

Who, What, Where, When (and Maybe Even Why)? How the Experience of Sexual Reward Connects Sexual Desire, Preference, and Performance

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Abstract Although sexual behavior is controlled by hormonal and neurochemical actions in the brain, sexual experience induces a degree of plasticity that allows animals to form instrumental and Pavlovian associations that predict sexual outcomes, thereby directing the strength of sexual responding. This review describes how experience with sexual reward strengthens the development of sexual behavior and induces sexually-conditioned place and partner preferences in rats. In both male and female rats, early sexual experience with partners scented with a neutral or even noxious odor induces a preference for scented partners in subsequent choice tests. Those preferences can also be induced by injections of morphine or oxytocin paired with a male rat's first exposure to scented females, indicating that pharmacological activation of opioid or oxytocin receptors can “stand in” for the

sexual reward-related neurochemical processes normally activated by sexual stimulation. Conversely, conditioned place or partner preferences can be blocked by the opioid receptor antagonist naloxone. A somatosensory cue (a rodent jacket) paired with sexual reward comes to elicit sexual arousal in male rats, such that paired rats with the jacket off show dramatic copulatory deficits. We propose that endogenous opioid activation forms the basis of sexual reward, which also sensitizes hypothalamic and mesolimbic dopamine systems in the presence of cues that predict sexual reward. Those systems act to focus attention on, and activate goal-directed behavior toward, reward-related stimuli. Thus, a critical period exists during an individual's early sexual experience that creates a “love map” or Gestalt of features, movements, feelings, and interpersonal interactions associated with sexual reward.

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We have evolved a nervous system that acts in the interest of our gonads, and one attuned to the demands of reproductive competition.

—M. T. Ghiselin (1973)

Erotic fetishism makes an idol of physical or mental qualities of a person or even merely of objects...because they awaken mighty associations with...sexual pleasure.

—R. v. Krafft-Ebing (1886/1929)

The first cut is the deepest...

—Cat Stevens (1967)

Introduction

Imagine yourself walking along a busy street when suddenly you smell something that reminds you of your very first love.

The odor is familiar, comforting, and despite the terrible adolescent angst that accompanied the breakup, it elicits a complete and happy memory of exciting experiences you shared. To another person, that smell may well rekindle horrible memories of abuse and pain. And to a third person, the smell has no meaning whatsoever. Now consider another scenario. You are at a bar with a good friend watching others and selecting those who are the sexiest. Although at first you both agree on some rudimentary symmetries and body types, the discussion quickly degenerates around particular features: you like brunettes while your friend likes blondes, you like almond-shaped eyes, while your friend likes round eyes, you like long faces while your friend likes round faces, you like a particular set of dimples while your friend cannot stand dimples, you like a particular size of breasts or pectorals, while your friend likes skinny. You like the one dressed in leather, while your friend likes the one in the business suit. It is even worse when the talk turns to personality characteristics. You like them loud, unbridled, and maybe a bit dangerous, while your friend likes them demure, soft-spoken, reliable, and boring. Eventually, you agree to disagree on who is hot and who is not.

If the ultimate drive for reproductive success causes us to select potential sex partners with epigamic characteristics that denote good genetic material, health, wealth, higher social status, and good potential parental investment (e.g., Buss, 1994), why would we ever have a difference of opinion? Why would we have “a billion wicked thoughts” (Ogas & Gaddam, 2011) instead of just a few that denote reproductive success? Why would we ever need to learn anything about, or from, sex? We should simply be drawn to men that are big and strong enough to tear the flesh off bears, and/or younger women with ample breasts and optimal waist-to-hip ratios, and then copulate as much as possible, preferably in the position(s) that provide the most effective stimulation for impregnation, and, of course, only when his sperm count is high and she is ovulating. But who are we to pick? Do we all possess the *same* degree of desired physical characteristics as those we want to mate with? Of course, the answer to that rhetorical question is no. Moreover, *mating* is clearly not the only reason we have sex and, in fact, may be second to a more proximate master: pleasure (with Tantric liberation coming a distant third). Indeed, sexual behavior in some species facilitates sociosexual goals; for example, brief female–female mounting in bonobos that promotes peaceful interactions among males (Furuichi, 2011; Hohmann & Fruth, 2000).

A nervous system that is prepared to copulate also needs to be flexible and learn strategies that maximize copulatory success in an ever-changing world. But what defines success? In order to have sex, we must first be able to respond to hormonal and neurochemical changes that signal our own sexual desire and arousal and distinguish it from other sympathetic activation, such as anxiety. This ability underlies our moment-to-moment level of sexual arousability (as conceived by Whalen, 1966) and defines a large part of the internal state that is commonly referred to as “sex drive.” Second, we must be able to make

sense of external cues that signal sexual attraction and receptivity in others (e.g., Salu, 2011). This ability requires a complex mix of instinct, learning, and feedback: a neural organization that allows for incentive-based motivation and expectancy (Bindra, 1968, 1974; Bolles, 1972; Toates, 1986). We must be able to identify external stimuli that predict where potential sex partners can be found, to seek out, solicit, court, or otherwise work to obtain sex partners, distinguish external cues and behavioral patterns of potential sex partners from those that are not sexually receptive, and to pursue sex partners once sexual contact has been made (Pfaus, Kippin, & Coria-Avila, 2003). In this way, we move in time from distal to proximal to interactive, with an ever-increasing load on sensory processing and motor sophistication as we interact more and more with a moving and sentient sensory stimulus.

Neural mechanisms also exist that allow sexual responding to become habitual or automated with practice and such processes may underlie the ability of desired features in others to be identified and responded to quickly (e.g., Ortigue & Bianchi-Demicheli, 2008) and of sexually experienced individuals to be less affected by treatments that disrupt sexual responding in sexually naïve individuals (e.g., Pfaus & Wilkins, 1995). Similarly, neural mechanisms exist that allow the stimulation received during sexual contact to be perceived as rewarding. Such reward alters subsequent behavior, for example, by contributing to the formation of preferences for salient stimuli associated with positive sexual reinforcement (Pfaus, Kippin, & Centeno, 2001), just as individuals develop preferences for stimuli associated with drug or food reward (Berridge, 2009; Robinson & Berridge, 2001). Many of these aspects of sexual responding go well beyond the traditional focus on copulation or genital reflexes/blood flow. Although some appetitive responses that individuals make prior to copulation are not specific to sexual behavior, they can be considered “sexual” if they are conditioned using sexual reward as the positive reinforcer (Pfaus, 1999). This is as true for appetitive bar pressing in male rats (e.g., Everitt, Fray, Kostarczyk, Taylor, & Stacey, 1987) as it is for giving flowers and remembering birthdays in men. Thus, we learn about *who* makes us feel desire, about *what* we like, and *where* we like it, and we learn what to do to get it.

It is becoming increasingly clear that there is a critical period of sexual behavior development that forms around an individual’s first experiences with sexual arousal and desire, masturbation, orgasm, and sexual intercourse itself. During this period, the sensory and motor mechanics of the behavior become integrated and crystallized along with the development of preferences for ideal activities and physical features of a partner. Such preferences often violate societal “norms” (e.g., as in the development of fetishes or paraphilias) and so-called “evolutionary laws” regarding features that represent genetic and reproductive strength, appearing more to be based on an egocentric evaluation of salient reward- or pleasure-related characteristics that differ from one individual to another. The formation of such experience-based

preferences can be found in historical texts, such as Stendhal's "Principle" in his work *De L'Amour* (1822), described explicitly in case histories, such as those in Krafft-Ebing's *Psychopathia Sexualis* (1886/1929), and more theoretically in the "love maps" proposed by Money (1986). This critical period may well form on the foundation laid by previous critical periods, especially those associated with attraction to other- or same-sex individuals, which itself may form on the foundation laid by a critical period for gender typical versus atypical behavior, and the sense of self as "female" or "male."

In this article, we propose a neurodevelopmental trajectory of sexuality that considers how innate predispositions are forged into successful sexual behaviors, expectations, and desires, based on an individual's experience with reward and capacity to link reward to cues that predict it. The integration of genetic and experiential factors in determining behavior is consistent with older ideas of the complementary nature of ultimate and proximate causality (Tinbergen, 1963) and new ideas concerning the role of epigenetic factors (e.g., Bale, 2011). A popular reading of genetic causality seems to infer that behaviors are fixed or hardwired in the brain, whereas learning infers that such brain mechanisms and the behaviors they underlie are flexible. We want to emphasize at the outset that even so-called "fixed action patterns" are subject to experience and that subsequent epigenetic changes in gene transcription and protein synthesis in neurons can alter the expression of behaviors differently in different individuals. Evolutionary pressures alter the costs and benefits of any behavior, and experience with reward (and possibly punishment) maintains the cost-benefit ratio. We note that this ratio may change in different environmental conditions, sometimes quickly and radically. Those who can learn to respond in the wake of sudden changes to a niche (e.g., a decrease in population density) will likely out-reproduce those who do not learn. Thus, ultimate and proximate causes of behavior are complementary. We posit that reward mechanisms sit in the middle of these two domains.

Genetic and Hormonal Conditions and Predispositions

Sexual activity or partner preferences that stray from so-called "normal" are often attributed to genetic or hormonal differences. Such differences are believed to create different brains that process the world differently, or to generate physiological factors that predispose individuals to certain sexual dysfunctions, such as lifelong premature ejaculation (Waldinger, 2008) or erectile dysfunction (Bancroft & Janssen, 2000).

Biomarkers

A number of genetic and neural correlates of male homosexuality have been reported as "female" phenotypes (assumed to be due to either perinatal feminization and/or demasculinization). For example, relative to heterosexual men, gay men possess a smaller

female-like interstitial nucleus III of the anterior hypothalamus (LeVay, 1991), a larger female-like suprachiasmatic nucleus (Swaab, Gooren, & Hoffman, 1992), and in male-to-female transsexuals a smaller female-like central region of the bed nucleus of the stria terminalis (Zhou, Hofman, Gooren, & Swaab, 1995). Of course, it is not known whether those neuroanatomical differences actually contribute to the sexual orientation of the individual or whether they simply reflect an unrelated endpoint of some differentiated developmental process. Biomarkers have also been suggested for a distinct (and not putatively feminized or demasculinized) "gay" genetic makeup in the expression of the X-linked marker Xq28 (Hamer, Hu, Magnuson, Hu, & Patatucci, 1993), in the 2D:4D ratio of gay men relative to heterosexual men (e.g., Robinson & Manning, 2000), in a leftward directional handedness asymmetry (Martin, Puts, & Breedlove, 2008), hair-whorl direction (Rahman, Clarke, & Morera, 2009), visuospatial performance tasks (Collaer, Reimers, & Manning, 2007), and in the fraternal birth order effect (Blanchard, 2007; Blanchard & Lippa, 2007; Bogaert & Skorska, 2011; Rahman, 2005; Vasey & VanderLaan, 2007). Handedness and general IQ also appear as correlates in incarcerated male pedophiles (Cantor, Blanchard, Bobichaud, & Christensen, 2005; Cantor, Klassen et al., 2005), and cerebral white matter deficiencies in the superior fronto-occipital and right arcuate fasciculi have been found in incarcerated male pedophiles relative to an incarcerated non-pedophilic male population (Cantor et al., 2008), suggesting that frontal output (responsible for executive function and behavioral inhibition) of pedophilic individuals is compromised.

Sex Differences and Steroid Hormones

Another source of innate differences in sexual function involves the pattern of circulating steroid hormone levels that differ between the sexes. This occurs in two phases in mammals: (1) an "organizational" phase in which the male phenotype differentiates from the female "default" through the combined action of androgens and estrogens during a critical perinatal period that "sculpt" a male brain; and (2) during a subsequent "activational" phase in which gonadal steroid secretion acts on those differentiated brain regions to activate the neuroendocrine systems necessary for reproduction and the behaviors that will bring it about (Bonthuis et al., 2010; Lenz & McCarthy, 2010; Nelson, 2005). Thus, the brains of male mammals are differentiated from the female default by early hormone actions, which lead to different patterns of sexual responding in adulthood driven by two distinct steroid hormone secretion patterns, one continuous (male) and one cyclic (female).

The cyclic nature of estradiol, testosterone, and progesterone action in females leads to changes in sexual responding and increases in sexual arousal and desire around the time of ovulation in all vertebrate species, including humans (Slob, Ernste, & van der Werff ten Bosch, 1991; Stanislaw & Rice, 1988), although a smaller increase has been reported around the time of menstruation

(Singer & Singer, 1972). The hormonal milieu during the periovulatory follicular phase alters the way in which visual sexual stimuli are processed in women (Gizewski et al., 2006; Krug, Pihl, Fehm, & Born, 2000; Mass, Hölldorfer, Moll, Bauer, & Wolf, 2009; Rupp et al., 2009), which presumably leads to a shift in the incentive value of the stimuli. Analogous findings have been reported in our primate cousins, for example, in approaches and solicitations made around the time of the mid-cycle estradiol peak in rhesus macaques (Wallen, Winston, Gaventa, Davis-DaSilva, & Collins, 1984) and in the appetitive and consummatory sexual behaviors that characterize the periovulatory period of female rats (e.g., Beach, 1976; Erskine, 1989; McClintock, 1984; Pfaff, 1980, 1999; Pfaus et al., 2003). This contrasts with the relatively stable and continuous testicular androgen secretion in mammalian males (and its reduction to neural androgens or aromatization to neural estradiol in different regions of the brain) that maintains sexual arousability and responsiveness in a relatively continuous manner (Hull & Dominguez, 2007).

Biological Differences in Mating Strategy

Although a number of innate differences in mating strategies between species have been described, perhaps the most studied is the partner preference displayed by monogamous prairie voles relative to promiscuous meadow or montane voles (Lim, Hammock, & Young, 2004; Lim & Young, 2004; Winslow, Hastings, Carter, Harbaugh, & Insel, 1993; Witt, Carter, & Walton, 1990; Young & Wang, 2004). Differences in functional vasopressin and oxytocin receptor densities have been described between these two species of vole (Insel, Winslow, Wang, Young, & Hulihan, 1995) and, in particular, greater vasopressin 1A receptor density in the ventral pallidum (a motor output region that contributes to goal-directed behavior) of monogamous prairie voles compared to promiscuous voles (Lim, Hammock et al., 2004). Indeed, overexpression of this receptor in meadow voles by injection of an adenoviral vector that contains the whole receptor gene resulted in male meadow voles developing a significant partner preference for the first female they mate with (Lim, Wang et al., 2004). These data suggest strongly that a genetic difference in receptor density for those two neuropeptides results in a predisposition toward social recognition, affiliation, and pair-bonding, which, in turn, underlies the display of particular reproductive strategies in a species.

Temperament and Response Style

Finally, what is called “temperament” is believed to reflect innate differences in brain function that start in childhood and lead to individual differences in sensory processing and motor response styles. This results in stable personality traits such as extroversion, introversion, impulsivity, and inhibition (Kagan, 1994). One of the first classification schemes was that of the ancient “humoral

doctrine” of Hippocrates (460–370 BCE). This doctrine described four human personality traits (sanguine, choleric, melancholic, and phlegmatic) that allegedly explained both individual and group differences in responding. Sexually speaking, someone who is sanguine and prone to humor and passion would likely process sexual stimulation more readily than the calm phlegmatic person who is prone to sluggishness. That latter individual may require more sensory stimulation to achieve a requisite level of arousal for sexual responding and may gravitate to highly arousing, naughty, even violent sex play. Likewise, an introverted individual may have less sexual experience than an extroverted individual based simply on exposure to social situations and concomitant availability of potential sex partners. The two may possess different sexual attitudes and different levels of sexual arousal and desire (Meston & Buss, 2007). Indeed, it is possible that whatever the genetic bases of temperament are also produce differences in the activation patterns of neurochemical systems that excite or inhibit sexual behavior (Pfaus, 2009). However, introversion in women is correlated with a history of childhood sexual abuse (Talbot et al., 2000), making it difficult to know what comes first, response style or particular sexual experiences that may reinforce response style. Differences in temperament can also change how drugs affect sexual behavior (Pfaus, Wilkins, et al., 2010), with one person’s “aphrodisiac” producing a loss of sexual function in another.

