The Pharmacology of Sexual Function and Dysfunction
J. Bancroft, editor

Context-sensitive variation in the regulation of erection

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Introduction

Is androgen necessary to maintain erectile function? Does ejaculation inhibit erection? Do dopamine D1 antagonists promote erection? The answer to these questions is, "It depends." And what it depends on is context -- the context in which erection is evoked. In turn, the context-sensitive nature of the answers to these questions probably indicates that the physiological regulation of erection varies from one context to another. The major goal of this paper is to compare several research models of erection, in the expectation that the similarities and differences among the models yield useful information about erectile function and its physiological control. The context-sensitive variation in regulation seems to be true of rats, which continue to be the most common subjects of physiological research into erectile function, and of humans, based on the more limited number of studies available. For this reason, the emphasis in this paper will be on rats, with occasional reference to humans and other species.

Research models of erection

The physiology of erectile function in rats and other animals has been studied using a considerable variety of research models, which may be thought of as contexts for erection. The more or less traditional contexts include copulation, reflexive erection in response to penile touch or pressure, pharmacological stimulation of solitary males, and lesions or electrical stimulation of the central or peripheral nervous system. To these contexts have been added, in the last few years, mechanical stimulation of the urethra (the urethrogenital reflex), noncontact (psychogenic) erection, and erection during sleep. Of course, many of these models are not mutually exclusive, e.g., one can study the effects of copulation on reflexive erection or the effects of lesions on erection *in copula*. A complete review of these models is beyond the scope of this paper, but it will be useful to describe some of them here in further detail. (The literature citations are necessarily also highly selective. Much of the uncited literature can be accessed through the reviews listed in the references.)

Copulation

Penile erection is a prerequisite for copulation, but studying erection *in copula* has not been easy [1]. This is especially true of the many species, such as rats and other rodents, in which intromission is brief and the penis is not readily seen before or after insertion. Direct measurement of intracavernous pressure during copulation has long since been achieved in larger mammals, but only recently in rats [2]. Hitherto, the relative success of erection *in copula* has been measured mainly by the "intromission ratio," which is the proportion of mount attempts that result in insertion [1,3]. However, not all failures of insertion are due to failures of erection. The behavior of the female and sensory factors in the male's perigenital area are

among the factors that contribute to variations in the intromission ratio, making it a less-than-perfect index of erectile function.

Reflexive erection

Males of many species develop erections in response to phasic tactile stimulation of the penis. In the rat, tonic pressure must be applied, which is accomplished by restraining the conscious male on his back, retracting the penile sheath to the base of the glans, and maintaining the male in this position. In this condition, males reliably respond with intermittent clusters of erections (see [1,3,4] for illustrations).

Drug-induced ("spontaneous") erection

A wide range of pharmacological agents, injected systemically or into the brain, induce erection in the absence of a sexual stimulus [1,5-8]. Although it has been said that the motor patterns accompanying such drug-induced erections in rats resemble intromissive or ejaculatory patterns, those familiar with copulation would be likely only to note a resemblance to the erections evident during postejaculatory grooming [9].

Noncontact erection

Erection may be evoked by a wide variety of erotic stimuli without direct contact, or by endogenous sexual stimuli, e.g., memories or fantasies. Such erections are commonly called "psychogenic" erections. (The many problems with this term have been reviewed elsewhere [10] and do not bear repeating here.) This type of erection is commonplace among primates [11-13], but had not been described for rodents until recently [14]. In rats, the motor pattern of noncontact erection closely resembles (and may be identical to) that of drug-induced erection.

Other models of erection

Among the many other *in vivo* models of erection, most involve anesthetized males. One instructive rat model has been the urethrogenital reflex, whose display requires lesions that isolate the spinal cord from the brain [15,16]. The reflex is evoked by mechanical stimulation of the urethra (probing with a catheter or pressure filling with fluid), and the response comprises a cluster of penile erections, expulsion of the contents of the urethra, and associated activity in the perineal nerves and striated penile muscles.

There have been several studies of erection in humans during sleep (nocturnal penile tumescence). Although semi-anecdotal reports of erection during sleep in animals have been available for many years, the first formal research has just been published [17,18]. Since virtually nothing is known about the physiological regulation of noncontact and sleep-associated erections, the advent of these models promises to open analytical windows into these processes.

Of the contexts described, the most natural ones are copulation, noncontact erection, and sleep; paradoxically, less is known about the regulation of erection in these contexts than any others. The relation of each of the other models to these contexts is unresolved, and in any case it should be noted that naturalness is an imperfect predictor of instructiveness.

Table 1. Characteristics of erection and effects of different treatments on erectile function of rats in various contexts.

Variables Studied	*Contexts for Erection*				
	Copulation	Reflexive (somesthetic)	Urethrogenital reflex	Apomorphine-induced	Noncontact
Characteristics					
Form (cups and flips)	+	+	+	+	+
Pressure (> systolic)	+	+	+	+?	+
Rate (> 0.5/min)	+	+	+	-	-
Duration (<5 sec)	+	+(er); -(cl) [a]	+(er); -(cl) [a]	-	-
Effects of Copulation					
Exposure to female only	↑?	↑	nd	nd	na
Intromissions	↑	↑	nd	0?	↑
One ejaculation	↓	↑ & ↓ [b]	nd	↑	↑
Sexual satiety	na?	↓	nd	↓	↓
Physiological Treatments					
Testosterone withdrawal	0	↓	0	↓	nd
$GABA_B$ agonist	0	↓	nd	↓	nd
Dopamine D2 agonist	0	↓	nd	↑	↑
MPOA stimulation	nd	nd	↑?	nd	nd
MPOA lesion	na	0	nd	nd	↓?
PVN lesion	0	↑	nd?	nd?	↓?
PGiN lesion	↑	↑	↑	nd	nd

Note. +/-: characteristic present/absent; ↑/↓/0: erectile function enhanced/depressed/unaffected; nd: no data; na. not applicable.

