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Sexual behavior in male rodents

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Abstract

The hormonal factors and neural circuitry that control copulation are similar across rodent species, although there are differences in specific behavior patterns. Both estradiol (E) and dihydrotestosterone (DHT) contribute to the activation of mating, although E is more important for copulation and DHT for genital reflexes. Hormonal activation of the medial preoptic area (MPOA) is most effective, although implants in the medial amygdala (MeA) can also stimulate mounting in castrates. Chemosensory inputs from the main and accessory olfactory systems are the most important stimuli for mating in rodents, especially in hamsters, although genitosensory input also contributes. Dopamine agonists facilitate sexual behavior, and serotonin (5-HT) is generally inhibitory, though certain 5-HT receptor subtypes facilitate erection or ejaculation. Norepinephrine agonists and opiates have dose-dependent effects, with low doses facilitating and high doses inhibiting behavior.

Keywords: Rats; Mice; Hamsters; Guinea pigs; Estradiol; Dihydrotestosterone; Testosterone; Medial preoptic area; Medial amygdala; Genital reflexes

Introduction

Reproductive behaviors and their neural and hormonal regulation vary widely across species. Yet much research has focused on relatively few animals. We describe the behaviors of male rodents and their neural, hormonal, and experiential regulation. We begin with rats, the most common subjects of laboratory research. We then describe the behaviors of male mice, hamsters, and guinea pigs, noting similarities and differences among species. Sexual behavior is highly interactive; here we concentrate on the male, keeping in mind that the contributions of the female are equally important. Because of the vast amount of research on rodents, and the page limits for this manuscript, we can cite only a small portion of it. For additional details, please consult Hull et al. (2006) or Hull et al. (2002).

Description of male rat copulatory behaviors and *ex copula* reflexes

Male rats usually begin a sexual encounter by investigating the female's face and anogenital region. Both partners may emit mutually arousing 50 kHz ultrasonic vocalizations. The male approaches from the female's rear, mounts, and gives several rapid shallow thrusts (19–23 Hz) with his pelvis; if he detects the female's vagina, he gives a deeper thrust, inserting his penis into her vagina for 200–300 ms (Beyer et al., 1981). He then springs backward rapidly and grooms his genitals. After 7 to 10 intromissions, 1 to 2 min apart, he will ejaculate. Ejaculation is characterized by a longer, deeper thrust (750–2000 ms) and much slower dismount (Beyer et al., 1981). It is accompanied by rhythmic contractions of the bulbospongiosus and ischiocavernosus muscles at the base of the penis, and of anal sphincter and skeletal muscles (Holmes et al., 1991). After ejaculation, he grooms himself and then rests during the postejaculatory interval (PEI), which may last for 6 to 10 min before resuming mating. During the first 50–75% of the PEI, the male will not copulate again and emits 22 kHz ultrasonic vocalizations. During the latter 25%, he may resume copulation if presented with a novel female or a mildly painful stimulus. After 7–8 ejaculations males reach satiety and usually will not copulate again for 1 to 3 days. Previous sexual experience confers greater copulatory "efficiency" and increased resistance to the effects of various lesions, castration, and stress (reviewed in Hull et al., 2006).

Copulatory ability is acquired between 45 and 75 days of age (reviewed in Meisel and Sachs, 1994). Prepubertal castration

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prevented the onset of mating behavior, and exogenous testosterone (T) or estradiol (E_2) hastened its development. Aging male rats lose the ability to ejaculate, which is not restored by exogenous T (Chambers et al., 1991). A decline in estrogen receptors (ER) (Roselli et al., 1993), but not androgen receptors (AR) (Chambers et al., 1991), may underlie the deficit in old males. *Ex copula* reflexes can be observed in several contexts. Spontaneous or drug-induced erections occur in the home cage or neutral arena. Volatile odors from an estrous female elicit noncontact erections, which may be a model for psychogenic erections in humans. In rats "touch-based" erections can be elicited by restraining the male on his back and retracting the penile sheath. These erections result from engorgement of the corpus spongiosum, which produces tumescence of the glans penis (reviewed in Hull et al., 2006; Meisel and Sachs, 1994). Anteroflexions also occur; these result from contractions of the ischiocavernosus muscle and erection of the corpus cavernosum, causing the penis to rise from its normal posteroflexed position. Occasionally, seminal emission occurs in this context. The continuing pressure of the retracted sheath around the base of the penis provides the stimulus for these touch-based reflexes. Finally, the urethrogenital reflex has been studied in anesthetized male and female rats as a model of orgasm in humans (McKenna et al., 1991). It is elicited by urethral distension, followed by release; it consists of clonic contractions of the perineal muscles.