In summary, innate genetic predispositions are assumed to underlie different sexual responses and partner preferences. Those differences may form generally around different hormone actions that sexually differentiate the brain and induce a differential activation of excitatory or inhibitory neurochemical systems, which leads to specific types of sensory processing and/or motor function. Together, they create individual brains with different sexual phenotypes and proneness to sexual excitation and inhibition, either as a spontaneous “drive” or in the presence of incentive sexual stimuli. Such differences are believed to underlie sexual orientation in humans and different species-specific mating strategies, such as monogamy or polygamy.

Associative Conditions

Another innate characteristic of brains is that they learn and remember. Brain function (and, therefore, behavior) is modified to a large extent by experience. The ability to form operant associations (Skinner, 1938) between motor actions (responses) and their consequences (reinforcers) and Pavlovian associations (Pavlov, 1927) between a neutral external cue that serves as a conditioned stimulus (CS) and different emotional states like pleasure, reward, or aversion, induced by an unconditioned stimulus (UCS), require a brain capable of experience-based synaptic plasticity, as in the formation of Hebbian circuits and neural networks that sensitize neural responses to stimuli (Hebb, 1949; Johnson,

LeDoux, & Doyère, 2009). There are a number of molecular events that shape such plasticity. These include: (1) the activation of growth factors that direct the formation of new synapses; (2) augmentation of intracellular events, such as transmitter receptor proliferation and the availability of second messengers linked to receptors; and (3) epigenetic factors, including DNA methylation or histone acetylation of genes to suppress or enhance the generation of proteins they code for that ultimately facilitate or inhibit individual responses that comprise the behavior. All three processes are stimulated and sensitized during phases of neuronal activation following the first encounter with a new sensory stimulus (see, e.g., McEwen, 2010). The emotional state induced by the consequences of that encounter feed back to strengthen or inhibit the likelihood of future encounters. Because the molecular protein synthetic events that subserve those phenomena take time, along with a degree of repeated experience with the conditions, the final form of the response accrues across a “learning curve” that can be defined individually or for a group of individuals exposed to the same stimuli and consequences. Regardless of the species, all neurons store the memory of salient events in this way (Kandel, 2001). Thus, activation of the network itself by a formerly “neutral” CS associated with it generates, as Pavlov said, a “representation of the UCS” which serves to predict, activate, and prime the emotional state. An incentive motivational account of Pavlovian conditioning (e.g., Bindra, 1968) has the CS activating a “central motivational state,” which moves the body in the direction of the goal (e.g., activates appetitive responses) and prepares it viscerally to act on the goal (e.g., salivation in response to a CS that predicts food; erection in response to a CS that predicts sexual gratification).

As with Pavlovian conditioning, a motor response that results in the arrival of a needed or preferred stimulus becomes strengthened, such that doing it on its own after it is learned can be reinforcing to a certain extent. Motor patterns also become automated with repeated activation, as in the development of “habits” or “routines” that require very little cognitive loading to be engaged once they are formed (Hull, 1943; Tolman, 1932). This also makes them extremely difficult to break without an extensive program of extinction and/or alternate reinforcement and, even then, spontaneous recovery can occur, showing the primacy of early relative to subsequent experiences. Thus, associative conditioning creates a brain in which the ends “justify” the means and in which the cues that predict the ends become conditioned incentives. To a brain that generates some degree of self-awareness (as in humans), conditioning results in circular reasoning and tautologies. When do we ever thank our bodies and ourselves for our pleasurable responses to salient erotic stimulation? Instead, we ascribe their valence and intensity to our sex partner(s), as in the phrase “you make me feel so good.” Of course, when such stimulation loses its arousing potential, as often happens when it is repeated over and over again the same way (and at intervals that produce tolerance, rather than sensitization), we tend to blame that loss on our sex partners no longer arousing us as they once did.

Setting the Stage

If we were creating a sexually reproductive universe, would we make sexual responses as “innate” as possible to assure that everyone would do the same thing at the right time with presumably the most optimal mate(s)? After all, like a male black widow spider or praying mantis, we may get only one crack at it. Yet, anyone who has had the opportunity to watch utterly inept sexually naïve male rats try to copulate no doubt wondered why there are so many rats. Like language, sexual desire, preference, and performance must be learned and crystallized before they appear as a relatively “automatic” set of species-specific responses. Essentially, genetic factors and early hormonal differentiation help to set the stage upon which experience creates the play. But the actors have to rehearse before the play can be performed properly. The sexual brain must have feedback systems that coordinate, facilitate, and crystallize the learning of appropriate and competent sexual responses. Those systems must link together the activation of both sympathetic and parasympathetic divisions of the autonomic nervous system by desired sexual stimuli with appetitive sexual behaviors directed at those stimuli and drive them into a coordinated set of consummatory (e.g., copulatory) responses. What kind of feedback is required and how can this be studied empirically?

Obviously, human sexual behavior is best studied in humans, but it is impossible to control the conditions under which humans have their first sexual experiences. Far too much occurs randomly and chaotically despite the best-laid plans. Therefore, we depend on animal models in which different aspects of sexual experience can be controlled methodically (for comprehensive reviews, see Ågmo & Ellingsen, 2003; Pfaus et al., 2003). Sexual behavior in animals, like that of humans, can be divided along appetitive and consummatory lines (Pfaus, 1999; Pfaus, Damsma, et al., 1990) and can be studied with respect to the stimuli animals are given to respond to and the motor patterns that become strengthened and automated with repeated sexual experience. Although the behavioral structure of sexual responding may be the same for all vertebrates, it is true that laboratory rats are not humans. Drawing conclusions from one species and applying it to another must be done with caution and an eye toward predictions made from one species about the functions of another, e.g., mechanisms underlying erection in males or sexual solicitations in females (Beach, 1950; Pfaus et al., 2003). We do not know if rats experience “orgasm” as we do, although at another level of analysis they clearly experience a sexual reward state that augments their responsiveness to cues associated with it.

Learning What to Do

In his seminal analysis of conditioning and copulatory behavior in male rats, Larsson (1956) demonstrated learning curves for baseline rates of mounts, intromissions, and ejaculations in male rats. Baseline rates were typically achieved in 3–5 trials to ejaculation

and were faster if males achieved more ejaculations in their initial trials. Notably, sexually naïve males typically took a long time to sniff and lick the female's anogenital region before mounting whereas some males never copulated at all despite repeated exposure to females and their progressively intense attempts to solicit copulation. Some sexually sluggish or non-copulating males (referred to colloquially as “duds” relative to the “studs” that copulate) could be stimulated to mount if unavoidable, low-level footshock, short-term pain (e.g., tail-pinch), or neutral stimuli paired with them were applied (Barfield & Sachs, 1968; Caggiula, 1972; Crowley, Poplaw, & Ward, 1973). Such stimuli also reduced the number of intromissions required for ejaculation in sexually active males (Beach & Fowler, 1959; Sachs, Macaione, & Fegy, 1974).

In other experiments, repeated exposure of the males to the copulation testing chambers for several days prior to their first exposure to the female increased the proportion that mounted to 100%, suggesting that the stress of a novel environment may preclude copulation in sensitive males (Pfaus & Wilkins, 1995). Endogenous opioids are activated in response to novelty stress (Izquierdo & McGaugh, 1987) and may disrupt copulation in sexually naïve males by μ receptor activation in an important hypothalamic region known as the medial preoptic area (mPOA) (Hughes, Everitt, & Herbert, 1990; Matuszewich & Dornan, 1992). Administration of the opioid receptor antagonist naloxone to sexually naïve males increased the proportion of males that copulated on their first test in a manner identical to that of preexposure to the testing chamber (Pfaus & Wilkins, 1995). In fact, naloxone had no effect in that study if males had been preexposed. In addition to genetic reactivity to novelty stress, sexually sluggish males were found to have decreased nuclear estrogen receptor in the mPOA relative to sexually active males (Clark, Davis, & Roy, 1985), suggesting a genetic factor that would either fail to activate excitatory pathways, or fail to disinhibit them in the presence of stressful inhibitory external cues.

Crystallization

Learning the appropriate set of appetitive responses is crucial to gaining access to sex partners and learning how to copulate properly is crucial to successful reproduction. Both types of responses become “crystallized” in an animal's behavioral repertoire. Many examples of this exist in the literature. In rats, those behaviors include performance in obstruction boxes (Jenkins, 1928; Moss, 1924; Stone, Barker, & Tomlin, 1935; Warner, 1927), straight-alley running (Beach & Jordan, 1956; Sheffield, Wulff, & Backer, 1951; Ware, 1968), maze learning (Drewett, 1973; Eliasson & Meyerson, 1975; Hetta & Meyerson, 1978; Kagan, 1955; Meyerson & Lindstrom, 1973; Warner et al., 1991; Whalen, 1961), crossing of electrified grids (Moss, 1924), nose-pokes and other attempts to “get to” a potential sex partner behind a wire-mesh screen (Damsma, Pfaus, Wenkster, Phillips, & Fibiger, 1992; Pfaus, Damsma, Wenkster, & Fibiger,

1995; Pfaus, Mendelson, & Phillips, 1990), digging through sand (Anderson, 1938), bar-pressing for a sex partner (Beck, 1971, 1974, 1978; Beck & Chmielewska, 1976; French, Fitzpatrick, & Law, 1972; Jowaisas, Taylor, Dewsbury, & Malagodi, 1971; Larsson, 1956; Sachs et al., 1974; Schwartz, 1956) or for a cue light associated with the arrival of a sex partner (Everitt, 1990; Everitt & Stacey, 1987; Everitt et al., 1987), and psychomotor stimulation in anticipation of the arrival of a sex partner (Mendelson & Pfaus, 1989). To gain access to receptive females, male guinea pigs learn to run an alley (Seward & Seward, 1940), male pigeons learn to peck keys (Gilbertson, 1975), and male stickleback fish learn to swim through rings (Sevenster, 1973). Male songbirds learn to sing particular songs that attract females (MacDougall-Shackleton, 2009; Mooney, 2009).

Larsson (1956) also found that, once established, individual patterns of copulatory behavior appear stable and relatively resistant to environmental change. Similarly, Pattij et al. (2005) demonstrated stable individual differences in ejaculatory latency in male rats that resembled those found in humans using the stopwatch method to determine intravaginal ejaculatory latency (e.g., Wal-dinger, McIntosh, & Schweitzer, 2009), and could be assigned statistically to groups of rapid, normal, and delayed ejaculators. In fact, such assignment predicted certain drug effects, such as the facilitation of ejaculation by the presynaptic 5-HT_{1a} agonist drug 8-OH-DPAT (which occurred in normal and delayed ejaculators, but not in rapid ejaculators). However, the early conditions under which copulatory patterns are established can alter the way that they appear in subsequent tests. For example, Larsson discovered an “enforced interval effect” (EIE) in which males that had the receptive female pulled out of the test arena for durations of up to 1 min would ejaculate with progressively fewer intromissions. Once established, this effect would last despite the fact that males had free access to females. However, although males given early experience with free copulation showed an EIE within a copulatory session, they would resume their “normal” pattern under conditions of free copulation.

In an elegant and well-controlled extension of the EIE, Silberberg and Adler (1974) trained sexually naïve male rats to copulate in three different conditions. Control males were allowed to copulate freely with sexually receptive females for 30 min on each of 20 tests of sexual behavior. Experimental males were allowed to achieve seven intromissions before the receptive female was removed during each test. A third group was yoked in time to the experimental group, but not in terms of a particular number of intromissions prior to the female being removed. A large and significant proportion of males in the experimental group consistently achieved ejaculation prior to the 7th intromission relative to males in the other groups. Intromissions thus could be interpreted as “operants” that brought about ejaculation and the intromission pattern (along with the ejaculation latency) could come under external control.

To examine the development of particular patterns of sexual responding, we have used unilevel pacing chambers with two

types of Plexiglas divider, one with four holes and another with one hole, that separate the chamber into two equal sides. The holes are small so that only the female can cross from one side to the other. This sequesters the male to one side and allows the female to control or “pace” the initiation and rate of copulation. However, this creates two distinctive pacing conditions, one in which the female has free access to the male (4-hole) and one in which she has relatively restricted access (1-hole) given that the male typically puts his head in the a hole (presumably trying to get to the other side). Of course, from the male’s perspective, the female is always available in the 4-hole condition whereas he has to wait longer in the 1-hole condition. Male rats given their first nine trials of sexual activity in one of the two pacing conditions developed significantly different patterns of copulatory activity (Ismail, Zhao, & Pfaus, 2008). Males trained in the 4-hole condition developed faster ejaculation latencies and fewer intromissions before ejaculation relative to males trained in the 1-hole condition (Fig. 1). Notably, when males in

each group were switched to the other condition on the 10th trial, they maintained their previously-established ejaculatory pattern, despite the difference in condition.

Beach (1956) proposed that two separate but interactive sexual mechanisms existed in male rats, an arousal mechanism (AM) and a copulatory mechanism (CM). The AM integrated distal olfactory, auditory, and visual cues from receptive females. When the cue strength became sufficiently intense, the AM activated the CM to initiate copulatory responding (mounts and intromissions). The CM then integrated tactile stimulation from the penis with each vaginal intromission, leading eventually to ejaculation and the highly stereotyped post-ejaculatory refractory period. Given that sexually naïve males can show preferences for receptive over non-receptive females and that they are responsive to sex odors from receptive females, the first unconditioned reinforcer in the cascade of sexual reinforcers would be sex odors. The goal would be getting to them. In Beach’s terms, this would be the primary function of the AM.

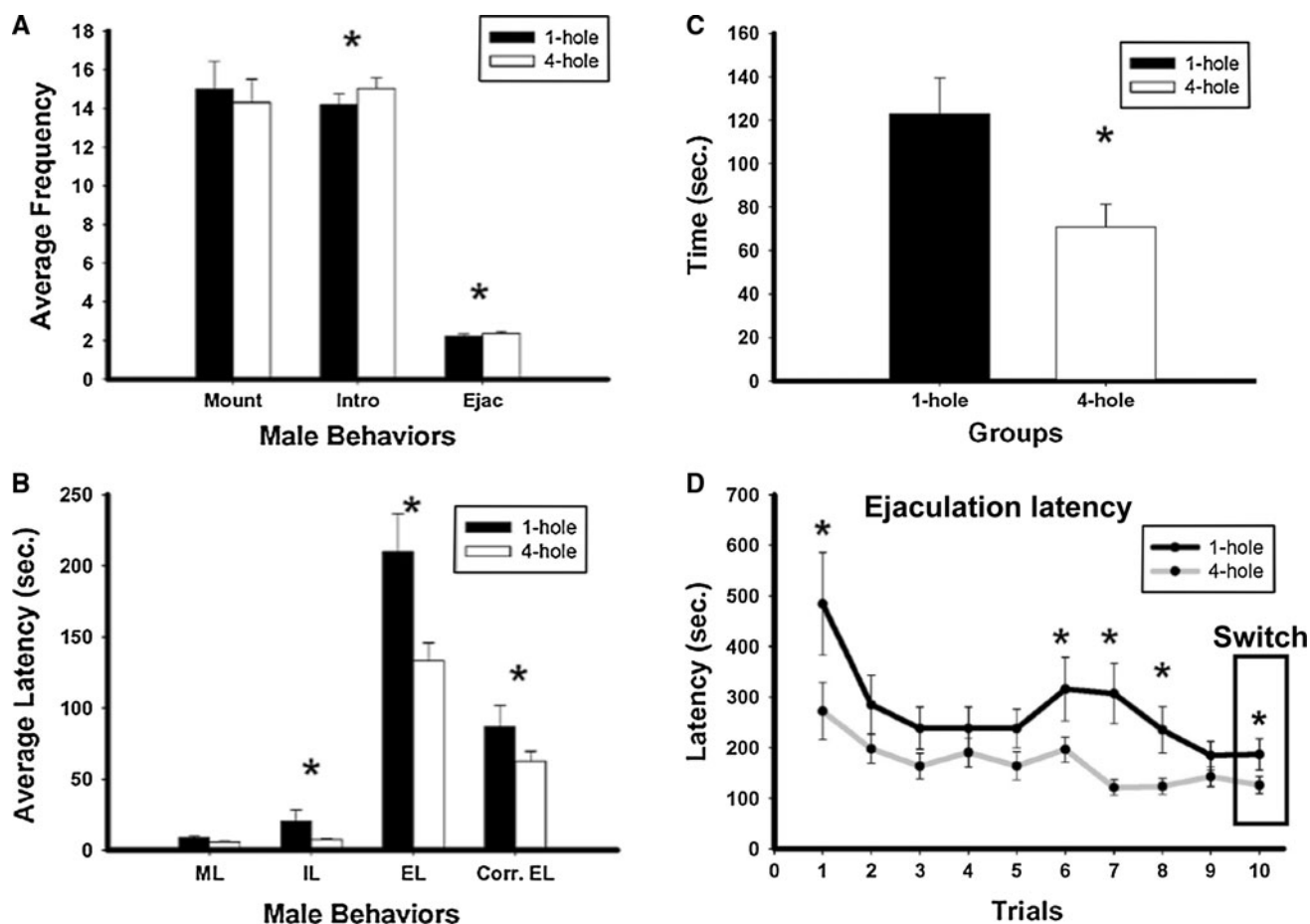


Fig. 1 Development of male rat sexual behavior in 1-hole vs. 4-hole unilevel pacing conditions. **a** Average frequencies of mounts, intromissions, and ejaculations during the nine conditioning trials in the two pacing conditions. **b** Average mount, intromission, and ejaculation latencies during the nine conditioning trials in the two pacing conditions.

c Average time (s) the females spent away from males during the nine conditioning trials in the two pacing conditions. **d** Ejaculation latencies in the two pacing conditions across the nine conditioning trials and during the 10th test when the males were switched into the other pacing condition

Whalen (1961) asked what the necessary stimulation must be for the development of copulatory behavior. The answer was penile stimulation. Whalen varied whether males achieved mounts without intromission, intromissions without ejaculation, or intromissions with ejaculation with sexually receptive females. On a final test, males were allowed to copulate to ejaculation with receptive females. Many rats that achieved only mounts during their sexual experience trials did not copulate whereas rats that achieved intromissions with or without ejaculation were able to copulate to ejaculation normally. Thus, exposure to sex odors alone was not sufficient to crystallize patterns of copulation; sensory feedback from penile stimulation was necessary. This makes penile stimulation a second goal or reinforcer in the cascade (and the first of the CM).