[a] Each erection tends to be < 5 s, but clusters of erections may last 10-15 s.

[b] Lower latencies suggest enhanced erectile function; reduced number and intensity of erections suggest impaired function

Similarities and differences among models of erection

Table 1 summarizes some of the formal characteristics of erection and the results of various experimental treatments in five of the contexts described above: copulation, reflexive erection, the urethrogenital reflex, drug-induced erection (with apomorphine used as a representative drug), and noncontact erection. The models and features to be compared were selected for the purposes of this chapter; other features may have yielded somewhat different lessons. The cell entries are a best estimate of current knowledge, but many of them may be expected to change in light of subsequent research or reinterpretation of existing studies. Limitations of space prevent discussion, or even documentation, of all the entries in the table, but reviews cited in the references can help locate the original sources.

Formal characteristics

The penis of most mammals comprises two erectile structures, the paired corpora cavernosa of the penile body and the singular corpus spongiosum of the glans penis. The forms of erection and the pressures developed within the penile corpora appear to be similar across many contexts. That is, they tend to be marked by erections of the penile glans, which assumes the shape of a "cup" or trumpet bell when intense, and of the penile body, which can display anteroflexions, or "flips" [1,3,4]. The normal blood pressure of the flaccid penis is substantially below diastolic pressure, but during moderate erections, achieved by the combination of vascular and smooth-muscle actions [1,8,19], intracorporal pressure commonly reaches or slightly exceeds systolic levels [2,15]. The most intense forms of erection require the additional action of the striated penile muscles [1,19], and can result in corporal pressures greater than 1000 mm Hg [2,18,19].

An occasional problem in research on erection is a failure (sometimes mine!) to specify whether erection is occurring in the penile body, glans, or both. This failure can result from an inability to observe the penis closely, e.g., during studies of copulation or drug-induced erections in rats. However, the importance of attending to the difference between penile bodies is revealed by various treatments or clinical conditions that have quite different effects on the penile glans and body [1,10]. For example, stimulation of the cavernous nerve causes erection of the penile body but not the glans [20], and cavernous nerve transection severely impairs body erections without major effects on glans erection [21].

In contrast to the general similarity of erectile form and pressure among contexts, the temporal pattern of erections may vary widely, a finding suggestive of differential central regulation. During reflexive erections, whether in response to touch/pressure or urethral stimulation, glans and body erections may occur separately or together in rapid and largely unpredictable succession. The rate and duration of erection may also vary considerably across contexts. The rate of intromissions under standard copulation testing conditions is 1-2/min, indicating an erection rate of at least that frequency. Information on the duration of erection *in copula* is less reliable, but the duration of intromission in rats has been estimated at 0.25-0.5 s. Erection rarely is evident before the intromissive thrust, and detumescence is substantially complete by the time the penis withdraws from the vagina, although some erection may persist during postintromissive grooming [1].

The duration of drug-induced erections, commonly 5-10 s, is much longer than erection *in copula*, but the rate of occurrence is low. Even with optimal doses of such highly effective drugs as apomorphine and oxytocin, the mean rate of erection is rarely greater than 4/hr

(0.07/min) [9,23,24]. However, because the natural (placebo) rate approximates zero, the occurrence of as few as 1-2 erections/hr may represent a statistically reliable increase. In rhesus monkeys the incidence of drug-induced erection appears to be much higher, perhaps because primate erections tend to be prolonged. For example, with an optimal dose of mCPP (a serotonin agonist), moderate-to-strong erections occur in about 25% of 10-s periods in which the genitals can be seen, compared with about 2% without drug treatment [25]. Prolonged erection after subcutaneous injection of apomorphine also occurs in men [26].

Complicating the comparison of the rate and duration of reflexive erections with other models is the fact that reflexive erections tend to occur in clusters: 5-10 erections of the penile body and/or glans may occur within a few seconds, followed by a period of 30-90 s before the next cluster. During a cluster, erections of the penile body (extensions and flips) may be as brief as those occurring during intromissions, but glans erections lasting more than 2 s are common. It has been proposed that a spinal pacemaker regulates the occurrence of erections during reflexive erection tests, and that the relatively high rate of erection is enabled by a relative absence of supraspinal control in this context [15,27-29]. In the freely moving male, erection is thought to be inhibited by the brain and brain stem, and disinhibited or stimulated under appropriate environmental cues [1,8,11,29]. A similar disinhibition may be accomplished naturally, as during paradoxical sleep (nocturnal penile tumescence) [30,31], or experimentally, as by lesions of the spinal cord or appropriate brain-stem structures [1,27-29,32,33]. This hypothesis has been supported by research on the urethrogenital reflex. This reflex apparently has no refractory period, perhaps because the very evocation of this response depends on lesions that free the spinal cord from descending inhibitory influences [15,16].

Noncontact erections look very much like drug-induced erections and have a similar 5-10 s duration [14], as does erection during postejaculatory grooming [34]. Conceivably, the long drug-induced and noncontact erections comprise a 5-10 s cluster of much briefer erections, similar to clusters of reflexive erections. (The degree to which grooming contributes to this longer duration in each context is still uncertain.) However, the rate of noncontact erection, commonly four during a 20-min test (0.2/min), is somewhat higher than with optimal drug doses. In rhesus, noncontact stimulation from females results in a three-fold increase in the percentage of genital observation periods with erection (from 15% to 45%) [13].