Hormonal factors in the activation of male rat mating behavior

Male sexual behavior in virtually all vertebrate species is dependent on T, secreted by the Leydig cells of the testes and metabolized in target cells to either E_2 (by aromatization) or dihydrotestosterone (DHT, by 5α-reduction). Plasma T is undetectable within 24 h of castration (Krey and McGinnis, 1990); however, copulatory ability decreases gradually over days or weeks. Five to ten days of T is usually required to reinstate mating (McGinnis et al., 1989). However, E_2 increased chemo-investigation and mounting by castrates within 35 min (Cross and Roselli, 1999). Therefore, rapid, probably membrane-based, hormonal effects may contribute to sexual motivation, but longer-term genomic effects are required for full restoration of mating.

The major hormone to activate sexual behavior in male rats is E_2, as proposed by the "aromatization hypothesis" (reviewed in Hull et al., 2006). DHT, which is nonaromatizable and has greater affinity for ARs than does T, is ineffective when administered alone. However, E_2 does not fully maintain male rat sexual behavior (McGinnis and Dreifuss, 1989; Putnam et al., 2003) or partner preference (Vagell and McGinnis, 1997). Thus, androgens contribute to motivation and performance and are also necessary and sufficient to maintain *ex copula* genital reflexes (Cooke et al., 2003; Manzo et al., 1999; Meisel et al., 1984). Although E_2 was ineffective in maintaining *ex copula* reflexes, it did maintain vaginal intromissions *in copula* (O'Hanlon et al., 1981). Sachs (1983) suggested that E activates a "behavioral cascade" that can elicit genital reflexes *in copula*, but cannot disinhibit them *ex copula*.

Effects of systemically administered drugs on male rat sexual behavior

Transmitters often act synergistically in multiple sites, and the site of action often is not known *a priori*. Therefore, systemic drug administration can be useful. Table 1 summarizes the effects on male rat sexual behavior of drugs and treatments that affect neurotransmitter function in more than one brain area.

Brain areas that regulate male rat sexual behavior

Chemosensory input from the main and vomeronasal systems is probably the most important stimulus for male rodent sexual behavior. Bilateral olfactory bulbectomy, which removes both the main and vomeronasal pathways, produced variable impairment of copulation and noncontact erections, with sexually naive males being more susceptible to impairment (reviewed in Hull et al., 2006). Information from the main and accessory olfactory systems is processed in the medial amygdala (MeA), along with somatosensory input from the genitals, relayed through the parvocellular portion of the subparafascicular nucleus (SPFp), which is also part of an ejaculation circuit in several species (reviewed in Hull et al., 2006). Input from the MeA, both directly and via the bed nucleus of the stria terminalis (BNST), to the medial preoptic area (MPOA) is critical for copulation in male rats (Kondo and Arai, 1995).

The MPOA is arguably the most critical site for orchestrating male sexual behavior. It receives sensory input indirectly from all sensory systems and sends reciprocal connections back to those sources, thereby enabling the MPOA to influence the input that it receives (Simerly and Swanson, 1986). It also sends output to hypothalamic, midbrain, and brain stem nuclei that regulate autonomic and somatomotor patterns and motivational states (Simerly and Swanson, 1988). Many studies have reported severe and long-lasting impairment of copulation following lesions of the MPOA (reviewed in Hull et al., 2006). However, male rats with MPOA lesions continued to show noncontact erections (Liu et al., 1997a,b) and bar-press for a light that had been paired with access to a female (Everitt, 1990). Everitt (1990) suggested that the MPOA is important only for copulation, and not sexual motivation. However, MPOA lesions impaired sexual motivation in other contexts, including preference for a female partner (Edwards and Einhorn, 1986; Paredes et al., 1998) and pursuit of a female (Paredes et al., 1993).