Whalen also asked whether mounts with or without intromission could augment the ability of male rats to learn to run a T maze and find a sexually receptive female. Males with 1 or 4 mounts alone, or 1 or 4 intromissions, both scored higher than chance (choosing the side with the receptive female more often than the non-receptive female). However, experience with intromissions produced a significantly higher percentage of “correct” responses, indicating that tactile stimulation of the penis summed with mounts (and other close interaction with the female during training) to augment the learning. López, Olster, and Ettenberg (1999) asked whether sexually naïve rats would run faster in a straight-arm runway if their prior copulatory experience was intromissions with or without ejaculation. Only rats that achieved ejaculation showed faster running times. Thus, it would seem that a cascade of reinforcing events, from perception of sex odors to chasing receptive females to penile stimulation during mounting to ejaculation, is necessary for the normal display of appetitive and consummatory sexual responses.

Resistance to Disruption

Sexual experience has profound effects on physiology and makes animals relatively resistant to treatments that disrupt sexual behavior. For example, compared with sexually inexperienced males, sexually experienced males have larger testes (Drori & Folman, 1964), heavier penises (Herz, Folman, & Drori, 1969), lighter body weights (Siegel, Nunez, & Wade, 1981), and increased secretions from accessory sex glands (Drori & Folman, 1964). Sexual experience has also been shown to ameliorate the disruptive effects of anosmia (Thor & Flannelly, 1977), castration (Lisk & Heiman, 1980; Fig. 2), penile deafferentation (Lodder, 1975), penile anesthesia with lidocaine (Fig. 3), and age (Gray, Smith, Dorsa, & Davidson, 1981). Gonadally intact, sexually experienced males prefer the odors of receptive females over those of non-receptive females whereas sexually naïve or castrated males do not display a significant preference (Carr, Loeb, & Dissinger, 1965; Carr, Loeb, & Wyllie, 1966).

We have shown that sexually naïve males are susceptible to the disruptive effects of novelty stress on copulation whereas

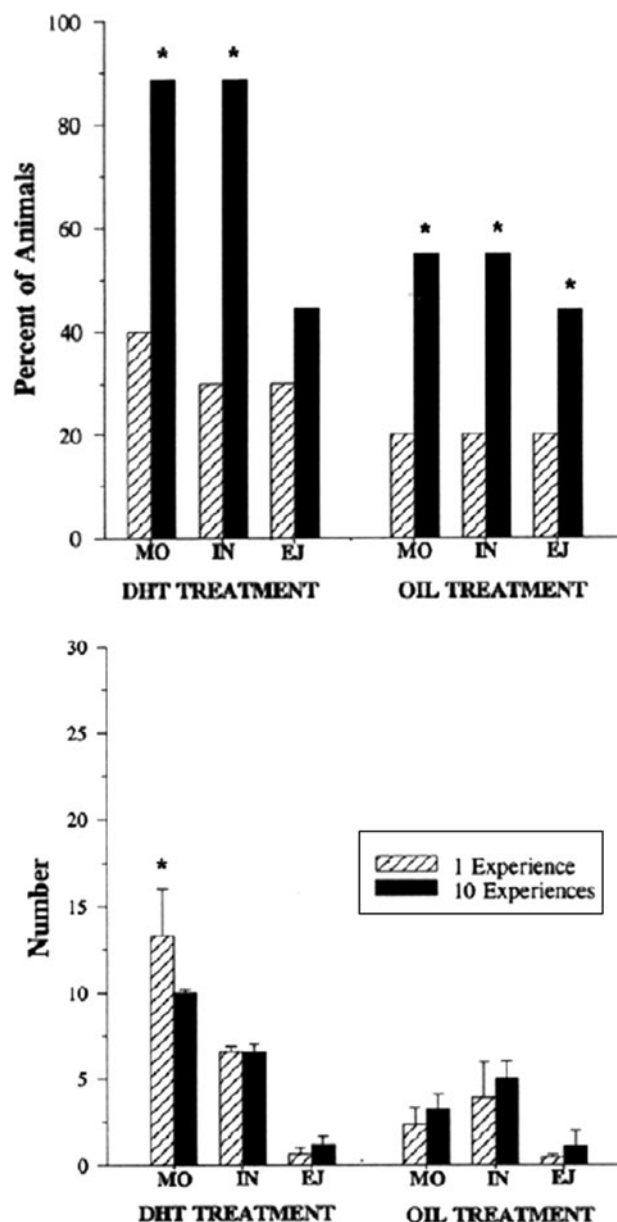


Fig. 2 Effects of castration with or without dihydrotestosterone treatment on consummatory sexual behaviors of male rats. *Top* Proportion of males displaying mounts, intromissions, and ejaculations a month after castration. *Bottom* Frequencies of mounts, intromissions, and ejaculations a month after castration. Males were given either 1 or 10 trials of sexual behavior to one ejaculation each prior to castration. * $p < .05$ compared to oil-treated controls

males with 10 prior multi-ejaculatory sexual experiences are not (Pfaus & Wilkins, 1995). Although both sexually naïve and experienced males that were placed into a novel testing apparatus displayed behaviors consistent with a fear state (e.g., freezing followed by exploration near the walls of the chamber), the sexually experienced males responded immediately to the introduction of a sexually receptive female with the initiation of copulation whereas most of the sexually naïve males ignored the receptive female for a long period of time, and, as noted above,

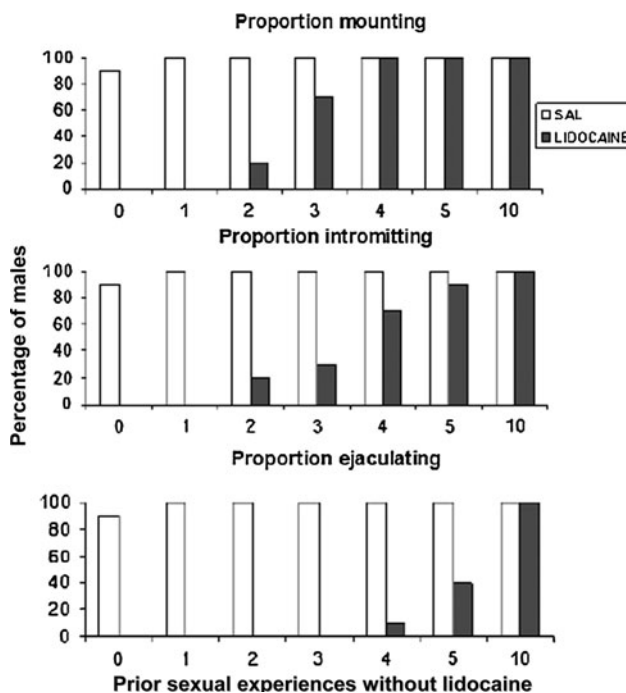


Fig. 3 Effect of the topical anesthetic lidocaine (5% topical cream) or saline applied to the penis of male rats on the proportion of males that mount, intromit, and ejaculate as a function of prior sexual experience. Males received either 1, 2, 3, 4, 5, or 10 prior experiences to one ejaculation before the application of lidocaine or saline. For percentages of 60 or lower, $p < .05$

some sexually naïve males did not initiate copulation, although novelty-induced opioid transmission in certain regions of the brain leads to an endogenous state in which copulatory behavior is suppressed, the induction of this state in males with sexual experience was not sufficient to suppress copulation once the female was placed into the chamber.

Learned Inhibition

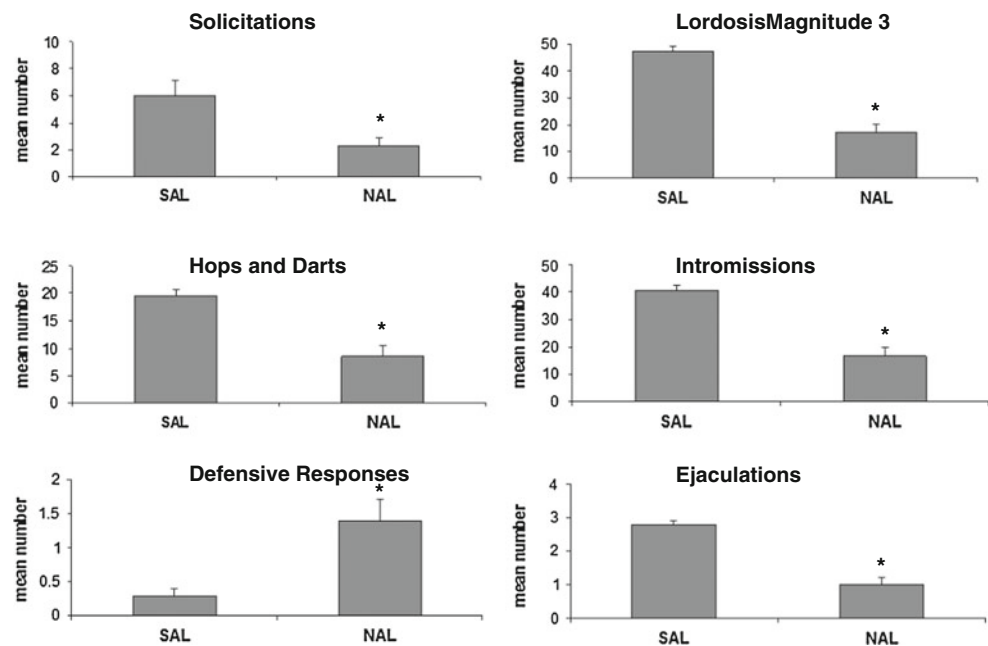
Sometimes animals have to learn what *not* to do. Sexually experienced male rats learn not to attempt copulation with sexually non-receptive females. This was shown when males that had 10 prior multiejaculatory trials at 4-day intervals with females were presented with a sexually non-receptive female (Pfaus & Pinel, 1989). All males attempted to mount those females despite their attempts being thwarted aggressively by the females' defensive behaviors. When males were presented sequentially with sexually non-receptive and receptive females in alternating trials, the males learned not to mount the non-receptive females over the course of approximately five trials while maintaining high rates of sexual responding on trials with sexually receptive females. Interestingly, a low dose of alcohol increased the proportion of males that attempted to mount the non-receptive females in a subsequent test, showing that alcohol possesses disinhibitory properties only if animals were inhibited in the first place.

When presented with a sexually inactive male rat, sexually receptive and experienced females will solicit the males with increasing vigor before mounting them repeatedly (Afonso & Pfaus, 2006; Beach, 1968). This “female–male mounting” (FMM) behavior was displayed only when the gonadally-intact females were sexually receptive, when ovariectomized (OVX) females were primed with estrogen, and was terminated abruptly if the males finally “got it” and mounted back. Thus, it is regarded as a “super-solicitation” behavior. Importantly, FMM is displayed by sexually naïve females presented with a castrated, sexually inactive male on their first exposure to males. However, if the males never mounted back (as the long-term castrates do not), the FMM behavior diminished over five successive trials (Afonso, Bablekis, & Pfaus, 2006). It is as if the females learned that this behavior does not successfully stimulate the males to mount them, although it could be restored if the males mounted intermittently. Fully receptive female rats also learned to suppress both appetitive and consummatory aspects of sexual behavior if they are paired with an explicitly nonrewarding state. We have created such a state with injections of the opioid receptor antagonist drug naloxone. Females were given their first six experiences of copulation with sexually vigorous males at 4-day intervals in unilevel pacing chambers either under the influence of naloxone or saline. On the 7th test, all rats were injected with saline. Females that had experienced sex without opioid reward showed dramatic reductions in solicitations, hops and darts, lordosis, and increased defensive responses compared to control rats and received fewer intromissions and ejaculations from the males (Fig. 4). As the half-life of naloxone is approximately 1–2 h in plasma (Fishman, Roffwarg, & Hellman, 1973), it is highly improbable that the reduction was due to a long-term or sustained action of naloxone itself. It is more likely that it stemmed from an expectancy of nonreward during sex.

Neural Correlates

Whereas critical periods of perinatal and pubertal steroid hormone action alter brain structure and function within hypothalamic, limbic, and cortical regions associated with sexual arousal and desire, experience with salient sexual stimulation (and reward) also changes or refines brain structure and neurochemical function (Pfaus, 2009). For example, whole-brain endorphin content increases significantly in male rats following repeated ejaculations (Szechtman, Hershkowitz, & Simantov, 1981). Copulation of sexually naïve rats to one ejaculation results in sensitized dopamine release and greater induction of the immediate-early gene product Fos (a marker of neuronal activation) in the nucleus accumbens (NAc) in response to a female behind a screen, relative to males allowed to intromit only during their first experience or that remain sexually naïve (Biały & Kaczmarek, 1996; Bradley & Meisel, 2001; López & Ettenberg, 2002). Males allowed 10 multiejaculatory experiences with sexually receptive females have increased numbers of dendritic spines (and therefore synapses) in the NAc relative to males allowed one multiejaculatory experience. Males

Fig. 4 Effects of acquiring sexual experience under the influence of saline or naloxone (5 mg/kg, ip) on appetitive and consummatory sexual behaviors in OVX female rats primed fully with estradiol and progesterone. Females received six multiejaculatory experiences at 4-day intervals prior to the final test in which all rats received an injection of saline



allowed 16 multiejaculatory experiences have increased glucose metabolism in limbic structures relative to sexually naïve males or those allowed three multiejaculatory experiences (Sakata, Gonzalez-Lima, Gupta, & Crews, 2002). Those data suggest that experience with ejaculation in males activates endogenous opioid reward systems and sensitizes mesolimbic systems associated with incentive motivation in male rats (Robinson & Berridge, 1993). Experience with paced copulation in females appears to activate the same reward and incentive systems. Females that mount sexually inactive males show increased Fos induction in the mPOA, ventromedial hypothalamus (VMH), and medial amygdala, but females that either do not mount or that have learned not to mount over five trials with castrated, sexually inactive males do not show Fos induction in those regions (Afonso, Lehmann, Tse, Woehrling, & Pfaus, 2009).

Sexual experience also activates the cerebellum. Sexually naïve male rats allowed to copulate to one ejaculation at 4-day intervals showed activation of the cerebellar vermis (notably lobule 7) whereas males given non-copulatory exposure to females had relatively little activation (Manzo et al., 2008). Using an identical paradigm, dynamic increases were found in GAD-65 (assessed by RT-PCR), the enzyme that converts glutamate into the inhibitory neurotransmitter GABA, during the first three ejaculations experienced by males that were sexually naïve at the beginning of the experiment (Bolivar-Duarte, Silva, Manzo, & Pfaus, 2012); however, this increase had dropped back to baseline levels by the fourth ejaculation. Thus, the acquisition of baseline rates of sexual behavior in male rats appears to correspond to dynamic reorganization of the cerebellar vermis, consistent with the critical role of the cerebellum

in motor habit learning (Salmon & Butters, 1995). It is tantalizing to consider that the particular pattern of sexual responding that crystallizes in animals is mediated by dynamic changes in cerebellar function during their initial sexual experiences.