From these comparisons, it seems clear that although the basic form of erection is similar among the different research models, the rather different rates and durations of erection may already reflect differences in the physiological systems regulating erection in the different contexts. Further support for such differences emerges from comparisons of the effects of various treatments on erection in the different contexts.

Effects of copulation

The differential effects of ejaculation on erection in different contexts are particularly revealing, but we consider first the effects of lesser amounts of copulation.

In several contexts, allowing a male a few intromissions prior to a test, or even noncontact exposure to an estrous female, increases the probability of erection during the test. By definition, noncontact erection reveals the erectogenic effect of exposing males to estrous females [14]. However, males exposed to estrous females for as little as two minutes also had shorter latencies in subsequent reflexive erection tests [35]. Similarly, intromissions or mere exposure to females appear to increase the intromission ratio during subsequent copulation tests. Three intromissions did not reliably enhance apomorphine-induced erection [9], although the

small sample size in this study renders conclusions tentative. It is therefore premature to judge whether erectile contexts will respond differentially to antecedent sexual stimulation that stops short of ejaculation. However, the differential effects of ejaculation are already evident, and we turn now to these.

The waning of erection in men and many other mammals after ejaculation is well known, as is the subsequent "refractory period" during which sexual stimulation fails to restore erection. Therefore, as one might expect, rats that copulate to sexual satiety fail to show reflexive erections [29,36] and do not display erection when treated with apomorphine [9]. The effects of sexual satiety on noncontact erections, the urethrogenital reflex, and sleep-associated erections have not been tested. (Studying the effect of sexual satiety on erection *in copula* is problematic. The strict criterion of sexual satiety is usually the absence of intromission within 30-60 min after the preceding ejaculation. In practice, males rarely mount after the ejaculation that begins satiety, and hence their erectile function during attempted copulation can not be assessed.)

The effects of a single ejaculation on erectile capacity in different contexts are more instructive for present purposes than are those of satiety. The apparent erectile incompetence during the refractory period of rats was demonstrated some years ago by applying mildly painful shock to the flanks of males at 30-sec intervals after ejaculation [37]. Prior to ejaculation, shocks were immediately followed by pursuit of the female and mounting, usually leading to intromission. In the first minutes after ejaculation, these shocks yielded no response, or merely orientation toward the female; then successive shocks yielded progressively greater approach toward the female, eventuating in mounts. The first of these mounts usually failed to result in intromission, but ultimately the males mounted and intromitted sooner than they would have without shocks. These data suggested that a substantial fraction of the normal refractory period is required for the male to recover erectile competence, and it was estimated that that fraction was similar to the absolute refractory period, during which the male vocalizes at about 22 kHz and is unresponsive to estrous females [38,39].

Since that time, however, converging results from erection tests in several other contexts indicate that erectile potential returns sooner after ejaculation than had earlier been inferred. In fact, some tests have demonstrated that ejaculation can facilitate erection. For example, in reflexive erection tests begun immediately after the first ejaculation, the latency to the first erection is about 1 min, rather than the customary 4-6 min [36]. Additional evidence for this facilitative effect of ejaculation in rats is that ejaculation reverses the inhibitory effect on reflexive erection of such diverse treatments as local anesthesia of the penis [40], removal of the penile sheath [41], and treatment with $GABA_B$ agonists [42]. Clearly, any lack of erectile competence *in copula* after ejaculation in rats can not be attributed entirely to mechanisms in the penis, the peripheral nerves, or the spinal cord. Rather, much of the problem with tumescence after ejaculation is likely to lie in the failure of brain mechanisms to stimulate or to disinhibit these lower systems.

By observing rats in another context, we have recently seen further evidence that erectile competence returns well before the male resumes copulation. In a study of the effects of copulation on apomorphine-induced erection in solitary rats [9], males were injected with apomorphine or vehicle immediately after the last of three intromissions, after ejaculation, or after no sexual contact. After copulatory stimulation, vehicle-injected males unexpectedly displayed erections similar in form, latency, and number to those induced by apomorphine.

The mean latency to erection after ejaculation in these control males was less than 3 min, barely more than half of the normal postejaculatory period.

We have now observed more directly the erections of 12 rats during their first postejaculatory interval, and also monitored their 22-kHz vocalizations (unpublished data). As just noted, these vocalizations continue through 50-75% of the postejaculatory interval, and the period during which they occur has been thought to mark the absolute refractory period, during which the male is considered insensitive to sexual stimulation [38,39]. The balance of the postejaculatory interval is thought to be the relative refractory period, during which progressively weaker sexual stimuli become sufficient to prompt the male to resume copulation. All 12 males in this study had erections during the postejaculatory period. (The normal erections with grooming that start immediately after ejaculation and continue for up to 30 s were excluded from these analyses.) The first postejaculatory erection tended to precede the last of the 22-kHz calls, although the mean difference (0.81 min) did not approach significance ($t(11)=1.31$, $p > 0.20$). These data suggest that in freely moving rats the resumption of erectile function after ejaculation roughly coincides with the end of the absolute refractory period. However, 3/12 males had erections within 90 s of ejaculation, and 7/12 males had at least one erection before the end of their 22-kHz vocalizations. The presence of females during the postejaculatory interval evidently contributed to the occurrence of erections. When the females were removed immediately after ejaculation, only 6/12 males displayed erections (relative to 12/12, $x^2 = 5.56$ with Yates correction, $p < 0.02$). We infer that the male is sensitive to sexual stimulation from the estrous female throughout the postejaculatory interval, resulting in an increasing probability of erection during that interval, well before copulation is normally resumed. (It is also noteworthy that only half the males vocalized when the female was absent during the postejaculatory interval, although there was no correlation between the tendency to vocalize and to erect. This reduced probability of vocalizing in the absence of females may be the first evidence to support the hypothesis that the 22-kHz vocalizations function in male-female communication [43], rather than being an epiphenomenal sequel to ejaculation [44]. Ample data support a communicative function for the 40-60 kHz vocalizations [38].)