Conversely, stimulation of the MPOA facilitated copulation, but did not elicit mating in sated males (Rodríguez-Manzo et al., 2000). Stimulation also increased intracavernosal pressure in anesthetized males (Giuliano et al., 1996) and elicited the urethrogenital reflex without urethral stimulation (Marson and McKenna, 1994a,b). The MPOA does not project directly to the lower spinal cord, where erection and seminal emission are controlled; thus, it must activate other areas that, in turn, elicit those reflexes.

The MPOA is the most effective site for hormonal stimulation of mating in castrated rats; however, T or E_2

Table 1
Effects of systemically administered drugs on male rat sexual behavior

Transmitter altering drugs	Effects on sexual behavior	References	Remarks
Dopaminergic			
DA agonists	+	(Malmnas, 1976; Mas et al., 1995; Niikura et al., 2002; Rodriguez-Manzo, 1999; Scaletta and Hull, 1990)	DA agonists also facilitated copulation in short-term (Malmnas, 1976) and long-term (Scaletta and Hull, 1990) castrated rats.
DA antagonists	−	(Ågmo and Picker, 1990; Ahlenius and Larsson, 1990; Lopez and Ettenberg, 2000, 2001, 2002b)	
Noradrenergic			
NE agonists	+	(Clark et al., 1984; Clark et al., 1985; Clark, 1995; Rodriguez-Manzo, 1999; Smith et al., 1987; Tallentire et al., 1996)	Although noradrenergic drugs appear to facilitate male sexual behavior, high levels of peripheral NE activity inhibit erections (Stefanick et al, 1983) by vasoconstricting penile arteries.
NE antagonists	−	(Clark and Smith, 1990)	
Serotonergic			
5-HT agonists	−/+	(Ahlenius and Larsson, 1991, 1998; Ahlenius et al., 1989; Cantor et al., 1999; Coolen et al., 1997; Frank et al., 2000; Marson and McKenna, 1992; Millan et al., 1997; Schnur et al., 1989; Steers and deGroat, 1989; Vega Matuszcyk et al., 1998)	Stimulation of 5-HT_{1A} may promote ejaculation, but inhibit erections.
5-HT antagonists	+	(Rodriguez et al., 1984)	Stimulation of 5-HT_{2C} may facilitate erections, but inhibit ejaculations Stimulation of 5-HT_{1B} may inhibit ejaculation.
Acetylcholinergic			
Systemic ACh agonists	−	(Maeda et al., 1990; Zarrindast et al., 1994)	Systemically administered muscarinic agonists may facilitate copulation and erections, although contradictory results have been reported. These effects may be mediated, in part, by peripheral influences on penile muscles and/or the parasympathetic nervous system.
Systemic ACh antagonists	−		
Opiate			
Opiate agonists	−	(Ågmo and Paredes, 1988; Gomez-Marrero et al., 1988; Leyton and Stewart, 1992.	A possible explanation for these apparently contradictory effects is that low to moderate levels of endogenous opioids may facilitate sexual motivation and genital reflexes; however, exogenous opiates or high levels of endogenous opioids may inhibit those same functions.
Opiate antagonists	+/−	(Leyton and Stewart, 1996; Rodriguez-Manzo and Fernandez-Guasti, 1995; Pfaus and Wilkins, 1995; Sachs et al., 1981; van Furth and van Ree, 1994)	
Nitric oxide			
NO agonists	+	(Benelli et al., 1995; Ferrari et al., 2002; Giuliano et al., 2003)	Although NO is a major facilitator of parasympathetically mediated erections, it may inhibit sympathetically mediated seminal emission and ejaculation (Moses and Hull, 1999).
NO antagonists	−	(Benelli et al., 1995; Bialy et al., 1996; Hull et al., 1994)	

implants in the MPOA did not fully restore copulation, and DHT implants were ineffective (reviewed in Hull et al., 2006). Therefore, both ER and AR in the MPOA contribute to copulatory ability of male rats; however, hormonal effects elsewhere are required for full activation of behavior.