Learning Where to Do It

Whereas the crystallization of responses to unconditioned sexual incentives and copulatory behavior itself appears to be conditioned by genital stimulation, learning where to find sex partners, or optimal places to experience copulation, are conditioned by sexual pleasure or reward. Contextual factors, such as settings, are important components of positive sexual experiences for both men and women (e.g., Basson, 2001; Hoon, 1984; Kinsey, Pomeroy, & Martin, 1948; Kinsey, Pomeroy, Martin, & Gebhard, 1953; McCarthy, 1977). Salient cues in the environment may be associated with sexual reward in such a way that they increase arousal or desire directly in their presence. Such is the case with places that are associated with sexual gratification. Animals often display a preference to remain in a context that has been paired consistently with access to a reward (e.g., drugs of abuse, highly palatable foods, a mate) over a context that has not. This conditioned place preference (CPP) is typically demonstrated in an apparatus with two distinctive compartments that are connected to either side of a third neutral compartment (Fig. 5). During training, the compartments are paired differentially with unconditional stimuli (e.g., one side is paired with a sex partner, food, or a rewarding drug, and the other side is paired with either

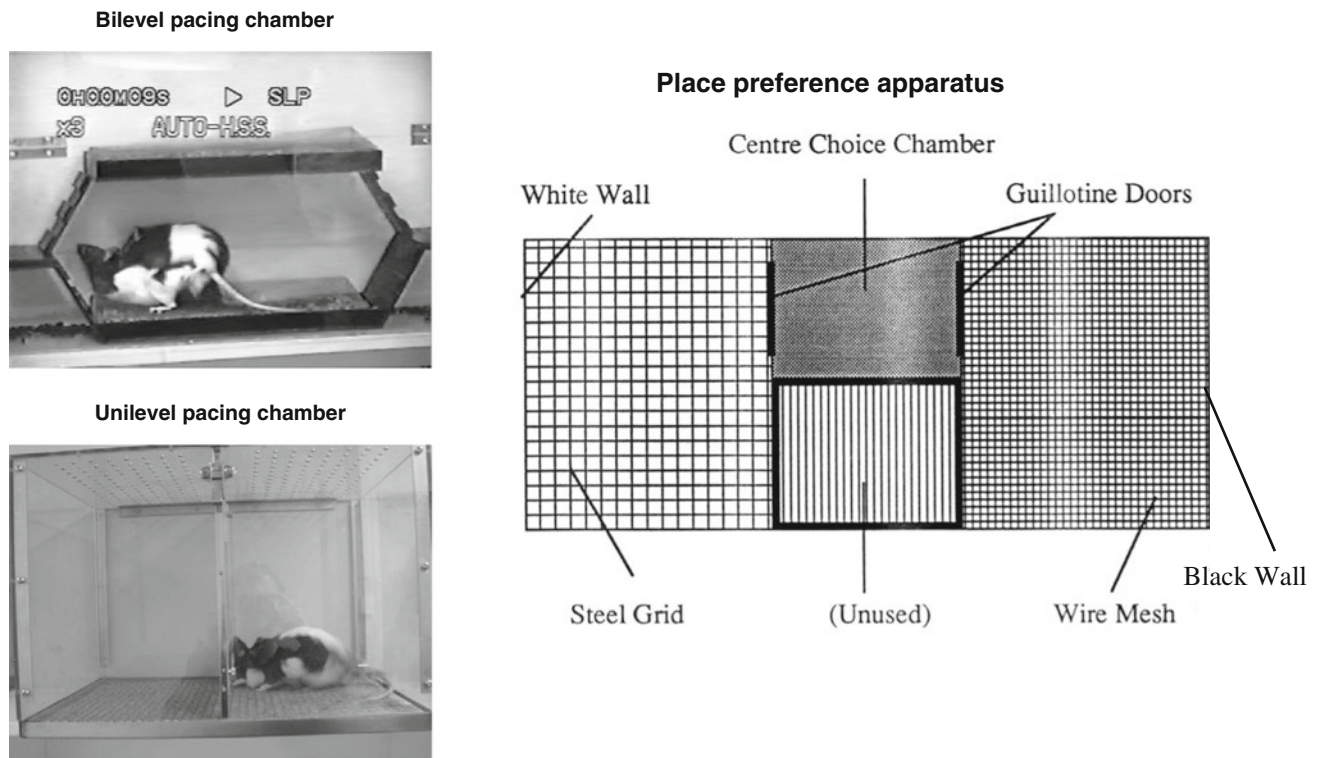


Fig. 5 Apparatus used to test CPP. Rats are allowed different types of copulatory experience in either bilevel or unilevel pacing chambers after which they are transferred to one side of a CPP box. On alternating trials, rats receive 15 min of no copulation in the pacing chamber, after which they are transferred to the other side of the CPP box. On the final test, rats are placed

into the central start compartment, the guillotine doors raised, and rats are allowed to roam freely from one side to the other over a specified amount of time. The amount of time spent in each compartment is marked by photo-beam breaks between the compartments, and tabulated automatically

nothing or a control manipulation). On the final test, the animal is placed into the neutral compartment with the two doors on either side opened to allow free access to either compartment. CPP is said to have developed if the subject spends significantly more time in the reward-paired compartment than the other compartment. Stimuli or events that are capable of supporting CPP are referred to as “rewards” rather than “reinforcers,” because the subject has never been required to move into the paired compartment to experience them. Thus, CPP is not reinforced, per se, because it is displayed spontaneously on the final test. However, the increased time spent in the side paired with reward is clearly conditional upon the Pavlovian association of those contextual cues with the reward state.

In male rats, sexual CPPs have been established using two different conditioning procedures. In one, copulation to ejaculation is allowed to occur within one of the distinctive environments and this environment is subsequently preferred over one in which no copulation occurred (Everitt, 1990). CPPs developed by this procedure are referred to as “copulatory CPPs.” Copulatory CPPs can be maintained by intromissions alone whereas prevention of intromission disrupts a previously established CPP (Hughes et al., 1990). In a second procedure, male rats are allowed to copulate to ejaculation in a separate testing chamber and are then transferred

immediately to one distinctive compartment of the CPP apparatus. As with the first testing procedure, the other distinctive compartment is paired on intermediate days with a control condition (usually no copulation). Following such training, the compartment paired with copulation is preferred over the other compartment (e.g., Ågmo & Berenfeld, 1990). A CPP induced by this procedure is referred to as a “post-ejaculatory CPP.” Demonstrations of post-ejaculatory CPPs might appear puzzling at first glance because the CS (i.e., the distinctive environment) is presented after the UCS (copulation to ejaculation), in what learning theorists call “backward conditioning” (that would not be expected to yield conditional responding to the environment). However, if the neural reward state induced by ejaculation is the unconditional stimulus, then the pairing of environmental cues with it is simultaneous. Thus, post-ejaculatory CPP can be accounted for by the rules of Pavlovian conditioning.

CPPs have also been demonstrated in female rats and hamsters. Oldenburger, Everitt, and de Jonge (1992) found that when copulation occurred within one of the distinctive compartments of a CPP apparatus, female rats showed a weak CPP. Subsequently, Paredes and Alonso (1997) and Paredes and Vazquez (1999) demonstrated a robust CPP in female rats that depended on whether the females were able to pace the rate of copulation with-

out having to employ defensive behaviors. This was accomplished using unilevel pacing chambers bisected by a Plexiglas divider with one or more small holes that only the female can pass through (Erskine, 1985, 1989; Paredes & Alonso 1997; Paredes & Vazquez, 1999). The male was sequestered on one side of the chamber and the female was then free to pace the copulatory contact by running from side to side whenever she wanted. Like males, females acquired a strong preference for a distinctive environment only if they were placed into the CPP box immediately after paced copulation. No preference was found if the copulation was unpaced prior to placement in the CPP box (meaning that it had occurred in the same pacing chamber but without the divider). Thus, for a female rat, CPP develops only if she has been able to control the initiation and rate of copulation freely without having to use defensive behaviors.

Although a sexually vigorous male rat is a clear UCS for approach and solicitation in female rats (e.g., Ågmo, 1999), contextual cues associated with pacing elicit a conditioned sexual reward state in those females. However, these results may also indicate the presence of an unconditional aversive state during unpaced copulation. To examine this possibility, Afonso, Woehrling, and Pfau (2006) allowed female rats to copulate in two unilevel pacing conditions using Plexiglas dividers that had either 4 holes or 1 hole. This was done to eliminate the possibility of an “aversive” state resulting from unpaced copulation. Trials were conducted sequentially at 4-day intervals and each pacing condition was paired with one of the distinctive sides of a CPP apparatus, in a counterbalanced fashion. Control groups contrasted the 4-hole or 1-hole condition with a no-divider condition (as was done by Paredes & Alonso, 1997).

Control females developed significant CPP for either the 1-hole or 4-hole condition, relative to unpaced copulation with no divider. Those control data replicate the findings of Paredes and Alonso (1997) and indicate that both the 4-hole and 1-hole condition were rewarding relative to the unpaced (no divider) condition. However, they do not rule out the possibility that the real distinction being made was between an aversive condition (unpaced copulation) and a rewarding condition (paced copulation). This was addressed in the group allowed to contrast the 4-hole vs. 1-hole condition. In this group, females developed significant CPP for the 4-hole condition relative to the 1-hole condition, suggesting strongly that copulatory CPP reflects a true sexual reward state in females. Similarly, Jenkins and Becker (2003) found that female rats developed significant CPP for paced relative to unpaced mating, but also for unpaced mating in which the experimenter removed the male for a period that approximated the female's imposed interintromission interval, relative to unpaced mating in which male removal did not occur. Thus, female rats develop CPP for sex at their own preferred intervals. Taken together with the results of Matthews et al. (1997), these data suggest that reward comes from the sexual stimulation that females receive, namely mounts with intromission, so long as that stimulation occurs at the desired time intervals.

What about paced copulation leads to CPP in females? Meerts and Clark (2009) reported that artificial vaginocervical stimulation (VCS) applied with a 1 ml syringe plunger at 200 g of pressure for 2 s at 30-s intervals, for a total of 15 stimulations, induced a reliable CPP in OVX females primed with estradiol and progesterone. Given that VCS stimulates both internal clitoris and cervix, we asked whether clitoral stimulation (CLS) alone could induce CPP (Cibrian-Llenderal et al., 2010; Parada, Chamas, Censi, Coria-Avila, & Pfau, 2010). In these studies, CLS was administered either with a lubricated paintbrush or a small cotton-tipped vibrator at preferred intervals for 10–15 min over 5–6 reinforced sessions. Both types of stimulation induced robust CPP. Importantly, clitoral reward can be induced in OVX females with or without hormone priming (Parada, Abdul-Ahad, Censi, Sparks, & Pfau, 2011), indicating that sexual reward is independent of steroid priming, although such priming would normally be required for females to experience CLS from mounts with pelvic thrusting (Pfaff, Montgomery, & Lewis, 1977).

Domjan and Hall (1986) demonstrated that male Japanese quail will stay in the vicinity of a window in their home cage through which they could see a sexually receptive female during a pre-copulatory period. However, this behavior developed only if the males had the opportunity to copulate with the female after the pre-copulatory period. A variant of this procedure, similar to that used to study anticipatory motor responding in rats, was used by Balthazart, Reid, Absil, Foidart, & Ball (1995) to study the role of hormones and brain dopamine systems in conditioned sexual behavior in quail. Male quail were placed into a chamber that contained a window and sliding door at one end through which the male could see a sexually receptive female. After a 10-min period, the sliding door opened and the animals could interact freely. As in Domjan and Hall (1986) and Mendelson and Pfau (1989), only males that copulated with the females during this period developed the behavior, in this case, a preference to stay close to the window in the pre-copulatory period of subsequent tests. Castrated males did not develop this conditioned proximity behavior nor did males that did not copulate. Castration also reduced the time spent near the window males trained prior to castration, and subsequent replacement with testosterone or estradiol restored the behavior. Subsequently, Castagna, Ball, and Balthazart (1997) reported that nomifensine, a dopamine re-uptake inhibitor, decreased the appetitive social proximity response, but increased the frequency of mount attempts. In contrast, amfonelic acid, a compound that enhances dopaminergic tone, increased aspects of both appetitive and consummatory sexual behaviors. Thus, brain dopamine systems in birds and mammals seem to have analogous functions in the control of appetitive or conditioned sexual approach behaviors.

Although both copulatory and post-ejaculatory CPP procedures produce effects of similar magnitude in male rats, there are differences in the underlying neurobiology. The opioid receptor antagonist naloxone disrupts both copulatory and post-ejaculatory CPPs, but in different ways. Ågmo and Berenfeld (1990) found that the development of post-ejaculatory CPP was blocked

by injections of naloxone prior to each training session. Conversely, the development of a copulatory CPP was unaffected by naloxone prior to each training session (Meharrra & Baum, 1990). However, once a copulatory CPP had developed, its expression was blocked by naloxone injections prior to the final test (Hughes et al., 1990; Meharrra & Baum, 1990).

There is also evidence that the site of action of naloxone is different for these effects. Ågmo and Gomez (1993) found that naloxone's disruption of the development of post-ejaculatory CPP occurred following infusions into the mPOA whereas infusions of naloxone into this brain region did not disrupt the expression of a copulatory CPP (Hughes et al., 1990). In females, pacing-related CPP was blocked by systemic injections of naloxone (Paredes & Martinez, 2001), or following infusions of naloxone to the mPOA, VMH, or medial amygdala, but not the NAc (Garcia-Horsman, Ågmo, & Paredes, 2008). These data suggest that common opioid systems in the brains of male and female rats are activated by sex-related cues (Paredes & Martinez, 2001) and constitute a primary reward signal. Indeed, as mentioned above, repeated ejaculations increase whole-brain endorphin content in male rats (Szechtman et al., 1981). As with approach behaviors toward sex-related odors, castration disrupts the expression of a copulatory CPP on the first postoperative test in male rats (Hughes et al., 1990; Miller & Baum, 1987), and acquisition of a copulatory CPP was blocked by naloxone in castrated, but not gonadally-intact, male rats (Meharrra & Baum, 1990). Endocrine responses have also been examined in male rats following exposure to contextual stimuli associated with copulation. Kamel, Mock, Wright, & Frankel (1975) reported that serum testosterone, luteinizing hormone, and prolactin levels were elevated after 45 min of exposure to an arena in which prior copulation occurred. Although dopamine antagonists have not been reported to alter the development or expression of copulatory CPPs in either male or female rats, or postejaculatory CPPs in male rats (Ågmo & Berenfeld, 1990; Garcia-Horsman & Paredes, 2004), Meisel, Joppa, and Rowe (1996) found that the development of a copulatory CPP in female hamsters was blocked by injections of the D2-receptor antagonists sulpiride or raclopride prior to each training session.

In summary, sexual reward in the form of ejaculation in male rats, or paced copulation in female rats, involves the activation of brain opioid systems. A similar effect may underlie the copulatory reward in male and female Japanese quail. This is reminiscent of the generalization made by some opiate addicts that the drug effect reminds them of the pleasure experienced at orgasm (Pfaus & Gorzalka, 1987), an effect referred to explicitly as a "pharmacogenic orgasm" by Chessick (1960). As with the reward state induced by heroin or cocaine, both male and female rats spend more time in contexts associated with state induced by sexual reward. Moreover, conditioned contextual stimuli associated with those reward states activate pituitary and gonadal hormone release in male rats, suggesting a priming or "occasion-setting" response that gets male rats ready to copulate.

Learning When to Do It

When to have sex seems straightforward in terms of arousal, desire, and opportunity. If you have all three, you are all set. But that is a big "if"! Sexual arousal is almost always conditional upon the provoking stimuli being adequate to activate the necessary sympathetic (e.g., increased heart rate) and parasympathetic (e.g., genital blood flow) divisions of the autonomic nervous system. Desire often depends on whether the stimuli are competent as incentives and what else might be going on at the time. And opportunity is often fleeting.

