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Sexually conditioned incentives: Attenuation of motivational impact during dopamine receptor antagonism

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Abstract

The motivational impact of sexually conditioned incentives was examined in two experiments. In Experiment 1, male Long–Evans rats copulated to ejaculation in the presence of one of two scents (orange or almond extract) on five separate occasions. On alternating days, subjects spent an equal amount of time in social isolation with the opposing scent. Following the 10-day conditioning regimen, subjects ran more rapidly down an operant runway toward a goalbox containing the sex-paired scent (CS+) compared to trials on which the isolation-paired scent (CS −) or no scent was provided. In Experiment 2, comparably conditioned male rats were first given a baseline runway trial with an unscented goalbox. The following day, subjects were pretreated with one of four doses of haloperidol (0.0, 0.075, 0.15, or 0.30 mg/kg ip) 45 min prior to being tested in the runway for their motivation to approach either the CS+ or CS − scents. Control subjects given vehicle injections performed comparably to subjects from Experiment 1, taking significantly less time to approach the CS+ than an unscented goalbox. This decrease in run latency was not observed in subjects within the 0.075 and 0.15 mg/kg haloperidol groups. Subjects in the 0.30 mg/kg haloperidol groups took significantly more time to approach both the CS+ and CS − compared to their baseline run times. These data reveal that an olfactory cue associated with sexual reward becomes a conditioned incentive capable of eliciting approach behavior, and that dopamine receptor antagonism (at moderate but not high doses) selectively attenuates this cue-induced motivation.

Keywords: Motivation; Copulation; Incentive; Conditioning; Dopamine; Haloperidol

1. Introduction

Numerous specific factors influence the activation of sexual motivation, such that reproductive behavior only occurs under certain conditions. Some factors are internal, in the sense that they are rooted in the physiological state of the organism, and may further be categorized as static (e.g., male-typical sexually dimorphic brain regions) or dynamic (e.g., changing levels of steroid hormones). These factors often bias the ''interpretation'' of perceived external factors, or stimuli within the local environment of an organism that are reproductively significant (Stewart, 1995). Termed incentives, these stimuli may carry either positive or negative valence, depending on whether they tend to elicit approach or avoidance behavior, respectively (Bindra, 1976; Bolles, 1975; Toates, 1986).

Sexual incentives include the range of stimuli associated with conspecific members of the opposite sex (for heterosexual organisms), as long as they fall within certain attractiveness parameters determined by the relative importance of partner age, health, reproductive status, etc. (Agmo, 1999; Beach, 1942, 1976; Stewart, 1995). For male mammals, including laboratory rats, female cues that reflect behavioral estrus (e.g., pheromones, proceptive displays) generally carry significant positive incentive value and tend to elicit approach behavior (Eliasson and Meyerson, 1981; Hetta and Meyerson, 1978; Landauer et al., 1977; Merkx, 1983; Vega Matuszczyk and Larsson, 1993; Vega Matuszczyk et al., 1994). In our laboratory, we have previously shown that such cues are inherently attractive to adult male rats, since sexually naïve subjects demonstrate a stronger motivation to approach estrous

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females over nonestrous females or other males (Lopez et al., 1999).

Primary female incentives form only one class of stimuli males find sexually inviting. Environmental stimuli that become associated with successful copulation, known as secondary or conditioned incentives, can also increase sexual motivation (Agmo, 1999; Stewart, 1995). Everitt (1990) demonstrated that male rats trained under second-order instrumental conditions learn to bar-press for presentation of a light previously associated with copulation. Mendelson and Pfaus (1989) tested sexual motivation in male rats through use of a bilevel chamber in which males were periodically allowed to copulate with receptive females. After several experiences, males became behaviorally activated (specifically displaying multiple level changes) when placed into the chamber, indicating that the local environment had acquired motivational significance. Additionally, male rats spend a majority of their time on a sex-paired side of a conditioned place-preference apparatus, even if conditioning consists of only a single ejaculation (Agmo and Berenfeld, 1990). Males also demonstrate an ejaculatory preference for receptive females marked with a scent previously paired with successful copulation (Kippin et al., 1998). Lastly, both male rats and Japanese quail initiate copulation and achieve ejaculation sooner with receptive females if a conditioned incentive is present (Domjan et al., 1986; Zamble et al., 1986).