Other research points to the conclusion that the effects of ejaculation on reflexive erectile function in rats are mediated by the brain and, to a lesser extent, by the spinal cord. That is, spinal blocks at the thoracic level, which presumably eliminate influences from the brain upon the spinal cord, did not restore reflexive erections in sexually sated males, but further reduced the erection latency after a single ejaculation [29].

To recapitulate, in humans, rats, and many other species, ejaculation usually leads rapidly to detumescence of the penis, which is commonly thought not to be "ready" for erection until at least several minutes later. (Canids that form a copulatory tie are among the exceptions, in that ejaculation occurs soon after insertion, but erection is maintained throughout the tie.) However, tests in several *ex copula* contexts indicate that, at least in rats, penile erection can occur soon after ejaculation, and therefore a good part of any *in copula* impotence is probably mediated more rostrally than the penis and the spinal cord.

Neuroendocrine mediation

Hormones The endocrine mediation of erection provides further evidence for context specificity in the physiological regulation of erection. The testosterone-dependence of somesthetic (touch-mediated) reflexive erection in rats is well established [1,45], and

erections induced by apomorphine or oxytocin are similarly dependent on testosterone [46,47]. In contrast, the urethrogenital reflex is evoked as readily in long-term castrated males as in intact males [15]. This independence of erection from androgen is also evident during copulation. Long-term castrated rats that are treated with estradiol readily mount estrous females, achieve intromission in a normal proportion of their mounts [48], and display electromyographic activity of the penile muscles that is at least as intense as that of intact males [49]. It remains to be seen whether such males achieve normal intracavernous pressures, but penile body and glans erection during copulation is clearly not testosterone-dependent in rats.

There is also a remarkable difference in the relative testosterone sensitivity of human erection in different contexts. Erectile function during sexual encounters may be severely impaired in hypogonadal men, and their nocturnal penile tumescence is much less intense, although it occurs at a frequency similar to that of eugonadal men [11,30,31]. However, the erections of hypogonadal men in response to erotic films are indistinguishable in intensity and duration from those of normal men [11,30,31]. This greater response to visual erotica may indicate a qualitatively different regulatory system [11,30], but quantitative differences can not be ruled out. That is, erotic films may provide stimulation so intense as to activate systems that are hyposensitive as a result of low testosterone levels [10,50].

Drug effects. Pharmacological studies, especially ones analyzing the effects of GABAergic and dopaminergic drugs, provide striking evidence for the differential regulation of erection in different contexts. As with the steroid regulation of erection, the control of erection by GABA presents the problem of resolving the difference between qualitative and quantitative context-sensitive differences. Baclofen, a $GABA_B$ agonist, inhibited apomorphine-induced erections in rats [51]. Males treated with baclofen also displayed a dose-dependent decrease in reflexive erections, whether injected systemically (1-2 mg/kg) [4] or intrathecally at the L5-S1 level (0.2-0.8 μg) [42]. However, this baclofen-induced impairment of erectile function was not evident during copulation, as no measures of this behavior were changed reliably by either route of administration. In particular, the intromission ratio, the measure most likely to reflect reduced erectile function, was similar in all treatments. It remains to be determined whether copulation provides such intense stimulation as to counteract the inhibitory effects of baclofen, or whether GABAergic systems are more involved in mediating reflexive erections than erection *in copula*.

Dopaminergic agents are among the most effective and frequently used drugs to promote erection in isolated, freely moving rats, and apomorphine, a mixed D1/D2 agonist, has been promoted as a reference model for the study of erections [22]. Increases in brain dopamine resulting from sexual stimulation have added to interest in the dopaminergic mediation of erection [52]. Nonetheless, it is fair to say that there is not yet a consensus on the role of dopamine in sexual behavior, and opposing views on the particular contribution of D1 and D2 receptors are illustrative. According to one hypothesis [53], activation of D2 receptors promotes erection, whereas stimulation of D1 receptors inhibits erection. Hull [54] has taken nearly the opposite view, i.e., D1 activation stimulating erection, D2 activation inhibiting it, except that low levels of D2 activation are thought to enable the excitatory effects of D1 agonists. Not surprisingly, these opposing conclusions arise from very different effects observed in rats after similar drug treatments, sometimes with the very same drug. Thus, Zarrindast et al. [53] reported that the D1 antagonist, SCH23390, promoted erections, whereas

the same drug, as tested by Hull et al., inhibited erections. Similarly, Hull et al. [54] and others [55] found that quinelorane, a D2 agonist, inhibited erection, whereas Zarrindast et al. [53] using quinpirole and bromocriptine as D2 agonists, observed an increase in erections. Quinelorane also has facilitated erection in rhesus monkeys [13]. Although several procedural differences distinguish the research of Zarrindast [53] from that of Hull [54], one contrast that stands out is the very different contexts in which erections were evoked [10]. Zarrindast et al. observed erections only in solitary, freely moving males. Hull et al. relied primarily on data from reflexive erection tests. The limited data available on rhesus monkeys were gathered in a noncontact erection context, but masturbation could not be ruled out as a contributing factor. Clearly additional information will be necessary to help weigh the accuracy of the competing hypotheses about dopaminergic regulation of erection, but it seems likely that closer attention needs to be paid to the context in which the effects of drugs on erection are tested. Conceivably, each of the hypotheses will have merit if it proves that the relative contribution of D1 and D2 receptors varies with the context in which erection occurs.