Sexual arousal and desire are constrained further by experience. In addition to habituation that occurs when one does the same thing over and over, or the inhibition that occurs during a refractory period, the reward-related occasion setting mentioned above may well underlie the ability of external cues (and in their most obvious manifestation, fetish objects) to control sexual arousal and thereby control when to have sex. Inanimate objects, such as articles of clothing, particular forms and textures, and, in fact, any antecedent tactile, olfactory, auditory or visual stimulation, can during an animal's initial experiences with sexual reward, come to control both arousal and desire. Thus, the development of paraphilias may well follow the same pattern of Pavlovian and operant sexual learning discussed above.

Some opportunity is constrained by hormonal activation. Obviously, having a sexual "heat" makes things simple, constraining sexual arousal, desire, and behavior to the periovulatory period when estrogens and progestins can stimulate it (Pfaff, 1980, 1999). However, despite the fact that women's desire peaks around the time of ovulation (Stanislaw & Rice, 1988), we and some of our primate cousins (e.g., rhesus macaques, Goy, 1978) can have sex anytime throughout the cycle. And males *can* learn when it is appropriate and not appropriate to attempt copulation depending on the receptive versus defensive behaviors of the female (Pfaus & Pinel, 1989). Male rats also display "psycho-genic" or noncontact erections in response to unconditioned sex odors of sexually receptive females (Sachs, Akasofu, Citron, Daniels, & Natoli, 1994), an effect that is facilitated mildly by brief olfactory, visual, and auditory contact with inaccessible receptive females, moderately by experience with mounting alone, and dramatically by full copulatory experience to ejaculation (Sachs & Liu, 1997). Thus, although erections can be induced by presumably "prepotent" unconditional olfactory stimuli, the stimuli become far more effective—perhaps even sensitized—by pairing them with the state induced by sexual reward.

What about other sensory cues? In his classic work *Psychopathia Sexualis*, Krafft-Ebing (1886/1929) presented numerous case histories (almost all male) of fetish development in which particular inanimate objects, actions or states of arousal induced by painful stimulation (e.g., spanking, piercing the skin, etc.) or other tactile sensations (e.g., the feeling of feathers) became associated with an individual's first sexual erection or first set

of sexual experiences to orgasm. In some of those cases, the initial experience occurred prior to the normative age of puberty, suggesting that the individual may well have been in precocious puberty or that at least his genital responses were in a state of relative sexual awakening. Often, the individual would masturbate to ejaculation while reminiscing about the early event and/or fantasizing about experiencing it again with others. Of course, the fetish became problematic when it was attempted with an unwilling partner or when the individual was caught engaging the fetish in public (e.g., hiding in bushes and spilling water from a pitcher on an unsuspecting woman's bustier). The case histories were often accompanied by a psychological profile of the individual, noting a history of odd behavior and any potential eugenic abnormalities (e.g., low level cognitive functioning) that ran in the family. Given that such behavior was not "normal" in its day, and that the individual appeared to suffer from some genetic basis for abnormal behavior in general, it was easy to conclude that the sexual behavior was a "psychopathic" symptom of a more general genetic-based syndrome. And, after all, how could it serve reproduction if an individual can't get an erection unless he or his partner wears leather or lace? Surely, such objects did not play a central role in our species' evolutionary sexual history.

An alternate hypothesis from an incentive-based analysis is that *anything* that predicts sexual reward becomes an occasion setter for sexual arousal (and maybe desire too). But here is where the situation gets dicey. Whereas sexual reward may be studied objectively in animals, in humans the notion is muddled in peculiar definitions, along with particular phases of the human sexual response (Pfaus, 1999). It is also the case that human subjects in laboratory settings show relatively weaker effects than are typically observed in animals. This may be due to the fact that the typical human subject has already acquired sexual experience prior to the study, an effect that reduces the possibility of robust conditioning. Thus, the sexual UCSs used may not create a "strong enough" sexual reward state to condition the particular CSs, especially as they are not occurring during an early critical period of sexual behavior development.

There have been several notable attempts to condition sexual arousal in humans (see Hoffmann, 2012). Rachman (1966) and Rachman and Hodgson (1968) found that following pairing with erotic visual slides, a pair of women's boots was able to elicit erections in men. Similarly, McConaghy (1970, 1974) demonstrated conditioned erection elicited by colored circles or squares paired previously with erotic videos or still pictures in heterosexual and homosexual men. A particularly informative study by Kantorowitz (1978) examined the nature of association between the UCS and conditioned arousal induced by still pictures. For each subject, three different slides were paired with the plateau, absolute refractory, and later resolution stages during and after masturbation to orgasm. During subsequent testing, stimuli paired with the plateau phase produced an increase in penile erection whereas stimuli paired with the refractory phase produced a decrease in erection. Stimuli paired with the later resolution phase had no

effect. Remarkably, those responses were still present after 3 months. Lalumière and Quinsey (1998) reported significant conditioned genital arousal in heterosexual men to a picture of a moderately attractive, partially nude woman that was paired with a video depicting highly arousing sexual interaction. A control group that received access to the picture alone (without the video) showed habituation.

Regarding women, Letourneau and O'Donohue (1997) failed to find significant effects of conditioning on sexual arousal. However, it was noted that the UCSs (erotic films) produced only moderate levels of arousal whereas in studies with male subjects such stimuli produced high levels of arousal. Thus, this failure to demonstrate conditioned arousal in women may have been due to an ineffective UCS. Indeed, Both, Laan et al. (2008) found that neutral pictures of male headshots paired with 2 s of intensely pleasurable vibrotactile CLS produced greater vaginal pulse amplitude (VPA) during extinction in the paired versus unpaired groups. In another study, stimuli were presented briefly (30 ms), followed by a masking stimulus (Both, Spiering, et al., 2008). Although only the paired group showed increased VPA to the CS during the first extinction trial, there was no increase in the conscious affective value of the stimulus. Finally, Hoffmann, Janssen, and Turner (2004) varied the duration and relevance of a CS (abdominal area vs. a gun) that was paired with short erotic film clips in both men and women. Interestingly, when the stimuli were presented subliminally for brief durations, the relevant abdominal stimulus increased arousal in both men and women. However, when the stimuli were presented for longer periods prior to the erotic film clips, a sex difference emerged in which the relevant CS alone (abdominal area) induced genital arousal in men, but the presumably irrelevant stimulus alone (gun) induced genital arousal in women. This latter effect may indicate that women require CSs that increase autonomic arousal to a higher extent than men, a potential corollary of the "discordance" experienced by women, but not men, between genital and subjective sexual arousal (Chivers & Rosen, 2010).

Several studies have attempted to demonstrate instrumental control of sexual arousal in men and women. Rosen, Shapiro, and Schwartz (1975) found that given feedback and contingent monetary reinforcement, men learned to become sexually aroused in the absence of erotic stimuli. Other studies have found that men can suppress (Rosen, 1973; Rosen & Kopel, 1977) or increase (Reynolds, 1980) penile erection with instructional feedback; however, those studies failed to demonstrate learning effects across trials. Given similar instructions, women can increase their vaginal pulse in the absence of erotic stimulation (Zingheim & Sandman, 1978) or decrease vaginal pulse in the presence of erotic stimulation (Cerny, 1978), but, again, no learning effects were reported. In summary, the evidence regarding instrumental control of sexual arousal is limited to the one report in which monetary reinforcement and feedback were provided.

Can animals show sexual arousal in response to cues associated with sexual arousal or reward? Graham and Desjardins

(1980) placed sexually naïve male rats in a chamber scented with a methyl salicylate (wintergreen oil) CS for 7 min before transferring them to an adjacent chamber with an unscented receptive female for 15 min of copulation (UCS). Control males received CS alone, UCS alone or handling. Training occurred once a day for 14 days. On the 15th day, males were placed in either the CS or UCS chamber and trunk blood was taken within 15 min to assay for luteinizing hormone and testosterone. Exposure to females increased concentrations of both hormones in plasma whereas the CS was effective only in males in the paired group. Sachs and Garinello (1978) reported that placing male rats into a chamber in which copulation had previously occurred dramatically reduced the latency for males to display penile erections. Male rats trained to associate an almond odor with copulation to ejaculation (see below) initiated copulation faster with an almond-scented receptive female than with an unscented receptive female (Kippin & Pfaus, 2001b). Similarly, male marmosets trained to copulate to ejaculation with lemon-scented receptive females display erections and increased place preference in response to the odor alone relative to unpaired males (Snowdon, Tannenbaum, Schultz-Darken, Ziegler, & Ferris, 2011).

Placement of male rats into a holding cage has been used as a conditioned contextual stimulus to signal non-copulatory exposure to a receptive female behind a wire-mesh screen (Zamble, Hadad, Mitchell, & Cutmore, 1985; Zamble, Mitchell, & Findlay, 1986). Placing males into the holding cage prior to a final test of unrestricted copulation resulted in significantly shorter latencies to intromit and ejaculate relative to males placed directly from their home cages into the copulatory condition. Subsequent studies found that second-order conditioned stimuli (e.g., a plastic toy fish found in the holding cage) were effective in enhancing the same measures of arousal (Zamble et al., 1985) and such conditioning in sexually naïve or sluggish males could increase the proportion of males that copulated on a subsequent test (Cutmore & Zamble, 1988). Hollis, Cadieux, and Colbert (1989) demonstrated that repeatedly pairing a light with non-contact exposure to a receptive female resulted in conditioning of sexual behavior in male gouramies, a type of Labyrinth fish. They found that males receiving the conditioning treatment displayed significantly lower latencies to initiate copulation and lower levels of aggression towards females when the CS was presented before access to a female. Similar results have been demonstrated in Japanese quail. Male quail that received repeated exposure to females following the presentation of a CS light displayed significantly shorter latencies to initiate copulation when the stimulus was present compared to when it was absent (e.g., Domjan, O'Vary, & Greene, 1988).

Finally, if male rats are given their first copulatory trials wearing a Velcro tethering jacket, the jacket will become a CS+ for sexual arousal. Sexually naïve males in the paired group were given nine multi-ejaculatory trials at 4-day intervals with the jacket on, whereas males in the unpaired group received the same number of trials without the jacket. On the 10th trial, males in both groups

were assigned randomly to two subgroups, one with the jacket on and one with the jacket off, and given a final 30-min test of copulation. Males that had been trained without the jacket displayed normal baseline rates of copulatory behavior with or without the jacket, as did males trained with the jacket that had the jacket on during the final test (Fig. 6). In contrast, males trained with the jacket that had the jacket off during the final test displayed a severe copulatory deficit, including significantly increased mount, intromission, and ejaculation latencies, a decreased number of conditioned level changes, and a reduction in the proportion of males that achieved ejaculation during the test. The pattern suggests significantly diminished sexual arousal and desire and a failure to engage sympathetic tone for ejaculation (Pfaus, 2009). Thus, the jacket had become a CS+ for sexual arousal only in the paired group that had their early formative sexual experiences with it.

The ability of neutral olfactory and tactile stimuli associated with sexual reward to direct sexual arousal in males of a variety of species indicates a high degree of plasticity in the neural systems that control sexual behavior in general, rather than a specific genetic difference that makes some males susceptible to conditioning. Could this plasticity extend to the development of preferences for individual partner-related cues?

Learning *Who* to Do It With

Although it is clear that animals learn what to do sexually and where and when to do it, the question of *who* they prefer to do it with seems like it should be less affected by experience and more by innate, genetic, and species-specific causes geared toward reproductive success. And in the case of homosexuality, it would seem that innate causes play a large role in determining sexual orientation long before sexual activity and sexual reward is initiated. Indeed, sexual partner preferences that are not geared toward reproduction (as in homosexuality) or that are highly constrained by the presence or absence of inanimate objects (as in many paraphilias) should either not exist or should confer some other reproductive benefit. One such benefit could be related to kin selection (e.g., Wilson, 1975), as in the “gay uncle hypothesis” that has received much attention but little empirical support in Western culture (Bobrow & Bailey, 2001), although it appears to be supported among the Samoan *fa'afafine* (Vasey & VanderLaan, 2010). Yet, from a reward-based incentive view, there is absolutely no reason why partner-related cues that can be detected at a distance (such as sex, gender, race, hair color or length, facial features, body type) or more proximally (such as a multitude of personality characteristics) cannot also become conditioned by early experience with sexual reward, although there are important developmental constraints that make the preference for gender far less amenable to conditioning (see below).

Evidence of this in animals would provide strong support for the alternative hypothesis put forth here that the “genetic” basis of sexual preference rests in reward-based learning, as do

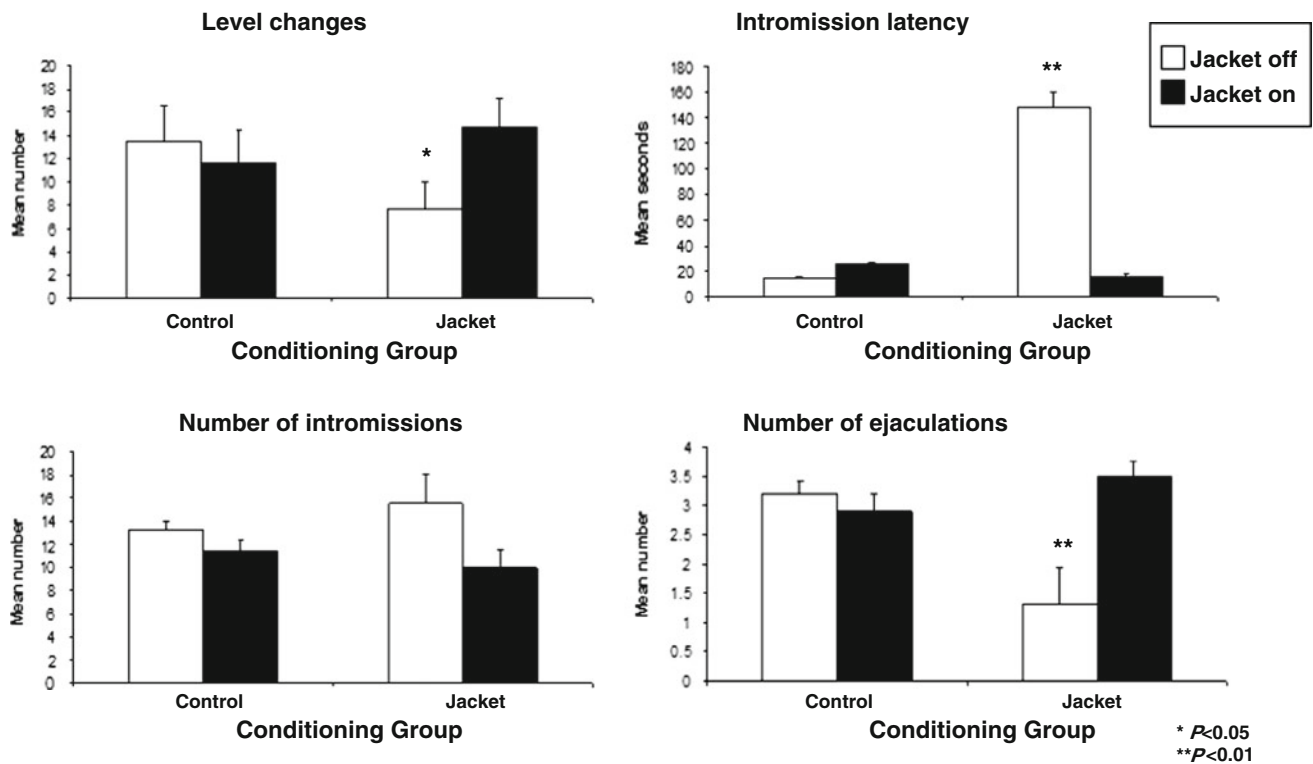


Fig. 6 Appetitive and consummatory sexual behaviors by male rats given their first nine trials of sexual behavior with or without a rodent jacket. On the final test, rats in each group either had the jacket on or off. * $p < .05$ between jacket on and jacket off conditions

virtually all other motivational and regulatory functions performed by organisms on this planet. This does not make it a “choice” except at an epiphenomenological level of interpretation. Once conditioned, sexual preferences should feel as natural and “hardwired” as one’s food preferences. And, in humans, the conditioning does not occur overnight, but rather through a progressive and iterative process that begins well before the periadolescent awakening of sexual arousal, and becomes relatively refined and fixed during formative experiences with masturbation and orgasm prior to actual sexual activity with other people, when further refinement and fixing occur. Interpersonal sexual reward would thus reinforce the already-established template.