MPOA microinjections of the classic dopamine (DA) agonist apomorphine facilitated copulation in gonadally intact and castrated rats and increased touch-based reflexes (reviewed in Dominguez and Hull, 2005; Hull et al., 2006). MPOA apomorphine also restored copulation in males with large amygdala lesions (Dominguez et al., 2001). Conversely, a DA antagonist inhibited copulation and touch-based reflexes and decreased sexual motivation without affecting motoric function (reviewed in Dominguez and Hull, 2005; Hull et al., 2006). These effects were anatomically and behaviorally specific.

DA is released in the MPOA before and during copulation (Hull et al., 1995; Sato et al., 1995). Again, there was both behavioral and anatomical specificity. Recent, but not concurrent, T was necessary for the DA increase and copulation (Hull et al., 1995). A major factor promoting MPOA DA release is

nitric oxide (NO), in both basal and female-stimulated conditions (reviewed in Dominguez and Hull, 2005; Hull et al., 2006). NO synthase immunoreactivity (NOS-ir) is positively regulated by both T and E_2 (Du and Hull, 1999; Putnam et al., 2005). NO is also important for copulatory performance, as a NOS inhibitor (L-NAME) in the MPOA blocked copulation in naive males, impaired mating in experienced males, and prevented the facilitation produced in saline-treated males by 7 pre-exposures to an estrous female (Lagoda et al., 2004). Input from the MeA is required for the DA response to a female, but not for basal DA levels (Dominguez et al., 2001). Chemical stimulation of the MeA resulted in increases in extracellular DA in the MPOA comparable to those produced by a female (Dominguez and Hull, 2001). There are no DA-containing neurons in the amygdala of male rats; however, some efferents from the MeA to the MPOA, and even more from the BNST, appeared to be glutamatergic (Dominguez et al., 2003). Reverse dialysis of glutamate into the MPOA increased DA release, an effect blocked by a NOS inhibitor (Dominguez et al., 2004). In addition, extracellular glutamate increased during copulation and rose to 300% of basal levels in the two-minute sample collected during ejaculation; reverse dialysis of glutamate reuptake inhibitors facilitated several measures of copulation (Dominguez et al., 2006). Similarly, glutamate microinjected into the MPOA increased intracavernous pressure (Giuliano et al., 1996) and the urethrogenital reflex (Marson and McKenna, 1994a,b) in anesthetized rats. Therefore, a consistent picture emerges, in which glutamate, at least in part from the MeA and BNST, facilitates copulation and genital reflexes, both directly and via NO-mediated increases in DA, which also contributes to the initiation and progress of copulation. Other neurotransmitters in the MPOA that may facilitate male rat sexual behavior are norepinephrine, acetylcholine, prostaglandin E_2, and hypocretin/orexin (hcrt/orx), whereas GABA and 5-HT may be inhibitory. Low levels of opioids may facilitate, and higher doses inhibit copulation (reviewed in Hull et al., 2006).

Electrophysiological recordings revealed that different MPOA neurons contribute to sexual motivation and copulatory performance (Shimura et al., 1994). Mating increases Fos-ir in the MPOA (reviewed in Hull et al., 2006), with greater increases in sexually experienced males, compared to naive ones, even though the experienced males had fewer intromissions preceding ejaculation (Lumley and Hull, 1999). Therefore, sexual experience may enhance the processing of sexually relevant stimuli.

The mesocorticolimbic DA tract, ascending from the ventral tegmental area (VTA) to the nucleus accumbens (NAc) and prefrontal cortex, is important for reinforcement and appetitive behaviors. It receives input from the MPOA (Simerly and Swanson, 1988) and numerous other sources. VTA or NAc lesions increased PEIs and decreased noncontact erections, but did not affect copulation (reviewed in Hull et al., 2006). Conversely, electrical stimulation of the VTA facilitated copulation (Markowski and Hull, 1995). Applications of drugs to the VTA or NAc primarily affected general activation, rather than specifically sexual behavior (reviewed in Hull et al., 2006). Mating activated Fos-ir in the NAc and VTA, and an estrous female-stimulated increase was enhanced by prior sexual experience (Lopez and Ettenberg, 2002a). Copulation and/or exposure to the odor of an estrous female increased DA release in the NAc (reviewed in Hull et al., 2006). Reverse dialysis of 5-HT into the anterior lateral hypothalamic area (LHA) decreased basal DA in the NAc and prevented the rise that otherwise occurred with the introduction of a female (Lorrain et al., 1999). Because 5-HT is increased in the LHA at the time of ejaculation (Lorrain et al., 1997), the resulting decrease in NAc DA may contribute to the PEI.