Neural effects. One of the most widely accepted conclusions concerning the physiology of sexual function is that lesions of the medial preoptic area (MPOA) permanently impair copulatory behavior [1,8]. Nonetheless, thirty years after the initial research on this effect, the interpretation of the effect is subject to dispute, and the role of the MPOA in erection is uncertain. The best evidence for an erectile function for the MPOA comes from electrical stimulation of this structure, which promotes erection in conscious, freely moving, solitary rats [32,33] and monkeys [12,56] and also in anesthetized rats [57,58]. The results of MPOA lesion studies are more ambiguous. Because males with MPOA lesions do not usually initiate copulation, there has been no assessment of the effect of such lesions on erection *in copula.* However, in a preliminary study, 7/9 rats that stopped copulating after MPOA lesions also failed to display noncontact erections [59]. The other side of this coin is that at least some males with MPOA lesions nonetheless had noncontact erections. Lesions of the MPOA have no effect on reflexive erections, suggesting that this structure does not regulate erectile function in that context [60]. These data indicate that at least in some contexts, erectile function survives lesions in the MPOA better than does the initiation of copulation. Tests for erection in other contexts will be needed to determine the generality of this conclusion.

The paraventricular nucleus (PVN) of the hypothalamus innervates the penis [61] and has reciprocal connections with the penile motor neurons in the spinal cord [62,63], but the functional implications of this anatomy have not yet been confirmed. Reflexive and spontaneous erections are affected by the infusion of apomorphine and other dopaminergic agonists into the PVN [24,64]. Lesions in the PVN reduced reflexive erection latency without affecting other parameters [65], implying enhanced erectile function resulting from reduced descending inhibition. In contrast, in a preliminary study amino acid lesions of the parvocellular PVN reduced the proportion of males displaying noncontact erections [59]. In copulation tests, lesions restricted to the lateral parvocellular area of the PVN resulted in reduced latencies to initiate copulation and to resume copulation after ejaculation, but the number of mounts and intromissions were unaffected, and no effect on their ratio was reported [66]. The effects of PVN lesions on erections in other contexts have not yet been tested. (One difficulty in discovering effects of lesions in these and similar studies is that there may be redundant systems. Also, neural plasticity after lesions may mask their effects on erectile function, whereas acute treatments like drug infusion would not be affected by plasticity. It should also be noted that negative results of PVN and other lesions in behavioral studies must be

interpreted conservatively, because such lesions may affect penile pressure during erection to a degree undetectable by available behavioral measures.)

The brain structure with the clearest, most uniform involvement in erectile function in different contexts is the medullary nucleus paragigantocellularis (PGiN). This nucleus, like the PVN, has reciprocal connections with the spinal motor nuclei innervating the penis [16,62]. A clear role for the PGiN in erection was demonstrated initially by showing that bilateral lesions of this nucleus were as effective as spinal transection in permitting evocation of the urethrogenital reflex [16]. This inhibitory function in erection was also evident in tests for reflexive erection [67] and copulation [68]. A role for the PGiN in other erectile contexts awaits appropriate tests, but to date all evidence points to an inhibitory function for the PGiN in all erectile contexts.

We turn finally to the regulation of erection by the spinal cord and peripheral nerves. It is commonly believed that reflexive erections are regulated by the lumbosacral cord and pelvic nerves, whereas noncontact (psychogenic) erections are controlled by the thoracolumbar cord and hypogastric nerves [1,7,8]. Space does not allow a reexamination of this question here, but in a recent review [10] I argued that the oft-cited evidence for this case of differential regulation was not compelling. Rather, all contexts may share similar spinal and peripheral neural control. If that be true, then as one progresses from the forebrain to the brain stem and spinal cord, the neural and neurochemical regulation of erection may be less and less context-sensitive. Conversely, as one progresses centrally from the penis and rostrally from the spinal cord, the regulation of erection may become more context-specific, possibly because of an increasingly particular involvement of sensorimotor systems in effecting erection in different contexts.

Conclusion

Each of the several research models for the study of erection has contributed toward understanding the physiology of erection, but it is commonly assumed, at least implicitly, that inferences based on one model, or context, can be validly applied to other models. As we have seen, however, comparison of the similarities and differences among the results yielded in different contexts suggests that this assumption is not always warranted. It appears that the several models of erection are not all modeling the same erectile process, and closer attention to the different outcomes of the models may yield important lessons about differences in the physiological regulation of erection in different contexts.

Acknowledgments

Supported by research grants from NICHD (HD08933) and the University of Connecticut Research Foundation. I thank Jacqueline Sachs for her excellent editorial advice and a great deal more, and James D. Rose for his suggestion, in another context, to compare the characteristics of different research models of erection. For some of the ideas in this paper I owe an intellectual debt to John Bancroft and Julian Davidson, whose research on hypogonadal men sensitized me to the context-dependency of erectile physiology, and to C. S. Sherrington's concept of the "final common path."