There is growing evidence that the monoamine neurotransmitter, dopamine, plays a crucial role in mediating the behavioral activating effects of primary and secondary incentives across a variety of motivational domains (Berridge and Robinson, 1998; Blackburn et al., 1987, 1989, 1992; Horvitz, 2000; Ikemoto and Panksepp, 1999; Kiyatkin, 1995; Mogenson et al., 1980; Phillips et al., 1991; Robbins and Everitt, 1996; Salamone, 1994, 1996; Schultz, 1998; Schultz et al., 1997; but see Beninger and Hahn, 1983; Beninger and Herz, 1986; Horvitz and Ettenberg, 1991; McFarland and Ettenberg, 1995, 1998, 1999). This includes both approach behavior towards positive incentives such as food, and avoidance of and withdrawal from aversive stimuli (Salamone, 1994). Certainly, dopamine has long been recognized as an important stimulatory agent of male sexual motivation (for reviews, see Bitran and Hull, 1987; Everitt, 1990, 1995; Hull et al., 1999; Melis and Argiolas, 1995; Pfaus and Everitt, 1995; Wilson, 1993). Drugs that enhance dopaminergic transmission generally cause an increase in sexual motivation, while drugs that block dopaminergic action tend to inhibit sexual motivation (Everitt, 1990; Pfaus and Phillips, 1989, 1991; Lopez and Ettenberg, 2001).

However, many of the experimental methodologies employed in this research area confound the relative motivational impact of primary and secondary sexual incentives, making the interpretation of dopamine's exact effect somewhat difficult. For instance, subjects are often trained to emit an operant response (such as press a lever or traverse an alley) in order to gain access to a receptive female (Everitt, 1990; Moses et al., 1995; Warner et al., 1991). Administration of dopamine receptor antagonists under these conditions decreases the rate and/or intensity of operant responding. Unfortunately, it is unclear as to whether the reduced responding is occurring because of a reduction in the incentive value of the female herself (who resides within the test apparatus), the value of local conditioned cues, or the value of the operant response itself (Domjan et al., 1992). Additionally, dopamine receptor antagonism may block the reinforcing nature of the sexual encounter and thus lead to an extinction of operant responding (Ettenberg, 1989; Wise, 1982).

In order to address these issues, the current experiment was designed with the following goals in mind: (1) to establish a sexually conditioned incentive following a minimum of sexual experience, (2) to experimentally isolate the motivational impact of a conditioned incentive, independent of other external factors, and (3) to examine dopamine's role in mediating the positive value and behaviorally activating effects of a sexually conditioned cue. In order to isolate the effect of a secondary incentive, we developed an experimental protocol in which subjects do not receive sexual experience within the same apparatus used to test their sexual motivation. Thus, a sexually reinforced operant response is not established. Male rats are conditioned to associate two neutral olfactory cues with copulation and social isolation respectively, within a Plexiglas arena. The incentive value of these cues is subsequently tested by presenting each of them individually to subjects within a straight-arm operant runway. The subjects' approach behavior towards the scent (located within the goalbox) is taken as an objective measure of its motivational value. This procedure allows for the examination of sexual motivation induced by sexually conditioned cues independent of the effects of primary female incentives, as subjects never perceive nor encounter a female within the runway apparatus. Through administration of haloperidol prior to runway trials, the effects of dopamine receptor antagonism on the incentive value of a previously established conditioned cue can also be tested.

2. Method

2.1. Animals

A total of 93 male and 50 female Long–Evans rats were obtained from Charles Rivers Laboratories (Wilmington, MA). The males ranged from 80 to 100 days old and the females from 80 to 150 days old at the start of testing. All animals were housed individually in hanging wire cages within a 22 °C vivarium environment maintained under a reverse 14:10 light–dark schedule (lights on 2300–1300 h). Food and water were provided on an ad-libitum basis. Prior to arrival in the vivarium, the males were group housed but did not have access to females. Therefore, they were sexually naive insofar as they lacked heterosexual copulatory experience.

2.2. Surgery

All females were ovariectomized (OVX) through a single lower abdominal incision 1–8 weeks prior to testing using standard aseptic surgical techniques and under deep anesthesia. For 30 females, anesthesia was induced by intraperitoneal (ip) administration of a mixture of 90 mg/kg ketamine and 2 mg/kg xylazine, in a volume of 1 ml/kg. For 20 females, isoflurane gas anesthesia (4% induction, 2% maintenance) was given. All animals were pretreated with 0.3 mg/kg ip atropine (Pittman-Moore, Washington Crossing, NJ) 15 min prior to the induction of anesthesia in order to reduce potential respiratory problems. Females received at least 1 week of postoperative care prior to initiation of the experiment.

2.3. Inducing female sexual receptivity

Receptivity was induced in the female rats via hormonal administration consisting of subcutaneous (sc) administration of 15 μg of estradiol benzoate (in 0.1 ml sesame oil) 48 and 24 h before testing, with an additional sc injection of 500 μg progesterone (in 0.1 ml propylene glycol) 3–5 h before testing. Steroid hormones were purchased from Sigma Chemical Company, St. Louis, MO.