Features Conditioned by Sexual Reward

To study the effects of Pavlovian conditioning on sexual preferences, we took as our lead the findings of Graham and Desjardins (1980) above. Could a male rat’s primary sexual experiences with scented females come to elicit a preference for scented partners in a choice paradigm?

Kippin, Talianakis, Schattmann, Bartholomew, and Pfaus (1998) trained male rats to associate an almond odor smeared on the back of the neck and anogenital area of females that were either sexually receptive or non-receptive. Males in the Paired group received sequential access to scented receptive and unscented non-receptive females at 4-day intervals for nine trials each. Males in

the Unpaired group received the opposite order of association, such that the scent was on the non-receptive females and no scent was on the receptive females. Another group of males received Random pairing of almond odor with the receptive and non-receptive females. On the final test, males were placed into a large open field for a 5-min acclimation period, after which two receptive females were placed equidistant from the male, one scented and the other unscented. The choice of female for first mount, intromission, and ejaculation and the distribution of mounts, intromissions and ejaculations throughout the 30-min open field test were recorded.

Males in all groups copulated with the females closest to them, displaying no significant preference of female to receive their mounts and intromissions. However, males in the Paired group ejaculated preferentially with the *scented* females, choosing them significantly more than the unscented females to receive their first ejaculations, and more often to receive their ejaculations throughout the test. Males in the Unpaired had the opposite preference, choosing to ejaculate first, and more times overall, with the unscented females. Males in the Random group did not show any ejaculatory preference. Interestingly, males in the Unpaired group displayed a preference to mount and intromit with the unscented females on the final test, suggesting that the almond odor had acquired conditioned inhibitory properties that dampened their interest in now-receptive females bearing the odor. In fact, those males showed robust avoidance behavior toward the scented

females during the final test (an effect that was responded to with increased solicitations on the part of those females).

Subsequent studies established that the conditioned ejaculatory preference (CEP) developed only if males were in the vicinity of the females during their post-ejaculatory refractory period (Kippin & Pfau, 2001a) and was more robust if males had more ejaculations (Kippin, Samaha, Sotiropoulos, & Pfau, 2001). It did not develop if males were allowed only to intromit or if the female was removed immediately after ejaculation. An analysis of the conditioned response showed that males became “choosy” during the last three mounts prior to ejaculation and directed those mounts at the female bearing the familiar cue (Kippin & Pfau, 2001b). This is a period in which males are sensitive to their impending ejaculation and emit a 50 kHz call that attracts females immediately prior to ejaculation (McGinnis & Vakulenko, 2003). Using unilevel pacing chambers bisected by a Plexiglas partition that contained either 1 or 4 holes, males were shown to develop significant CEP only when trained in the 1-hole condition, in which they had to wait longer between intromissions, had more intromissions before ejaculation, and longer ejaculation latencies compared to males in the 4-hole condition (Ismail, Gelez, Lachapelle, & Pfau, 2009), suggesting that the ejaculatory reward state may rest on increased parasympathetic arousal during copulation, something that occurs naturally in bilevel pacing chambers as the males must chase the females in order to copulate with them (Pfau, Mendelson et al., 1990). Finally, Erskine (2005) raised the issue of whether such partner preferences might be displayed in more natural contexts (e.g., between different strains of partner). So, instead of neutral olfactory cues on the same strain of partner, we varied the strain of partner (pigmented Long-Evans rats vs. albino Wistar rats) associated with the ejaculatory reward state (Ismail, Jones, Graham, Sylvester, & Pfau, 2011). Pigmented Long-Evans males received nine multi-ejaculatory copulatory training trials with either pigmented or albino females in a 1-hole pacing chamber. In a final open field test with two females, one pigmented and one albino, the males chose the strain of female associated with the 1-hole condition significantly for their first ejaculation. However, the males chose pigmented females significantly for their second ejaculation only if they were associated with the 1-hole condition. This suggests that a degree of “assortative” choice (in which animals have a natural preference for less related members of their own strain, or at least that look a little like them) may strengthen the development of CEP (for a discussion of optimal in- and out-breeding as it relates to assortative mating, see Bateson, 1983).

Association with reward can also reduce the impact of aversive stimuli. For example, although rats initially reject a bitter morphine solution that replaces their drinking water, they learn to like the bitter taste as the morphine reward state sensitizes over time (Zellner, Berridge, Grill, & Temes, 1985). The sexual reward state in males is clearly powerful enough to condition a preference for a neutral odor, so we asked whether it could also blunt the impact of an aversive odor like cadaverine, a polyamine that is produced in decaying flesh. Rats are well known to bury aversive

smelling objects such as noxious food, dead conspecifics, and anesthetized conspecifics speared with cadaverine (Wilkie, MacLennan, & Pinel, 1979), so cadaverine is considered unconditionally aversive.

We gave male rats their first nine sexual experiences with either cadaverine-scented females (unanesthetized, of course), or unscented control females. A third group of males was given habituation to the cadaverine odor in their home cages and copulation trials with unscented females (Pfau et al., 2001). On the 10th trial, males from the three groups were placed into an open field and allowed to copulate freely with two receptive females, one scented with cadaverine and one unscented. Males in the control group pursued the unscented females selectively and ejaculated exclusively with them. Males that had been habituated in their home cages did the same. In contrast, males that had copulated previously with cadaverine-scented females pursued, copulated, and ejaculated with both females, indicating that the aversive properties of cadaverine had been diminished after pairing with sexual reward. Four days later, males received a wooden dowel that had been saturated in cadaverine into their home cages. Males in the control and habituated groups avoided the dowel, and some attempted to bury it. In contrast, all males in the cadaverine-paired group made contact with the dowel and more than half picked it up and gnawed on it, as they would if the dowel had been laced with something hedonically positive like estrous vaginal secretions or chocolate.

First and foremost, these findings demonstrated that a simple Pavlovian conditioning paradigm can modify male rat sexual strategies away from an assumed innate polygamous preference for novel females toward a preference for familiar females. Second, they showed that male rats can distinguish copulation from mating, as the conditioned preference was not displayed in the Paired group for choice of female for mounts and intromissions but rather for ejaculations. Third, the association of the odor with sexually non-receptive females induced a conditioned inhibitory state that compelled males to avoid sexually receptive females bearing the odor on the final test. Fourth, the state induced by ejaculation was the critical UCS, especially if it occurred on a background of high arousal. Finally, an unconditionally aversive odor (cadaverine) was made less aversive and possibly conditionally appetitive by pairing with sexual reward.

Female rats also show olfactory conditioned partner preference for males associated with a pacing-induced reward state (Coria-Avila, Ouimet, Pacheco, Manzo, & Pfau, 2005). This was accomplished easily in unilevel pacing chambers in which the paced condition involved the placement of either a 1-hole or 4-hole Plexiglas divider through which the female could regulate the initiation and rate of copulation. The non-paced condition involved copulation in the same chamber but without the divider. Females in the Paired group were given paced copulation with males that have had the almond odor smeared on their necks and anogenital area versus non-paced copulation with males that have had distilled water smeared on the same areas. After four paced versus non-paced trials, females were placed into a large

open field with two tethered males, one scented and the other unscented, and choice of male to solicit, copulate with, and receive ejaculations from, was recorded. Females for which the odor was paired with the paced condition selectively solicited, copulated with, and received ejaculations from the scented male. Females that had the odor explicitly unpaired or paired randomly with pacing did not display a preference.

As with males, females showed a similar preference for strain cues associated with paced copulation (Coria-Avila et al., 2006), although it was stronger if the strain associated with paced copulation was their own. Interestingly, in that study, pigmented or albino females solicited whichever strain of male was associated with paced copulation, but received ejaculations preferentially from males of their own strain and only if that male had been associated with paced copulation. This also revealed a degree of assortative choice, especially for mating, and showed that females, like males, can differentiate copulation from mating. Finally, female rats that experienced manual CLS in the presence of a cotton gauze pad soaked in almond extract chose to copulate selectively with almond-scented males over unscented males during their first sexual experience in a large open field with both males (Parada et al., 2011). Interestingly, they did not show a preference to receive the scented male's ejaculations, suggesting that the VCS received from males during paced copulation induced a further reproductive or mate choice. It is not yet known whether this stems from specific stimulation of the cervix (and pelvic nerve) or from full stimulation of internal and external aspects of the clitoris. Experience with paced, relative to non-paced, copulation in unilevel chambers induces significant neurogenesis in the granular layer of the accessory olfactory bulbs (Corona, Larriva-Sahd, & Paredes, 2011), a region known to contain intrinsic memory systems related to pheromonal stimulation and recognition of conspecifics (Brennan, Kaba, & Keverne, 1990; Brennan & Keverne, 1997). Thus, as Darwin (1859) suggested, females are indeed more “choosy” than males in terms of choosing a male to copulate and mate with. However, like males, they base this choice on the external (epigamic) characteristics of the male associated with their own experience of a copulatory reward state.

Females also learn inhibitory associations. In addition to the effect of nonreward induced by training under the influence of the opioid receptor antagonist naloxone, sexual frustration in the presence of an inaccessible male can also induce an inhibitory state. Parada et al. (2011) gave sexually naïve female rats five trials of CLS in the presence of a sexually active male scented with almond behind a screen. On alternating days, the females received sham CLS in the presence of an unscented male behind the screen. During the final open field test with two males, one scented and the other unscented, females solicited selectively the *unscented male* and showed a trend to receive that male's ejaculations preferentially. At first glance, these data seem at odds with the fact that CLS induces a reward state. However, it was noted that females attempted to solicit the males behind the screen following CLS during the training trials, which, of course, were not successful because the

male was behind a screen. Thus, it is likely that the female was in a state of frustrated non-reward that she associated with the odor and generalized to the choice of male for her first sexual experience.

Neural Correlates

One of the strengths of the olfactory conditioned partner preference paradigm is that the odor can be presented alone in the animal's bedding or on a cotton gauze pad and neuroanatomical and neurochemical activation in response to the odor examined. This takes the mess of copulation (and interpretation based on different types or amounts of sensory stimulation) out of the analysis and makes the study far more cognitive in terms of examining responses made to a second-order conditioned cue. In fact, it is now possible using this paradigm to relate areas of the rat brain activated by the conditioned odor with areas of the human brain activated by visual erotic cues.

We have found significant activation of the immediate-early gene product Fos following presentation of the odor in paired versus unpaired groups in a number of brain regions that constitute a sexual circuit similar to that found activated in fMRI studies of sexual arousal and desire in men and women (e.g., Karama et al., 2002; Ortigue & Bianchi-Demicheli, 2008; Paul et al., 2008). These regions included cortical structures such as the medial prefrontal cortex, piriform cortex, insula, and anterior cingulate gyrus; limbic/motor regions such as the olfactory tubercle, nucleus accumbens, dorsal striatum, lateral septum, basolateral and medial amygdala; hypothalamic regions such as the mPOA, bed nuclei of the stria terminalis, anterior and lateral hypothalamus, and the midbrain anterior ventral tegmentum (a region that gives rise to the mesolimbic dopamine (DA) system) of males (Kippin, Cain, & Pfau, 2003) and females (Coria-Avila & Pfau, 2007) after presentation of the paired odor alone relative to the odor unpaired or random. Previous studies showed these regions to be activated by unconditioned olfactory or genitosensory stimulation during copulation (reviewed in Pfau & Heeb, 1997); thus, their conditional activation by the odor suggests that they are activating a representation of the UCS, as Pavlov (1927) originally suggested for all CS+s. Notably, a nearly identical set of regions is activated by stimuli that predict cocaine or heroin reward (Childress et al., 2008; Garavan et al., 2000), suggesting that these regions function together as a general system for appetitive arousal and desire related to reward.

We suggest that the conditioned cue acts as a “priming stimulus” to activate cortical, limbic, and hypothalamic circuits involved in the facilitation of sexual arousal and desire and/or in the suppression of inhibitory systems (Fig. 7). Some of those circuits involve selective processing of the sexual stimulation that generates the reward state (UCS), the olfactory stimulus (CS), and a system that integrates the CS and UCS so that animals can focus their attention and engage appropriate forward-directed locomotion toward the CS when it is present (Robinson & Berridge, 1993). What is immediately obvious from the figure is that systems for sexual

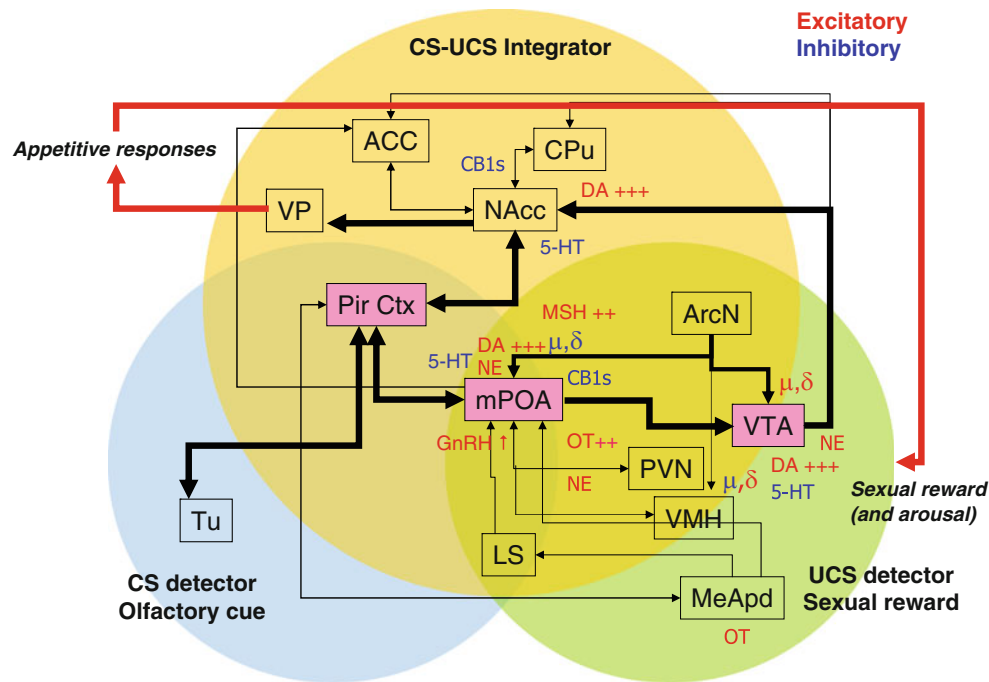


Fig. 7 Neural systems which are critical for the display of conditioned olfactory preferences in the rat. Appetitive behaviors made toward conditioned stimuli lead to sexual reward that is processed by three interactive systems. Two systems process olfactory stimuli and sexual reward relatively independently, whereas a third, mesolimbic DA system, acts to integrate both the conditioned olfactory cue and its rewarding sexual outcome. Three common regions, the piriform cortex, mPOA, and VTA, are activated in male and female rats by conditioned olfactory stimuli. Opioid actions in the VTA potentiate mesolimbic DA activation, whereas opioid actions in the mPOA inhibit sexual arousal and desire. Neurotransmitter systems or their receptors in red/lighter are excitatory for sexual motivation whereas those in blue/darker are inhibitory. Note that opioids can be excitatory in the VTA, inhibitory in the mPOA, or either in the VMH (depending on the receptor type). Dopamine, gonadotropin releasing hormone, melanocyte stimulating hormone, noradrenaline, and oxytocin are excitatory whereas serotonin, opioids, and the endocannabinoids are inhibitory. ACC anterior cingulate cortex; ArcN arcuate nucleus of the hypothalamus; CB1 cannabinoid type 1 receptor; CPU caudate-putamen (striatum); DA dopamine; δ delta opioid receptors; GnRH gonadotropin releasing hormone; LS lateral septum; MeApd posterior-dorsal nucleus of the medial amygdala; mPOA medial preoptic area; MSH melanocyte stimulating hormone; μ mu opioid receptors; NAcc nucleus accumbens; NE noradrenaline; OT oxytocin; PirCtx piriform cortex; PVN paraventricular nucleus of the hypothalamus; Tu olfactory tubercle; VMH ventromedial nucleus of the hypothalamus; VP ventral pallidum; VTA ventral tegmental area; 5-HT serotonin. Adapted from Pfaus, Ismail, and Coria-Avila (2010) (Color figure online)

reward and incentive responding overlap with systems proposed for sexual (and maternal) bonding (e.g., Young & Wang, 2004). These involve the interaction of at least three neurochemical systems, including DA, hypothalamic oxytocin (OT), and opioids that inhibit hypothalamic structures like the mPOA, but sensitize mesolimbic DA systems through a process of disinhibition (Kalivas & Stewart, 1991). This is strikingly similar Fisher's (2000) proposal of three primary emotional systems for mating, reproduction, and parenting.