The paraventricular nucleus (PVN) of the hypothalamus comprises a magnocellular division, which releases oxytocin and vasopressin into the circulation from the posterior pituitary, and a parvocellular division, which projects to several brain areas and the spinal cord. Excitotoxic lesions of the parvocellular portion decreased noncontact erections but did not impair copulation (Liu et al., 1997a,b). Similar lesions decreased the amount of semen ejaculated and the number of oxytocin-containing fibers in the spinal cord, but again did not affect copulation (Ackerman et al., 1997). Lesions that encompassed both divisions did impair copulation, as well as touch-based and noncontact erections (Liu et al., 1997a,b). Argiolas and Melis have provided an elegant picture in which DA, oxytocin, and glutamate (Melis et al., 2004) increase production of NO in oxytocinergic cells in the PVN, which then release oxytocin in the hippocampus (Melis et al., 1992), spinal cord (Ackerman et al., 1997), and elsewhere, thereby increasing erection and seminal emission and possibly enhancing copulation (reviewed in Argiolas and Melis, 2004). GABA and opioids inhibit these processes. This laboratory has also shown that DA (Melis et al., 2003), glutamate, (Melis et al., 2004), and NO (Melis et al., 1998) are released in the PVN during copulation.

Several additional brain areas influence male rat sexual behavior. 5-HT is released in the LHA at the time of ejaculation, as noted above, and microinjection of an SSRI into the LHA inhibited copulation (Lorrain et al., 1997). Therefore, this may be one site at which SSRI antidepressants act to inhibit sexual function. In addition, hypocretin/orexin (hcrt/orx) neurons reside in the LHA and are activated (Fos-ir) following copulation, and the numbers of hcrt/orx neurons decreased after castration (Muschamp et al., 2007). Furthermore, 5-HT inhibits hcrt/orx neurons in the LHA (Li et al., 2002). Therefore, a possible way in which LHA 5-HT inhibits sexual behavior is by inhibiting hcrt/orx neurons, which would remove their facilitative effect on VTA DA cell firing (Muschamp et al., 2007).

The nucleus paragigantocellularis (nPGi) of the medulla is a major source of inhibition of male rat sexual behavior. Lesions facilitated copulation and delayed sexual satiety (Yells et al., 1992). Similar lesions facilitated touch-based reflexes (Holmes et al., 2002; Marson et al., 1992) and allowed the urethrogenital reflex to be elicited without spinal transection (Marson and McKenna, 1990). Most of the axons projecting from the nPGi to the lumbosacral spinal cord contain 5-HT (Marson and McKenna, 1992). A 5-HT neurotoxin decreased the descending inhibition of the urethrogenital reflex, and application of 5-HT

to the spinal cord suppressed that reflex in spinal-transected rats (Marson and McKenna, 1994a,b). Thus, 5-HT from the nPGi is a major inhibitor of genital reflexes.

An ejaculation generator in the lumbar spinal cord comprises galanin- and cholecystokinin (CCK)-containing neurons, which showed Fos-ir only after ejaculating (Truitt and Coolen, 2002; Truitt et al., 2003). Lesions of these neurons severely impaired ejaculation; therefore, they not only carry ejaculation-specific sensory input to the brain, but also elicit ejaculation (Truitt and Coolen, 2002).

