore, pacing relies on the female's ability to discern sexual cues and execute appropriate motor behavioral responses. These findings have facilitated a more detailed and nuanced analysis of mating behavior. They shed light on the intricacies involved in the female's ability to modulate the mating process, highlighting the importance of understanding the underlying mechanisms and factors that contribute to the regulation of paced mating.[15,19]

The measurement of pacing is derived from meticulous behavioral observations, allowing researchers to delve into the various facets of the interaction. It entails focusing on two key components: (1) the exit percentage, which calculates the ratio of instances where the female rat separates from the male after a specific mating stimulus to the total number of mating stimuli, and (2) the interintromission interval, which measures the duration of time the female rat avoids the male following a particular mating stimulus. Both measurements exhibit an upward trend as the intensity of sexual stimuli increases, progressing from mounting to intromission, and ultimately to ejaculation. Consequently, pacing hinges upon the female rat's ability to discern the nuances of the sexual stimuli and execute precise motor behavioral responses. These intriguing findings have paved the way for a more comprehensive and nuanced analysis of mating behavior, unraveling the intricate dynamics involved in the process.[15,22]

The current focus revolves around the assessment of the motivational aspects of female rat sexual behavior through various methodologies and the identification of the favorable outcomes of regulated sexual interactions. In traditional laboratory settings, the sexual acceptability of female rats has been examined, revealing the readily observable attractive and aversive dimensions of sexual encounters. However, when female rats are granted the ability to modulate the pace of sexual stimulation, akin to semi-natural or natural conditions, the aversive attributes associated with mating tend to diminish. To gauge the positive effects of sexual experiences, researchers have employed the conditioned place preference method. Experimental setups have involved a two-compartment chamber, enabling female rats to freely navigate between sections while engaging in sexual interactions with male rats. The intriguing findings illustrate a distinct preference for one compartment over the other, indicating the development of a place preference. Moreover, even in instances where controlled sexual contacts transpire without ejaculation, female rats still exhibit a preference for the associated environment. Notably, the induced place preference resulting from regulated sexual interactions can be impeded by systemic administration of naloxone, a drug that antagonizes opioids, thereby implying the involvement of opioids in reward processes linked to regulated sexual interactions. In summary, controlled sexual interactions possess the potential to elicit positive effects and foster conditioning when conducted with sufficient intensity and duration.[23]

3.3. Importance of pacing behavior

Female rats have a remarkable ability to actively regulate the pace of their mating encounters, and this control plays a crucial role in their reproductive success. It is not simply the quantity of vaginal-cervical stimulation that determines the outcome, but rather how females perceive and respond to it. When given the autonomy to adjust the rate of intromissions, females exhibit a fascinating phenomenon: even with just a few well-timed intromissions, they have a high likelihood of experiencing pseudopregnancy. However, this rate is comparatively lower in females subjected to unregulated intromissions. As the number of intromissions increases, the disparity diminishes, yet females that maintain control over the pace consistently achieve higher rates of pseudopregnancy. Moreover, when females actively modulate the pace, the duration of estrus behavior is significantly shorter compared to those without regulation. These intriguing findings emphasize that while the regulation of mating pace may not be an absolute requirement for achieving pregnancy or pseudopregnancy, it highlights the active role of females in shaping their mating experiences, optimizing vaginal-cervical stimulation, and potentially yielding substantial physiological consequences.[15,24,25]

3.4. Sexual motivation

Traditionally, female sexual behaviors have been categorized as either "receptive" or "proceptive" behaviors. However, there has been a recent shift in focus among researchers to delve deeper into the complexities of female sexual motivation. Particularly, the term "proceptive" has gained significance as it implies that females actively contribute to initiating sexual behaviors. This paradigm shift has arisen due to the historical emphasis primarily placed on male sexual behaviors, which has drawn attention to the overlooked aspects of female sexual engagement. Nevertheless, the understanding that female rats require male stimulation to display lordosis following hormonal priming has occasionally perpetuated the perception of females as passive recipients influenced solely by hormonal and environmental factors. However, it is now widely acknowledged that females play an active and initiating role in sexual interactions, challenging conventional assumptions and underscoring the intricate nature of female sexual involvement.[15,26,27]

Despite the challenges, female rats in estrus exhibit remarkable determination as they bravely navigate through obstacles, even crossing an electrified grid, in their quest to reach a sexually competent male. Additionally, they display a distinct preference for the enticing scent emitted by sexually active males, prioritizing their company and dedicating a significant portion of their time to engaging with these fully sexually capable partners.[28–30]

Female rats display remarkable behavioral adaptations

to attain access to sexually active males. They actively engage in operant responses, demonstrating their willingness to perform specific actions to interact with sexually receptive males. Additionally, they develop conditioned place preferences, favoring the chambers associated with sexual activity over those where they are alone, indicating their strong motivation for sexual encounters. Furthermore, female rats exhibit conditioned place preferences for paced mating, highlighting their preference for controlled and rhythmic sexual interactions compared to uncontrolled mating scenarios. These behavioral observations underscore the intricate dynamics and active participation of female rats in their pursuit of sexual encounters.[27,31–35] However, it is important to note that in traditional testing conditions, not all aspects of female initiating behaviors are fully observed and understood. The perception of females as passive participants in sexual interactions may be influenced by the limitations of these testing conditions rather than accurately reflecting the complexity of female sexual behavior. Fortunately, experimental setups that empower females to exert control over sexual activity have emerged, offering a new and insightful perspective on female sexual behavior and motivation.[15,19]

4. Conclusion

Female rats exhibit remarkable and complex sexual behaviors during their peak sexual receptivity, known as estrus. The mating process involves a sequence of interactions between male and female rats, including mounting, intromission, and ejaculation. The female rat's receptivity is often assessed using the lordosis quotient (LQ), which quantitatively measures the percentage of time she displays the lordosis posture when mounted by a male. Female rats actively participate in mating, demonstrating proactive behaviors and communication signals to express their sexual interest. In natural settings, female rats display a diverse array of mating behaviors, adapting their approach and orientation according to their preferences and the environmental context. Pacing behavior, where females regulate the timing and pace of intromissions, is crucial for optimizing reproductive outcomes. It highlights the active role of females in shaping their mating experiences and underscores their ability to modulate the dynamics of sexual interactions. Overall, these intricate aspects of female rat sexual behavior emphasize their motivation, engagement, and control throughout the mating process.

Ethical approval

This study does not require approval from the Ethics Committee for Animal Experiments.

Authors contribution

BBK and MK: Research, planning, article scanning, writing-original draft & review. All authors contributed to the article and gave final approval of the version to be submitted.

Conflict of interest

There are no conflicts of interest associated with this research publication, according to the authors.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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