References

1 Meisel RL, Sachs BD. In Knobil E, Neill JD, eds. The Physiology of Reproduction. New York: Raven, 1994; vol 2, 3-105.
2 Giuliano F, Bernabé J, Rampin O, Courtois F, et al. J Urol 1994; 152:1271-1274.
3 Clark JT. In Conn PM, ed. Methods in Neurosciences, vol. 14, Paradigms for the Study of Behavior. New York: Academic Press, 1993; 32-53.
4 Leipheimer RE, Sachs BD. Physiol Behav 1988; 42:351-357.
5 Bitran D, Hull EM. Neurosci Biobehav Rev 1987; 11:365-389.
6 Dornan WA, Malsbury CW. Neurosci Biobehav Rev 1989; 13:1-15.
7 Foreman MM, Doherty PC. In Riley AS, Peet M, Wilson CA, eds. Sexual Pharmacology. New York: Oxford University Press, 1993; 87-113.
8 DeGroat WC, Booth AM. In Maggi CA, ed. The Autonomic Nervous System. Nervous Control of the Urogenital System. London: Harwood Academic, 465-522
9 Sachs BD, Akasofu K, McEldowney SS. Pharmacol Biochem Behav 1994; 48:423-428.
10 Sachs BD. Neurosci Biobehav Rev (in press).
11 Bancroft J. Human Sexuality and its Problems. 2nd ed. Edinburgh: Churchill Livingstone, 1989.
12 MacLean PD, Ploog D. J Neurophysiol 1962; 25:29-55.
13 Pomerantz SM. Pharmacol Biochem Behav 1991; 39:123-128.
14 Sachs BD, Akasofu K, Citron JH, Daniels SB, et al. Physiol Behav 1994; 55:1073-1079.
15 McKenna KE, Chung SK, McVary KT. Am J Physiol 1991; 261:R1276-R1285.
16 Marson L, McKenna KE. Brain Res 1990; 515:303-308.
17 Schmidt MH, Valatx J-L, Schmidt HS, Wauquier A, et al. Neuroreport 1994; 5:561-564.
18 Bernabé J, Giuliano F, Rampin O, Sachs BD. Int J Impot Res 6(Suppl 1):P19.
19 Schmidt MH, Schmidt HS. Sleep 1993; 16:171-183.
20 Quinlan DM, Nelson RJ, Partin AW, Mostwin JL, et al. J Urol 1989; 141:656-661.
21 Sachs BD, Liu Y-C. J Urol 1991; 146:900-905.
22 Heaton JPW, Varrin SJ, Morales A. J Urol 1991; 145:1099-1102.
23 Maeda N, Matsuoka N, Yamaguchi I. Brain Res 1990; 537:163-168.
24 Melis MR, Argiolas A, Gessa GL. Brain Res 1987; 415:98-104.
25 Pomerantz SM, Hepner BC, Wertz JM. Eur J Pharmacol 1993; 243:227-234.
26 Lal S. Prog Neuro-Psychopharmacol Biol Psychiat 1988; 12:117-164.
27 Hart BL. J Comp Physiol Psychol 1968; 65:453-460.
28 Sachs BD, Garinello LD. J Comp Physiol Psychol 1980; 94:530-535.
29 Sachs BD, Bitran D. Brain Res 1990; 528:99-108.
30 Carani C, Bancroft J, Granata A, Del Rio G, et al. Psychoneuroendocrinology 1992; 17:647-654.
31 Davidson JM, Rosen RC. In Rosen RC, Leiblum SR, eds. Erectile Disorders: Assessment and Treatment. New York: Guilford Press, 1992; 72-95.
32 Courtois FJ, MacDougall JC. Physiol Behav 1988; 44:165-171.
33 Courtois FJ, MacDougall JC, Sachs BD. Physiol Behav 1993; 33:721-726.
34 Holmes GM, Chapple WD, Leipheimer RE, Sachs BD. Physiol Behav 1991; 49:1235-1246.
35 Liu, Y-C, McEldowney SM, Akasofu K, Sachs BD. Soc Neurosci Abst 1992; 18:128.
36 O'Hanlon JL, Sachs BD. Behav Neural Biol 1980; 29:338-348.

37 Sachs BD, Barfield RJ. J Comp Physiol Psych 1974; 86:607-615.
38 Barfield RJ, Thomas DA. Ann NY Acad Sci 1986; 474:33-43.
39 Sachs BD, Barfield RJ. In Rosenblatt JS et al, eds. Advances in the Study of Behavior. New York: Academic Press, 1976; vol 7:91-154.
40 Stefanick ML, Smith ER, Davidson JM. Physiol Behav 1983; 31:63-65.
41 Lumia AR, Sachs BD, Meisel RL. Physiol Behav 1979; 23:273-277.
42 Bitran D, Miller SA, McQuade DB, Leipheimer RE, et al. Pharmacol Biochem Behav 1989; 31:657-666.
43 Barfield RJ, Geyer LA. J Comp Physiol Psychol 1975; 88:723-734.
44 Blumberg MS. J Comp Psychol 1992; 106:360-365.
45 Leipheimer RE, Sachs BD. Physiol Behav 1993; 54:1085-1090.
46 Heaton JPW, Varrin SJ. J Urol 1994; 151:797-800.
47 Melis MR, Mauri A, Argiolas A. Neuroendocrinology 1994; 59:349-354.
48 O'Hanlon JL, Meisel RL, Sachs BD. Behav Neural Biol 1981;32:269-273.
49 Holmes GM, Sachs BD. Horm Behav 1992; 26:406-419.
50 Davidson JM, Myers LS. In Rosen RC, Beck JG, eds. Patterns of Sexual Arousal. New York: Guilford Press, 1988; 158-186.
51 Zarrindast M-R, Farahvash H. Psychopharmacology 1994; 115:249-253.
52 Mas M. Neurosci Biobehav Rev In press.
53 Zarrindast M-R, Shokravi S, Samini M. Gen Pharmacol 1992; 23:671-675.
54 Hull EM, Eaton RC, Markowski VP, Moses J, et al. Life Sci 1992; 51:1705-1713.
55 Doherty PC, Wisler PA. Life Sci 1994; 54:507-514.
56 Perachio AA, Marr LD, Alexander M. Brain Res 1979; 177:127-144.
57 Marson L, McKenna KE. Brain Res 1994; 638:103-108.
58 Rampin O, Giuliano F, Courtois F, Brown K, et al. Int J Impot Res 1994; 6(Suppl 1):A1.
59 Sachs BD, Akasofu K, Citron JH, Daniels SB, et al. Neuroendocrinol Lett 1993; 315:344.
60 Stefanick ML, Davidson JM. Physiol Behav 1987; 41:439-444.
61 Marson L, Platt KB, McKenna KE. Neuroscience 1993; 55:263-280.
62 Monaghan EP, Breedlove SM. J Comp Neurol 1991; 307:370-374.
63 Wagner CK, Clemens LG. Brain Res 1991; 539:254-262.
64 Eaton RC, Markowski VP, Lumley LA, Thompson JT, et al. Pharmacol Biochem Behav 1991; 39:177-181.
65 Monaghan EP, Arjomand J, Breedlove SM. Horm Behav 1993; 27:122-131.
66 Hughes AM, Everitt BJ, Lightman SL, Todd K. Brain Res 1987; 414:133-137.
67 Marson L, List MS, McKenna KE. Brain Res 1992; 592:187-192.
68 Yells DP, Hendricks SE, Prendergast MA. Brain Res 1992; 596:73-79.