Description of male mouse copulatory behavior and penile reflexes

The mouse has become popular for behavioral studies, largely because of our ability to generate transgenics, knockouts, and knockdowns (see Burns-Cusato et al., 2004 for an excellent review). The male mouse begins an encounter by investigating the female's anogenital region, often lifting or pushing her with his nose. The male then presses his forepaws against the female's flanks and makes rapid, shallow pelvic thrusts. When his penis enters the female's vagina, his repeated thrusting becomes slower and deeper. After numerous intromissions, the male ejaculates, during which he may freeze for 25 s before dismounting or falling off of the female. There are many strain differences in mouse mating. For example, ejaculation latencies ranged from 594 to 6943 s, and the numbers of intromissions preceding ejaculation ranged from 5 to 142. PEIs ranged from 17 to 60 min, although introduction of a novel female decreased the PEI, with some males ejaculating on the first intromission with the new female (Mosig and Dewsbury, 1976). In place preference tests both intromissions and ejaculations were shown to be rewarding (Kudwa et al., 2005).

Touch-based reflexes have also been observed in mice. Unlike rats, intact male mice did not show spontaneous reflexes while restrained with their penile sheath retracted; however, abdominal pressure did elicit erections, but not anteroflexions (Sachs, 1980). The bulbospongiosus muscle contributes to erections during intromission and especially to cups (intense erections that hold semen against the female's cervix), which are important for impregnating a female (Elmore and Sachs, 1988).

Hormonal factors in the activation of male mouse mating behavior

T is more effective than either DHT or E_2 in restoring precopulatory and copulatory behaviors in castrated mice, with sensitivity to DHT and E_2 varying widely among strains (reviewed in Burns-Cusato et al., 2004). T can also have rapid effects, as it facilitated mounting within 60 min in castrates (James and Nyby, 2002). Synthetic androgens (5α-androstanediols) that can be aromatized to E, but not 5α-reduced to DHT, were even more effective than T in restoring sexual behavior (Ogawa et al., 1996). One strain, the B6D2F1 hybrid, recovered the ability to copulate about 3 weeks after castration without exogenous hormones (McGill and Manning, 1976). These "continuer" males depend on E_2; although the source of the E_2 is not clear, it may be produced in the brain (Sinchak et al., 1996).

Roles of hormones in specific brain areas of male mice

Implantation of T into the MPOA completely restored ultrasonic vocalization, partially restored urine marking, and had little effect on mounting or urine preference (Sipos and Nyby, 1996). However, additional implants of T in the VTA, which were ineffective alone, produced synergistic effects on mounting and urine preference. E_2 implants in the MPOA were as effective as T (Nyby et al., 1992).

Steroid receptor mutants

The testicular feminization (*Tfm*, or androgen insensitivity) mutation in mice, as well as other animals, results from deletion of a single base in the AR gene (reviewed in Burns-Cusato et al., 2004). *Tfm* males appear phenotypically female, are infertile, and engage in no sexual behavior if tested without exogenous hormones. Small testes secrete low levels of T and DHT. However, if these males are castrated and treated with daily injections of DHT, T, E, or E+DHT, they begin to show variable amounts of sexual behavior, including occasional ejaculations (Olsen, 1992). Mice lacking the ERα (ERαKO) show little sexual behavior, even when castrated and replaced with T (Rissman et al., 1999; Wersinger and Rissman, 2000a). This is not due to a lack of hormones as ERαKO males secrete more T than do wild-type mice, due to diminished ER-mediated negative feedback (Wersinger et al., 1997). Castration of ERαKO males and replacement with normal levels of T (Wersinger et al., 1997) or higher than normal levels of DHT (Ogawa et al., 1998) increased mounting, but did not restore ejaculation. Systemic injections of the DA agonist apomorphine restored mating and partner preference of ERαKO males to normal (Wersinger and Rissman, 2000b). However, apomorphine icv restored only mounts and intromissions (described in Burns-Cusato et al., 2004). Pubertal males lacking ERβ (ERβKO) acquired the ability to ejaculate later than did WT males, but were otherwise normal (Temple et al., 2003). Males lacking both ERs did not copulate at all when gonadally intact (Ogawa et al., 2000). However, apomorphine was able to stimulate mounting in most animals and intromitting in half; none ejaculated (described in Burns-Cusato et al., 2004). Genetic males lacking both the AR and ERα did not copulate, even after castration and replacement with T; however, the combination of E_2 replacement and systemic apomorphine did stimulate mounting in some animals (described in Burns-Cusato et al., 2004). Males lacking aromatase (ArKO) are unable to synthesize E but have normal receptors. Fewer ArKO males mounted, intromitted, and ejaculated, and had longer latencies when they did; however, about one-third of them were able to sire litters when placed with a female for a prolonged time (Bakker et al., 2002; Matsumoto et al., 2003).