As reviewed above, inhibition of opioid receptors with naloxone inhibits the development of sexual CPPs in both male and female rats and produces an expectancy of non-reward that inhibits sexual desire and behavior in female rats that have their first sexual experiences with the drug. Naloxone administration during training also inhibits the development of sexually-conditioned ejaculatory and partner preferences in male and female rats (Coria-Avila et al., 2008; Ismail, Girard-Bérault, Nakanishi, & Pfaus, 2009). In these studies, naloxone or saline was administered immediately before a male rat's first 10 multiejaculatory sexual experiences

with a scented partner or during a female's first five experiences of paced copulation with a scented partner (relative to five trials of non-paced copulation with unscented males that were interspersed). Rats were then given a final test in a large open field with two sexually receptive and vigorous partners, one scented and the other unscented, following saline injections. Rats trained with saline injections showed the partner preference reviewed above whereas rats trained with naloxone did not display the preference for the scented partner. In fact, males chose the *unscented* female significantly more frequently for their first ejaculation and females solicited the *unscented* male significantly more frequently and received more mounts, intromissions, and ejaculations from that male.

We have also found conditioned DA release in the NAc of Paired-trained male rats in response to the almond odor, but not in Unpaired-trained males (Fig. 8) and conditioned activation of Fos within parvocellular OT neurons of the paraventricular nucleus (PVN) that likely project to other forebrain regions. Fos was also found activated by the conditioned odor in magnocellular

with a scented partner or during a female's first five experiences of paced copulation with a scented partner (relative to five trials of non-paced copulation with unscented males that were interspersed). Rats were then given a final test in a large open field with two sexually receptive and vigorous partners, one scented and the other unscented, following saline injections. Rats trained with saline injections showed the partner preference reviewed above whereas rats trained with naloxone did not display the preference for the scented partner. In fact, males chose the *unscented* female significantly more frequently for their first ejaculation and females solicited the *unscented* male significantly more frequently and received more mounts, intromissions, and ejaculations from that male.

Dopamine release in the NAc

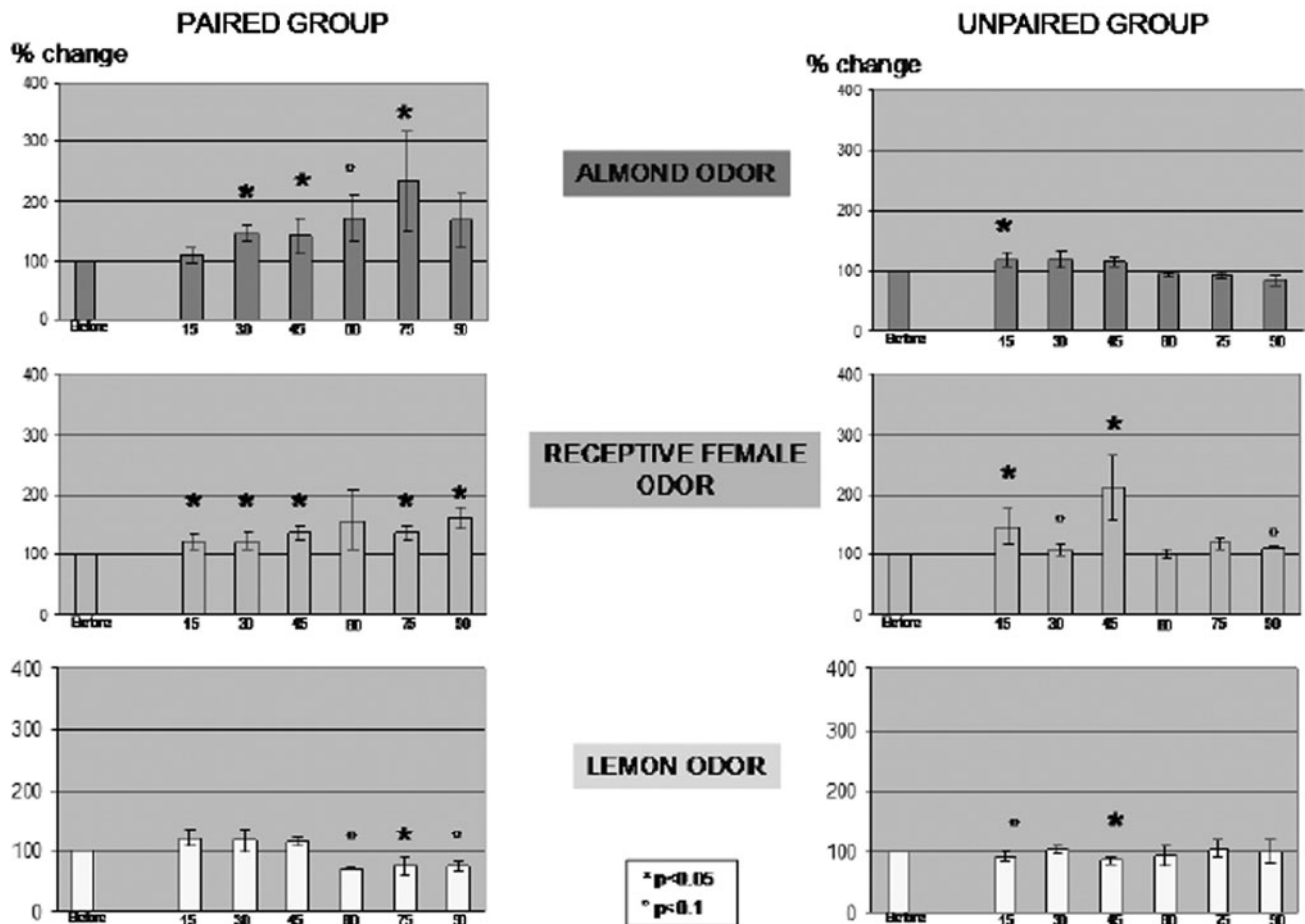


Fig. 8 Dopamine release in the nucleus accumbens of male rats in response to an almond odor paired or unpaired with sexual reward, estrous vaginal secretions, or a lemon odor unpaired in both groups. Unilateral dialysates were taken

every 15 min and analyzed via high performance liquid chromatography. Almond and lemon odors were presented on gauze. Estrous vaginal secretions were presented on Q-tips after vaginal lavage

vasopressin (VP) neurons of the supraoptic nucleus that likely project into the posterior pituitary. Systemic injections of OT (5 $\mu\text{g/kg}$), but not vasopressin, to sexually naïve male rats during their first exposure to almond-scented receptive females resulted in one-trial CEP.

These data suggest that conditioning in the putatively polygamous rat sensitizes a circuit similar to that activated in monogamous Prairie voles during their formative sexual experiences (Aragona et al., 2006; Young, Murphy Young, & Hammock, 2005; Young & Wang, 2004) and following parturition (Wang, Liu, Young, & Insel, 2000). The results of Aragona et al. (2006) are particularly instructive, as the sexual bond formation was inhibited by activation of D1 receptors, but facilitated by the activation of D2 receptors. This suggests a neural reorganization in mesolimbic terminals after formative sexual experiences that “seals the bond,” making it less likely for other stimuli to acquire associative strength.

Such an effect is consistent with modern theories of learning (e.g., Harris, 2011; Rescorla & Wagner, 1972) and has been implicated in the susceptibility to drug addiction, especially in terms of responding to cues that predict drug reward (Flagel et al., 2010), and more generally in response to food-related cues (Berridge, 2009; Blackburn, Pfaus, & Phillips, 1992). The interaction of OT and DA in the PVN, mPOA, VTA, and NAc of male rats induces penile erections and links them to appropriate appetitive sexual behaviors (Succu et al., 2007). Thus, opioid reward states may form the rudimentary mechanism of bonding because they sensitize DA release in the presence of reward-related cues compelling animals to focus their attention and goal-directed behavior toward those cues. Activation of brain OT systems (by DA or other means) adds a reduced social distance and bonding to this neurochemical reward state. Given that pharmacological activation of opioid receptors induces a direct suppression of both hypothalamic and pituitary OT secretion (Vuong, Van Uum, O'Dell,

Lufty, & Friedman, 2010), sensitized and potentially reorganized mesolimbic and hypothalamic DA systems must be a necessary intermediary. This is consistent with a multifaceted role of mesolimbic DA in incentive salience and response initiation (e.g., Blackburn et al., 1992; Robinson & Berridge, 1993).

Assortativeness

In social systems, assortativeness refers to a bias in favor of similar characteristics. This bias could be toward any outwardly definable (or distal) trait, including gender, race, size, age, dress, and more proximal traits, including socioeconomic status, political belief or religious orientation. In mating systems, assortativeness refers to choosing characteristics that are similar to oneself, as in species or strain (race/size) whereas disassortativeness refers to choosing characteristics that are dissimilar, such as the sex of the partner in heterosexual circumstances. Such choice is believed to reflect sexual imprinting, in which early postnatal (PN) conditions require the newborn to recognize and stick close to its mother or caregiver. Bateson (1983) defined heterosexual assortative mate choice for different species along an optimality curve between inbreeding and outbreeding, with a number of external and genetic weighting coefficients that define the costs and benefits of both. The choices are then made on the basis of dominant distal sensory cue(s), such as coloration in the Japanese quail studied by Bateson.

But all is not quite as it should be. Many different external cues can be imprinted during the early PN period depending on who (or what) happens to be in the right place at the right time (as in the famous picture of Konrad Lorenz with Greylag goslings following him). Several important studies have demonstrated that adult males mate preferentially with females that have attributes similar to those of the female(s) that nursed them early in life. Yamazaki et al. (1988) found that male mice nursed by foster mothers chose to mate with females that resembled their foster mother rather than females that resembled their biological mother. Similarly, adult male Lesser Snow Geese prefer the coloration of the female that nursed them over a different coloration (Cooke & McNally, 1975) and field studies (Cooke, Finney, & Rockwell, 1976; Cooke, Mirsky, & Seiger, 1972). One of the most provocative reports of sexual imprinting was that of Kendrick, Hinton, Atkins, Haupt, and Skinner (1998), who demonstrated that sexual partner preferences can be achieved between goats and sheep using cross-fostering to manipulate the imprinting process. In males and females of both species, sexual partner preferences were toward members of the opposite sex of the species of the foster, rather than biological, mother.

Is assortative mate choice dependent on mom per se or on a state of reward that her features are associated with? We have found that an olfactory cue associated with early PN reward in rats directs mate choice in adulthood (Ménard et al., in preparation). Newborn rats separated from their mothers display distress vocalizations that are reduced or eliminated by stroking their heads and backs with a soft fine paintbrush. Thus, stroking is both

negatively reinforcing (in the reduction of acute distress) and positively reinforcing as a reward (Sullivan & Hall, 1988). In the Ménard et al. study, we separated rat pups from their mothers for 15 min a day on PN days 1–10 and placed them on bedding scented with lemon (Paired) or left unscented (Unpaired). Pups were then stroked gently for the 15 min of maternal separation, after which they were returned to their mothers. On PN 60, after adolescence had been reached, the males were given their first sexual experience in an open field with two sexually receptive females, one scented with lemon and one unscented. All males in the Paired group ejaculated preferentially with the lemon-scented females whereas males in the Unpaired group did not display a preference. Imprinting alters neurogenesis and synapse formation in a variety of limbic and cortical brain structures associated with sensory coding, reward, emotion, and memory, especially the hippocampus and related cortical structures (Bolhuis, 1999; Moriceau & Sullivan, 2004). It is likely, therefore, that those changes essentially sculpt the bias in brain.

Experience and Expectancy

Experience leads to expectancy. Reward to desire. In a Pavlovian scheme, the CS comes to elicit a representation of the UCS and conditioned responses that lead to reinforcement strengthen the association. It is circular, but that is a fundamental property of the experience-driven brain plasticity that underlies Hebbian synapses. To the extent that “first cuts are the deepest,” and that first experiences with arousal and reward form a critical period of behavioral development and crystallization, the onset of sexuality then becomes a fluid critical period during which distal cues, proximal cues, and interpersonal cues that signal sexual reward are assembled into “wholes” or sexual Gestalts made up of desired features in potential sex partners (assembled perhaps hand-in-hand with desired activities with those partners). Individual differences in arousability, attention, temperament, reward intensity, and inhibition would then determine the success and timing of early sexual experiences. And if the process is iterative and additive, which it must be by definition, then new and unexpected experiences of greater sexual arousal and reward could refine the features further (e.g., as suggested by Morin, 1995) and lead to a conscious awareness that one has bonded sexually, emotionally, and romantically with another individual. Conversely, experiences with sexual non-reward could loosen or extinguish these associations, leading the features that were once in the “foreground” into the “background” (to paraphrase Köhler, 1929). However, if the process of reward learning is iterative and additive, it may never be completely possible to extinguish salient features entirely. Former drug addicts always want or crave some aspect of the early drug effect, even if the rewarding aspects of the drug had diminished prior to abstinence (Robinson & Berridge, 1993). This can be stimulated by cues that predict drug reward, and also by stress or other unexpected factors, and can lead to spontaneous recovery of drug taking

(Shaham, Erb, & Stewart, 2000), recovery of fears and phobias (Jacobs & Nadel, 1985), and perhaps also to the sexual gestalts and activities that we initially preferred.

Experience plays a vital role in some theories of sexual orientation. In his “exotic becomes erotic” theory, Bem (1996, 2000) provides support for the argument that gender-atypical behavior in childhood roots individuals into a biological framework in which same-sex activities become stronger predictors of sexual reward. This occurs in a social context in which gender role is fixed into “male” and “female” modes and imposed, and always confounded with sexual behavior. A number of studies have shown a strong correlation between gender nonconformity in childhood and subsequent homosexual orientation (e.g., Bailey & Zucker, 1995) and Bem’s own path analysis from a large sample of twins (Bem, 2000) reinforces this notion. So a first set of pieces in the puzzle of sexual orientation (and preference) comes from early interactions of genetic and sociocultural factors.

A second set of pieces comes from sexual experience itself. Storms (1981) argued that sex drive development occurs in concert with erotic development during a peri-adolescent period when individuals are moving from predominantly homosocial to heterosocial peer groupings. The content of an individual’s early sexual fantasies and desires is then consciously assessed in the context of actual sexual behavior and the dominant sociocultural definition of the appropriate gender and sexual orientation for that behavior, so that a convenient (and sometimes devastating) cognitive “label” ends up incorporated in one’s self-definition. And given the magnitude of sexual awakening in most people’s adolescent experiences, this addition to the self-definition is usually large and profound. One prediction in Storms’ theory is that sexual experiences that occur in the early phase of adolescence may be more likely to involve salient individuals in one’s same-sex social group. Interestingly, the modal retrospective age of puberty onset reported by the sample of gay men in Hamer et al. (1993) was between 11 and 12 years, somewhat earlier than the “normative” 12–13 years typically reported for boys in Western countries (Slyper, 2006). Of course, puberty does not occur suddenly but rather progresses in a cascade of events related to brain maturation, pituitary peptide hormone release, gonadal steroid hormone secretion, growth, and metabolism. Nevertheless, this leads us to entertain a tantalizing possibility that the X-linked genetic locus discovered by Hamer et al. could be related to a “female”-like timing of puberty onset. The Hamer et al. study can be mined for other gems of support for some of Bem’s and Storms’ ideas. The retrospective age of onset of first same-sex attraction had three phases, one from ages 5 to 8, a second from ages 9 to 13, and a third from 13 years on. The retrospective age of self-acknowledgement of homosexuality began just before the modal peak onset of puberty (approximately between 10 and 11 years), and rose steadily to age 17, then leveled off. Trailing this was the retrospective age of acknowledgement of homosexuality to others, which had a dynamic rise from ages 16 to 22, then leveled off in two phases, one from ages 22 to 32, and then less steeply after age 32. One

might imagine that exotic was becoming erotic through iterations of sexual reward achieved from formative same-sex sexual activities (starting, for example, with arousal, then rehearsal during masturbation, then actual sex play to genitally-based intercourse to orgasm) roughly between the ages of 11 and 16. It is not known from the data reported whether the men in that sample had experienced gender atypical behavior in that first period of attraction to other boys, but it is likely given the preponderance of supportive data.