Discussion - CONTEXT-SENSITIVE VARIATION IN THE REGULATION OF ERECTION

M. Baum

Can you comment on the role of androgens in the animal models which include electrical stimulation of the cavernous nerve?

B.D. Sachs

There have been studies (F. Giuliano et al. *J Neuroendocrinol* 1993, 5:677-683; TM Mills et al. *Biol Reprod* 1992; 46:342-348) demonstrating a facilitative role for androgens in the erectile response to cavernous nerve stimulation, but I would reserve judgment on the relevance of these studies to the androgenic regulation of erection in other contexts.

G. Wagner

When you talk about animals like rats that are pretty small, the surgery must be very refined. What do you feel about that?

B.D. Sachs

One of the reasons why the rat is preferred as a model for peripheral nerve experiments is that the nerves are quite coherent relative to the comparable nerves in dogs and cats, in which they tend to be more diffuse. It is true that there are potentially several branches of the cavernous nerve, and so there is a question when one cuts the cavernous nerve: has one cut all the fibers? The answer is that we do not have the anatomical studies yet that would allow us to make that judgement. It is easy enough to say that we have cut everything that we can see, but we do not know if we have cut everything that we cannot see. What one needs is tracing studies that have eliminated other routes from the spinal cord to the penis and then label the penis after cutting the cavernous nerves and see whether one still gets labelling in the spinal cord. Those experiments remain to be done but I think that in respect to stimulating or cutting the motor pudendal nerve, the sensory pudendal nerve, the hypogastric nerve and the cavernous nerve, the surgery with the appropriate instrumentation is really not

technically difficult.

B.J. Everitt

You mentioned that ejaculation actually facilitates or increases the probability of non-contact erections. Can you tell us about the time course of that and whether that is a uniquely rodent phenomena?

B.D. Sachs

We do not know whether it is uniquely a rodent phenomena until other species are examined. We first discovered this effect in a study in which we were looking at the effects of copulation on apomorphine-induced erection and found, to our great surprise, that the vehicle groups that had copulated, or indeed that had been exposed to females, showed erections during the post-ejaculatory interval at a time I judged to be prior to the end of the absolute refractory period. We were not monitoring other indices of this period, during which the male was supposed to be insensitive to cues from the female. But we have just completed another experiment in which we focused on that question and in which we monitored the male's 22-25 kHz vocalisations. They normally last 50 to 75% of the post ejaculatory interval and appear to define the absolute refractory period. We had 12 males and 7 of them showed erections before they stopped vocalising. The mean time to the end of vocalisation was about the same as the mean time to the first post-ejaculatory erection. A striking thing about this is that we also removed the female in the post-ejaculatory interval for one group and in that condition only 6 of the 12 males had erections, and that is a significant reduction from the 12 out of 12 that had erections when the female was present. Furthermore, only 6 of the 12 males, not necessarily the same six, vocalised during the post-ejaculatory interval. So this vocalisation seems to function importantly in the male-female communication or at least it is an index of male-female communication during the post-ejaculatory interval, in particular in that part of the post ejaculatory interval during which the male is supposed to be insensitive to the female. The fact that he displays these erections sometimes as soon as one minute after ejaculation suggests to us that the male is continuously sensitive to the presence of the female throughout the post-ejaculatory interval. Now, whether that will turn out to be true in some other species,

really remains to be seen. We assume it is not true with the human male but this has never been tested in an appropriate experimental setting.

J. Bancroft

I am keeping in mind possible species differences and I think we have to remember that there may be important differences in both central and peripheral mechanisms controlling erection in the rat and in man. Am I right in thinking that there is good evidence in the rat that reflex pathways in the spinal cord are very much testosterone dependent?

B.D. Sachs

The answer is that it depends on the context. With respect to the urethrogenital reflex, which is certainly spinally mediated, they are completely independent of testosterone. With respect to the somaesthetic reflexive erections that are touch-pressure induced, they are completely dependent on testosterone, and with respect to the copulatory context, so far as we know, they are testosterone independent.