Effects of systemically administered drugs on male mouse sexual behavior

Please see Table 2 for a summary of systemic drug effects on male mice and hamsters.

The roles of various brain areas in male mouse sexual behavior

Chemosensory cues are extremely important for sexual behavior in male mice (reviewed in Hull et al., 2006). However, the vomeronasal system may have an important, but not critical, role in mating. MPOA lesions severely impaired copulation in male mice, as in other species (reviewed in Hull et al., 2006). ERαKO had less nNOS-ir in the MPOA than WT or *Tfm* mice; therefore, E up-regulates nNOS-ir in mice (Scordalakes et al., 2002) as well as in rats.

Description of male hamster copulatory behavior

Mating behavior of hamsters differs in numerous ways from that of rats and mice (reviewed in Dewsbury, 1979). The female Syrian golden hamster remains in a lordosis posture continuously through successive copulations. Mating progresses more rapidly than in rats, with inter-intromission intervals of only 10 s and PEIs increasing from ~35 s after the first ejaculation to ~90 s after the ninth. Intromissions and ejaculations are longer, ~2.4 and 3.4 s, respectively. Hamsters also have more ejaculations than rats, often 9 or 10, followed by a series of "long intromissions," with intravaginal thrusting and no sperm transfer, prior to satiety. Detailed analysis of the hamster mating pattern, using accelerometric and polygraphic technique, revealed that trains of pelvis thrusting averaged about 1 s, though trains associated with mounts were longer than those with intromissions and ejaculations (Arteaga and Moralí, 1997). The frequencies of pelvic thrusting averaged 15 thrusts per second, although trains during mounts were slower. During intromissions there was a period without any thrusting, whereas during ejaculation, thrusting was of higher frequency (16.4/s) and less vigor. Long intromissions were characterized by ~6 to 25 s of slow intravaginal thrusting (1 to 2 per s). The duration of penile insertion was longer in ejaculations than in intromissions, but was shorter than in long intromissions.

Hormones

Lack of T during puberty impaired copulation after T replacement in adulthood, compared with castrates with T replacement during puberty (Schultz et al., 2004). Repeated sexual experiences did not compensate for these deficits. The odor of a receptive female activated Fos-ir in the MPOA even before puberty (Romeo et al., 1998), but did not increase the DA metabolite DOPAC (a measure of DA activity) until after puberty (Schultz et al., 2003). Therefore, puberty may be a second organizational period in which gonadal hormones permanently alter neural processing in areas that regulate sexual behavior (Romeo et al., 2002; Schultz et al., 2004).

Effects of systemically administered drugs in male hamsters

Please see Table 2 for a summary of systemic drug effects in mice and hamsters.

Table 2
Effects of systemically administered drugs on male mouse and hamster sexual behavior

Transmitter altering drugs	Effects on sexual behavior	References	Remarks
Dopaminergic			
DA agonists	+	Mice: (Sugiura et al., 1997; Rampin et al., 2003; Niikura et al., 2002; Szczypka et al., 1998)	DA-deficient mice were activated by L-DOPA and were more sensitive to L-DOPA and T (Szczypka et al., 1998).
DA antagonist	−	Mice: (Lopez and Ettenberg, 2002b)	
Noradrenergic			
NE indirect agonist	+	Hamsters: (Arteaga et al., 2002)	Increasing NE release with an α2 autoreceptor antagonist facilitated copulation.
Serotonergic			
5-HT_{1A} agonists	−	Mice: (Rodriguez-Manzo et al., 2002; Popova and Amstislavskaya, 2002)	5-HT_{1B} knockout mice were less impaired by serotonergic drugs, but needed more stimulation to ejaculate, possibly because of compensatory mechanisms (Rodriguez-Manzo et al., 2002).
5-HT_{1B} agonists	−	Hamsters: (Boscarino and Parfitt, 2002)	
5-HT reuptake inhibitor	−		
Nitric oxide			
nNOS knockouts	−	Mice: (Burnett et al., 1996; Kriegsfeld et al., 1999)	nNOS knockouts had normal erections, due to increased eNOS, but ejaculated with fewer intromissions; thus NO may help prevent "premature ejaculation".
NO antagonists	−		
GnRH			
GnRH icv	+	Hamsters: (Fernandez-Fewell and Meredith, 1995; Westberry and Meredith, 2003)	GnRH is released in response to female hamster odor.