Critical Periods and Bias: Disentangling Orientation from Preference

The data of Hamer et al. (1993) suggest the existence of at least three critical periods during the trajectory toward full sexual responsiveness: attraction, then arousal, and finally the emergence of a sexual reward system linked predominantly to genital pleasure and orgasm during and after puberty. The sexual nature of this last system is explicit: by the time people have incorporated sexual activity into their daily routines, they have already imbued it with names and given it personal and social definitions and values that are specific to it. Although the animal work reviewed above indicates a high degree of plasticity regarding the development of preferences for certain types of stimuli associated with sexual arousal and reward during an animal’s first experiences with genital stimulation and copulation, it does *not* reveal how sexual orientation toward members of the opposite or same sex develops. The development of sexual orientation then must form a “constraint” on learning (Gallistel, 1980; Lashley, 1951), biasing the subsequent development of sexual preferences toward the preferred gender. In fact, we argue that each critical period biases the formation of the next, although the next critical period follows the rules of an emergent property as far as the brain is concerned and cannot be reduced solely to the organization and activation that occurred in the previous period. That these critical periods emerge on a self-defining continuum is consistent with the trajectory outlined in Bancroft’s (2009) seminal review of sexual development.

To begin to understand how an orientation bias might develop, we much consider the role of two earlier critical periods, one of perinatal hormone-induced brain differentiation (McCarthy & Arnold, 2011) followed by another within the first 2–3 years of life linked to gender differentiation and the display of gender typical versus atypical behaviors. A cascade of developmental epochs or critical periods is depicted in Fig. 9 (and is contrasted with a neo-Piagetian cascade of stages of cognitive development that occurs during the same time frame, e.g., Demetriou, 1998; Piaget, 1967). These first two critical periods form according to a relative binary code linked to “male” and “female” (Money & Ehrhardt, 1972). Thus, we refer to sexual differentiation of anatomy and brain as the first critical period out of which should emerge an anatomical “boy” or “girl” that we assume has a brain differentiated accordingly. The second critical period differentiates gender-

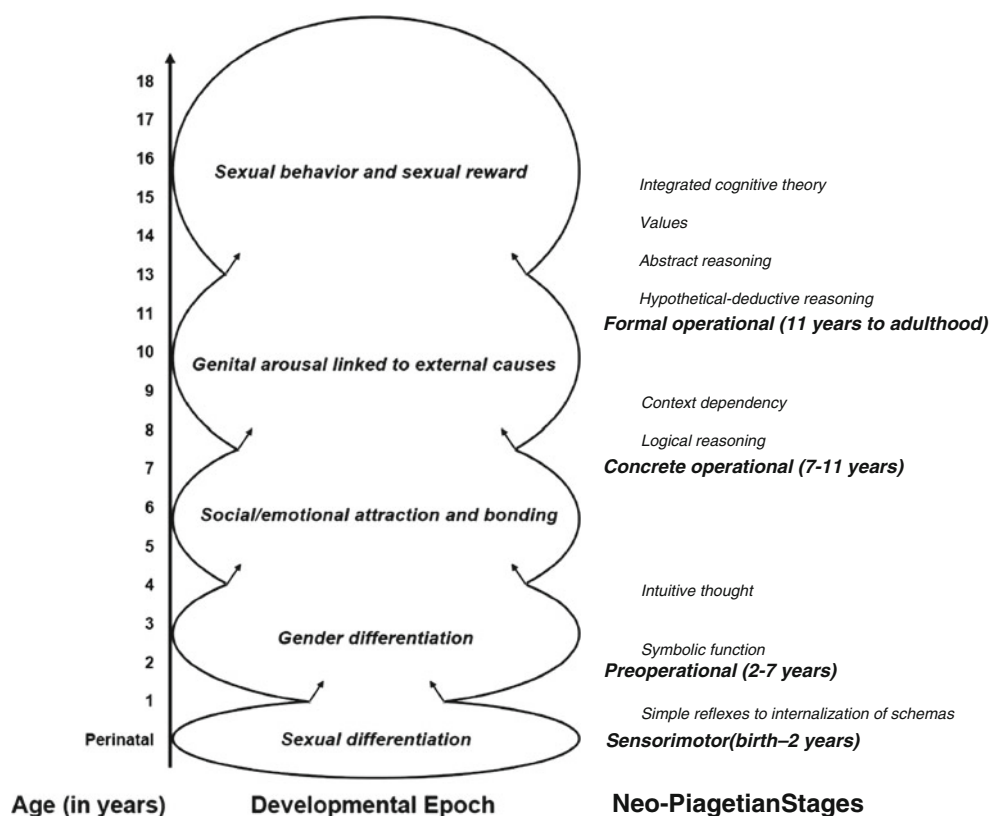


Fig. 9 *Left* Developmental epochs during which critical periods mold the development of sexual behavior as a function of age. *Right* Stages of cognitive development according to neo-Piagetian models age-matched to the critical periods. Orientation, we argue, derives from the first two epochs, although it is not recognized by an individual as a sexual orientation until the 4th or 5th epochs. Social development ensues during the 3rd epoch becoming more and more sociosexual, giving rise to general sympathetic and parasympathetic genital arousal that is more and more recognized as being caused by external circumstances. This gives rise to the 5th epoch when masturbation and copulation are achieved. During early experience with sexual arousal and reward, critical features of partners and objects are reinforced in both Pavlovian and operant ways, as are the necessary movements that predict and facilitate

sexual reward states. These are built upon prior critical period outcomes that allow individuals to identify themselves as “female” or “male” in terms of sex and gender, which in turn lays important cornerstones for social development and reinforcement. The developmental epochs occur generally around the ages of the widest spread although they can develop earlier or later depending on genetic and hormonal factors. Arrows indicate that the lower epoch blends into the next one such that there are predominant periods but no absolute start or end. An exception to this is the last epoch, which likely ends with a definitive sense of sex and gender, sexual orientation and sexual preferences for desired features and activities. Of course, peak sexual experiences can occur throughout the subsequent lifespan and give rise to an iterative redefinition of reward and preference

specific behavior (and perhaps self-identity as female or male). Overlaid onto this differentiation is the emergence of operant reward-based learning as it relates to the development of gender identity. During the second critical period, the individual experiences *intrinsic* reward acting as a male or female and this expression may be further rewarded or punished externally depending on whether the expression is gender typical or atypical. Thus, dressing and acting in a gender “appropriate” versus “inappropriate” manner leads to positive reinforcement (reward), negative reinforcement, or outright punishment. Gender atypical behaviors in Western culture typically lead to punishment and/or partial reinforcement (e.g., when one parent “accepts” the gender atypical behavior while the other does not). The impact of the reward or punishment, in turn, is affected by an individual’s temperament. What must be stressed here is that the tendency toward gender typical or atypical expression is intrinsically rewarding when the child engages in it.

Whatever brain mechanism(s) generate this bias become vitally important in the subsequent emergence of sexual orientation. The second critical period also generates conscious awareness of strain features (e.g., race and size) that define the traits of one’s family and/or clan, which can then be used to assess future assortative traits.

The third critical period forms around social and emotional attraction and rudimentary social bonding to opposite- or same-sex individuals. As cognitive development continues, individuals become more and more aware of peer groups, social structure, and the rules of engagement. During this time (roughly between the ages of 4 and 8, social and emotional attraction to opposite- or same-sex peers crystallizes and defines friendships and identity within a peer group social structure. The development of social bonds and hierarchies is also intrinsically reinforced and children who develop friendships and feel accepted have a very different

psychological trajectory compared to children that feel alone and without friends or outright ostracized. Thus, bonding itself is intrinsically rewarding and is signaled in a Pavlovian way by the individual features (typically facial and gender-related) of the other person(s). Storms (1981) argued that the predominant organization through this pre-pubertal period is homosocial, with boys having more friends that are boys and girls having more friends that are girls. However, in contrast to Storms' prediction, by the "magical" age of 10, gender nonconforming children are more likely to be in a predominantly heterosocial organization and experience more acceptance from opposite-sex peers than gender conforming children (Bailey & Zucker, 1995; Wallien, Veenstra, Kreukels, & Cohen-Kettenis, 2010). And superimposed on this third critical period is the conscious awareness of "grey zones" between other dichotomies (e.g., good and bad). Thus, during this third critical period, children may learn how good or bad it is to be gender typical or atypical in terms of the development of emotional and social bonds with others, gravitating naturally to friends and peer groups that are more accepting.

The fourth critical period involves the linkage of genital arousal to a state of general arousal that is associated with particular individuals or actions. This period, between approximately 8 years old and puberty, is associated with greater episodic awareness and context-dependency of events. Of course, genital arousal can occur anytime after the genitalia have been formed and certainly occurs well before puberty in a semi-spontaneous manner (driven in boys, for example, by bladder distention). It is also clear that tactile self-stimulation of the genitals can be perceived as pleasurable and comforting in young children. The linking of genital arousal (parasympathetic) to general sympathetic arousal during specific events involving persons, places, and things sets the stage for the pubertal linkage to sexual reward. It is, in essence, a dress rehearsal, and although the events do not have to be sexual in nature (e.g., Ramsey, 1943), they *can* be. This is the golden thread weaving through Krafft-Ebing's (1886/1929) case histories and the sudden emergence of sexually arousing events creates a set of antecedent biases on the type of external stimuli that will eventually be linked to sexual reward. But in the case of Krafft-Ebing's data, those events biased individuals toward fetish objects or highly arousing "naughty" behavior. Precocious puberty (that occurs before the normative time for girls and boys) adds a dimension of daring to this. Girls and boys who undergo precocious puberty are more likely to be norm-breaking, take risks, and engage in sexual masturbation, sex play, and sexual intercourse at an earlier age than people with normative onset puberty (Bancroft, 2009; Johansson & Ritzén, 2005; Kinsey et al., 1948, 1953). It is clear that the emergence of sexual arousal that leads to even a small degree of genital and sexual pleasure during the early phase of puberty creates a bias for sexual attraction and preference later on (e.g., Herdt & McClintock, 2000). This biasing occurs earlier in people with precocious puberty. It may well be during this phase that the groundwork for "exotic becomes erotic" is laid. For example, the groundwork for fetish development may be laid

during this period if the object or action results in high general and sexual arousal that predict some degree of reward.

To the extent that peri-pubertal experience with genital arousal biases the types of stimuli one can be attracted to, first experiences of sexual reward with those stimuli through masturbation or sexual intercourse during the fifth and final critical period powerfully reinforce those "pre-potent" biases (marking the events through which exotic truly become erotic). In this way, the critical periods generate a reward-based trajectory that moves first through gender-specific antecedents of sexual orientation and preference, to emotional and social attraction and bonding to others (based on gender and perhaps also strain), to awareness of genital arousal as a reward itself, and finally to *sexual* arousal, attraction, bonding, and motor responses that are reinforced by sexual reward with others (allowing people to differentiate lovers from friends for the first time). The preferred features move along a continuum as well, from distal features that are more pre-potent, such as gender, to those that are more flexible, such as hair length or color. It is becoming clear that children in the first 2 years of life are also able to distinguish features that play a role in assortativeness, such as race and size, depending on familial makeup and availability in the immediate peer group (Lam, Guerrero, Damree, & Enesco, 2011). It may well be that the ability to detect gender and strain in oneself and others precedes everything. Age-related features likely come next, defining the peer group during the third and fourth critical periods, and the pool of potential sex partners during the fifth critical period. Gender, strain, and age represent three of the most obvious group-related distal visual features. Surely there are more at a proximal distance, and more still when interaction adds interpersonal qualities to the mix.

Synthesis

We propose that the development of sexual "Gestalts" and sexual "scripts" (from the standpoint of both movements and language) are affected strongly by early formative experiences with sexual arousal and reward that feed forward to create desire for distal, proximal, and interactive features that predict the reward state. This occurs to some extent uniquely in the development of everyone's sexual preferences, although some commonalities may be easy to detect in terms of species-specific behavior or stimulation patterns, or as distal features of "attractiveness", such as the gender of the desired individual, race, age, body type, hair or eye color, facial features, and even the intergenerational styles of personal presentation (e.g., differences in facial structure, hair style, presence or absence of pubic, body, and facial hair of pin-ups from the first half of the twentieth century relative to the second half; see Gabor, 1973). It is likely, however, that some of those distal features, such as the gender of the desired partner, are relatively pre-potent, forming through mechanisms related to early critical periods of sexual differentiation and gender role

development, and reinforced naturally and intrinsically during periods of social and emotional attraction, and in the emergence of pleasurable genital arousal that is causally related to the gender of the individual that stimulates it. It is thus hard to escape the conclusion that there are as many sexual preferences as there are people, on a background of a gender orientation that has already been laid down. Every desired feature is to some extent a “fetish” that is sought after in the people we find attractive, in the styles they wear, and in the things they do (and we do with them). Although it is difficult to have rewarding sex with someone we are not attracted to, or worse, disgusted by, it is not impossible. As our rats have shown us, the unconditionally aversive odor of cadaverine can become less aversive and even conditionally desired when paired with a sexual-reward state during their early sexual experiences. There may be some features that are more “hardwired” at the outset, including those that define orientation and perhaps also those that contribute to assortativeness or optimal in- and out-breeding, and experience with sexual reward reinforces them considerably. One prediction of this is that people who experience sexual reward with someone of a non-preferred gender may well come to experience less aversion toward that type of sexual expression under certain circumstances (e.g., Pathela et al., 2006). This does not mean that sexual orientation and preferences can be altered once they are established. Reward gives us the power to know what we like, and directs our attentional mechanisms to focus on cues that predict the reward—to the exclusion of cues that do not, even if they *could*.

The fact that no one dies from lack of sex does not mean we don’t die trying. One of the important repercussions of making sex rewarding is that many individuals will try to do it despite the potential of predation or murder. Another repercussion is that a major source biological “determinism” for partner preference will be based on one’s own egocentric experience with cues that predict sexual reward. But this might make the most evolutionary sense of all, especially in a species in which individuals are, well, *individual* from a genetic and experiential perspective. If it is all about finding the “best” features of a mate that promote genetic survival, what then maintains diversity in a species, especially in those that are inbred or that live in unchanged environments? Shouldn’t the strong just eliminate the weak? Diversity in a species makes hybrid vigor possible and thus enhances survival across generations, especially when environmental changes occur in an unpredictable manner. Bonding to epigamic characteristics that are not associated with reproductive “strength” or “fitness” in one environment or epoch, may ensure survival in another. Moreover, reproduction may well be a fringe-benefit of sex that serves reward. As such, just having sex, especially good sex, makes an adult in any species “successful” from a more proximate sexual reward standpoint.

To the extent that mechanisms of sexual reward sensitize mechanisms of sexual bonding, it is likely that sexual reward and bonding merge in conscious awareness under the right circumstances

as romantic love (Aron, Fisher, Mashek, Li, & Brown, 2005; Fisher, Aron, Mashek, Li, & Brown, 2002), and bonded individuals can then begin to create the conditions for parental and even alloparental care. But they don’t have to. And that is as true for heterosexuals as it is for homosexuals and paraphilic individuals who favor inanimate objects. There is not one hormonal or gamete-related reason why gays and lesbians “can’t” reproduce, except that most do not desire heterosexual contact. Indeed, the number of gay men who provide sperm, and lesbians who become pregnant through artificial insemination, is growing in Western culture, as are the number of gays and lesbians who commit themselves to raising children. Does this reflect some emergent evolutionary change in homosexual brains or reproductive status? Probably not. More likely it reflects the fact that sexual reward and reproduction are separate and highly flexible processes that can interact under the right circumstances, and that our current cultural and legal climate has finally made it available.

The study of sexual learning in animals has given us a fresh perspective into the biological and social mechanisms of sexual reward and desire, and refined our knowledge of how patterns of sexual behavior crystallize during critical periods of early sexual experience. That allegedly polygamous rats show elements of monogamy suggests an extraordinary level of flexibility in brain function that can alter preferences dramatically as a function of early experience. Thus, Bagemihl’s (1999) concept of “biological exuberance” applies not just to homosexual behavior as a form of natural diversity, but to *all* forms of sexual expression and preference, no matter how constrained or socially sanctioned. To understand desire and preference we must understand reward and how it connects the external world to our internal representation of it.

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