S.M. Pomerantz

Can you just follow up on that? You said that they are testosterone-independent but are not they hormone-dependent? In other words, if there is not any oestrogen around will they still appear?

B.D. Sachs

We cannot answer that question because we cannot get them to mount without either oestrogen or testosterone. If you can suggest to me a preparation in which we have a male that has no steroids but will mount regularly, then we can find out whether erection is steroid-sensitive. I would say that with respect to oestradiol dependence, the somaesthetic reflexible actions cannot be maintained or restored with oestradiol. They can be restored or maintained with dehydrotestosterone.

J. Bancroft

You talk about context but is context related in any way to specific

neurotransmitters linked to the reflex pathways? I was told recently that serotonin, for example, was directly involved in this testosterone-dependant reflexive pattern in the spinal cord of the rat. Do you accept that? In which case your contexts are being mediated via different neurotransmitters pathways?

B.D. Sachs

The way I would like to answer that is by reiterating that as one moves centrally from the penis and rostrally from the spinal cord there is greater and greater context-sensitive divergence of the regulatory function. The serotonin regulation is primarily from the brain, so to the extent that the brain contributes differentially to these responses, I think we will find that the serotonergic regulation as well as the peptidergic regulation of erection will show increasing differentiation. The neural structures show differentiation with context, and that would be reflected in neurotransmitter differentiation.

J. Herbert

What role does mPOA play in female sexual behaviour? Relative to the VMA, for example.

J.G. Pfaus

The mPOA seems to play a different role depending upon the context. If the female can pace the copulatory contact, lesions of the mPOA do precious little. If she cannot pace the copulatory contact, lesions of the mPOA actually facilitate lordosis. So, in the non-paced condition, it is normally seen as a site which is producing some kind of tonic inhibition on lordosis and if it is disinhibited by the lesion then you get facilitated lordosis. Given that the context is different when a female can pace and you do not see the effect of the lesion, that would suggest that in certain cases it may be playing a role either to facilitate lordosis or to inhibit lordosis only in the case when the female cannot pace. In the case where she can pace it either plays no role or it may play a very subtle role. Oestrogens induce opioid peptide synthesis in the VMN, which is projected to three sites of the brain, at least three that we know of: the mesencephalic central grey, where it may play an inhibitory role in lordosis, lateral septum and the mPOA. We

know absolutely nothing about what opioids within the mPOA do to female sexual behaviour. It may very well be the case that they could disinhibit lordosis by producing some sort of tonic inhibition within the mPOA, and that may be one way that oestrogen then serves to facilitate lordosis.

M. Baum

I agree with what you are saying and that is for two reasons: first, for the appetitive situation, large preoptic area cytotoxic lesions in females have absolutely no effects on their inclination to approach and interact with males. And these animals do not show lordosis, they show a receptive posture also which was perfectly normal in those animals.

J. Herbert

Can I just come back to this business of the function of the MPOA? I am not totally convinced that the effect of MPOA is essential for consummatory sexual behaviour. In studies with chemical manipulation of the mPOA, males rush around as they would do with a MPOA lesion, they look for the female like mad and they never mount. They just look as if they had forgotten how to do it just as in the case of mPOA lesions. They would still bar-press for a female under second order conditioning but again they would not copulate. But the big difference is this: if you delay the infusion until after the male has done the first mount, there is no effect. The male goes on as if he had water or CSF into his mPOA. That does not mean that it is not doing anything because if you cheat and instead of putting the male back with the same female, you put it back with a different female, suddenly it looks lesioned again. So once he has started going with that female despite the fact that his MPOA is becoming neurochemically disabled, he is going probably normally; change the female and he suddenly shows a difference again. That seems to me to raise serious questions about the mPOA which are not simply answered by saying it has to do with consummation.

B.J. Everitt

Can I just comment on that? First of all, I think, it is a red herring to talk about that kind of chemical manipulation of the brain as a lesion. It is not helpful to think

about it that way. If you wanted to make that kind of comparison, I think one of the things you could do if you wanted to disable all of the neurons in an area acutely in the same paradigm, for example, after intromission, is to infuse a local anaesthetic in the preoptic area, and I think that in this case you could indeed talk of the effect of a reversible lesion. To say that infusing β-endorphin to control the activity of one population of opioid-sensitive neurons, is the same as lesioning the whole area is completely incorrect. We must take into account the potential richness of the neurochemical interactions that occur in the preoptic area, and presumably these different chemical address systems are subserving different responses. And again, we can look to the cortex and to the effects of the monoamines and see that is true. Manipulating one or other amines selectively in the same area of the cortex changes the information processing in remarkably different ways, and each of these effects is totally different from lesioning the entire cortical domain. Now, as regards to the fact that you lose the inhibition of behaviour when you let the behaviour start before you infuse the compound, it may be that one of the reasons for this might be that once the male is set in train, his sequence of responding to the female in terms of the repetitive, and rather spinal cord generated rhythmic acts of mounting and intromitting, it is hard to stop him unless you change the rules by which the male engages in the behaviour in the first place. I think it is very hard to disentangle that interpretation from one which may be right and indeed, if it is, is more interesting, but one which nonetheless remains speculative.

S.M. Pomerantz

I just want to bring up a paper that again addresses the importance of differentiating consummatory and appetitive effects of mPOA lesions. This paper by Slimp et al (Brain Research 142: 105-122, 1978) demonstrated that rhesus monkeys with mPOA lesions retain the ability to ejaculate, but only through masturbation and not through copulatory behaviour.