The roles of various brain areas in male hamster sexual behavior

Bilateral olfactory bulbectomy or combined deafferentation of the main and accessory olfactory systems permanently abolished sexual behavior (reviewed in Hull et al., 2006). Deafferentation of the accessory olfactory system had variable effects, with experienced males being less affected (Meredith, 1986). Mating-induced increases in Fos-ir in the main and accessory olfactory bulbs were specific to chemosensory stimuli, rather than to mating (reviewed in Hull et al., 2006).

Either T or E, but not DHT, implants into the MeA restored copulatory behavior in castrated male hamsters (Wood, 1996). Thus, hormonal activation of the MeA is sufficient for expression of sexual behavior in male hamsters. Projections from the MeA travel via the stria terminalis and ventral amygdalofugal pathway to the BNST, MPOA, and other areas. Cutting the stria terminalis delayed and slowed copulation, and combined cuts of both pathways eliminated copulation (Lehman et al., 1983).

As with many other species, the MPOA is critical for sexual behavior in male hamsters. However, steroid implants in castrates have variable effects and are not sufficient to restore behavior fully (Wood and Newman, 1995). Chemosensory cues activated Fos in the MPOA of male hamsters (Kollack-Walker and Newman, 1997). nNOS-ir is co-localized with gonadal steroid receptors in the MPOA, and castration decreased nNOS-ir (Hadeishi and Wood, 1996). As in rats, extracellular DA levels rose in the MPOA of male hamsters presented with an estrous female; this increase was blocked by bilateral or ipsilateral, but not contralateral or sham, bulbectomy (Triemstra et al., 2005).

Description of male guinea pig copulatory behavior

Male guinea pigs engage in several species-typical precopulatory behaviors, including nibbling the female's fur on her head and neck, sniffing her anogenital region, and making guttural sounds while either circling the female or shifting his weight on his two rear feet while keeping his forepaws stationary (Thornton et al., 1991). The male then approaches the female from the rear, places his chest over the female's back while clasping her sides, and begins pelvic thrusting, which usually results in a vaginal intromission (Valenstein et al., 1954). Males can intromit at a rate of approximately 1 per minute (Thornton et al., 1991), and 80% can ejaculate in a 15-min test (Butera and Czaja, 1985). Although a male that ejaculates with a single female usually does not reinitiate copulation within the next hour, he may copulate with a different female (Grunt and Young, 1952).

Hormones

Unlike in male rats, systemically administered DHT can fully restore copulation in castrated male guinea pigs (Butera and Czaja, 1985). Furthermore, DHT implants into the MPOA were also sufficient to activate copulation in castrates (Butera and Czaja, 1989).

Summary

Although there are differences in the copulatory elements among rodents, the hormonal factors and neural circuitry that control those elements are similar. Both E and DHT contribute to the activation of mating, although E is more important for copulation, and DHT, for genital reflexes of rats, mice, and hamsters. Hormonal activation of the MPOA is most effective, although implants in the MeA can also stimulate mounting in castrates. Chemosensory inputs from the main and accessory olfactory systems are the most important stimuli for mating, especially in hamsters, although genitosensory input via the SPFp also contributes. DA agonists facilitate sexual behavior when injected either systemically or into the MPOA or PVN. 5-HT agonists, especially 5-HT_{1B}, tend to inhibit behavior, although 5-HT_{2C} agonists facilitate erection and 5-HT_{1A} agonists facilitate ejaculation (except in mice). Norepinephrine agonists and opiates have dose-dependent effects, with low doses facilitating and high doses inhibiting behavior.

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