2.4. Apparatus

Sexual conditioning took place within three cylindrical Plexiglas arenas (45-cm diameter, 40-cm height). Motivational testing occurred within a straight-arm runway consisting of a startbox ($25 \times 25 \times 20$ cm), an alley ($160 \times 10 \times 20$ cm), and a cylindrical Plexiglas goalbox (45 cm diameter, 40 cm height). Removable doors were located between the startbox and alley, and between the alley and goalbox. Infrared photocell emitter–detector pairs were located within the alley just outside the startbox and just inside the goalbox. Interruption of the photobeam outside the startbox initiated a timer that stopped when the subject entered the goalbox. This apparatus is comparable to that used successfully by our laboratory for studying other motivating goalbox events including conspecific male and female rats (Lopez et al., 1999), food (Chausmer and Ettenberg, 1997; Ettenberg and Camp, 1986a; Horvitz and Ettenberg, 1989; McFarland and Ettenberg, 1998), water (Ettenberg and Camp, 1986b; Ettenberg and Horvitz, 1990), and drugs of abuse (Ettenberg and Geist, 1993; Ettenberg et al., 1996; McFarland and Ettenberg, 1995, 1997).

2.5. Procedure

2.5.1. Phase 1: conditioning

Two experiments were conducted, each employing an identical conditioning phase. On alternating days, subjects were given copulatory sessions in the presence of one of two distinct scents, either orange or almond extract (Felbro Food Products), and isolation sessions in the presence of the other scent. Only one session per subject occurred each day. The scent paired with copulation will henceforth be referred to as the CS+, while the scent paired with social isolation will be referred to as the CS−. For half the subjects, the orange scent was the CS+ and almond the CS−, with the opposite being true for the other half. A total of five copulatory and five isolation sessions were given over the course of 10 days. This 10-day period made up the entire conditioning phase of both experiments for the majority of subjects.

On each day, half of the male subjects were paired with a sexually receptive female until they achieved one ejaculation or until 30 min passed, whichever came first. Those subjects not given sexual experience spent an individual amount of time in the arena alone. The length of each subject's isolation period was equal to the amount of time it took that same subject to copulate to ejaculation on the preceding day. For the first day of conditioning, noncopulating subjects were arbitrarily isolated for 10 min. On half of the days (determined randomly), copulatory sessions were conducted prior to the isolation sessions; on the remaining days, isolation sessions preceded the copulatory ones.

Immediately prior to each session, that day's scent was applied using a disposable wipe drawn along the top edge of the Plexiglas arena. On any given day, both copulatory and isolation sessions occurred in the presence of the same scent, such that the use of the two scents alternated day to day. At the end of all subject sessions each day, all three arenas were thoroughly cleaned with a 30% alcohol solution to remove any scent traces.

Periodically, some males would not immediately copulate with the introduced female, especially if it was their first conditioning session. In order to stimulate copulation, the initial female was replaced with a second, and sometimes third receptive female. If the male failed to copulate for 30 min, the session was ended. At the end of the 10-day conditioning period, an 11th day of conditioning occurred during which all previously noncopulating males were given an additional opportunity to copulate with a receptive female under identical circumstances as their earlier failure. If a subject failed to copulate on two or more conditioning sessions, including this 11th day, he was dropped from the experiment. Four males were dropped from Experiment 2 for this reason. No subjects were dropped from Experiment 1.

Female rats were rotated through hormone treatments such that receptivity was induced every 4 days. A different female was paired with a subject male each time he was given a copulatory session, such that over the course of the conditioning phase he was exposed to five different females (possibly more, if female replacement had occurred due to lack of sexual activity). If a female was placed with a male but did not demonstrate immediate and sufficient receptivity for successful copulation, it was removed and replaced with another female.

2.5.2. Phase 2: motivational testing

2.5.2.1. Experiment 1. All runway testing took place under red light conditions during the dark portion of the rats' photoperiod. Following the 10-day conditioning regimen, 16 male subjects were allowed to individually explore and habituate to the empty runway apparatus for 10 min on two consecutive days. Over the next 4 days, subjects were tested for their motivation to approach a goalbox placed under one of three conditions: unscented, CS+ scented, or CS − scented. Subjects were tested for the unscented goalbox (control condition) twice. For the scented-goalbox trials, a small glass container of the extract (holding approximately 30 ml) was placed, uncovered, at the far end of the goalbox 15 min prior to testing. On any given test day, all 16 subjects ran for the same goalbox condition; only one trial per subject per day was conducted. The order of trials across the 4-day testing period was randomized for three separate groups of subjects.

Individual trials were conducted using the following procedure: first, a subject male was placed into the startbox for 15 s. The start door was lifted and the subject was given access to the alley. Leaving the startbox interrupted an infrared photocell that triggered a timer, which stopped once the subject entered the goalbox. At this point, the trial was ended and the subject returned to his home cage. The next subject's trial was then initiated. This procedure continued, one animal at a time, until all 16 subjects were tested. The order of subjects run was held constant throughout the experiment.

The dependent measure of interest was run time, i.e., the time elapsed between the subject's leaving the startbox and entering the goalbox. Thus, we view run time as an objective index of each subject's motivation to approach the goalbox stimuli; shorter run times presumably reflect greater motivation.

2.5.2.2. Experiment 2. As in Experiment 1, all runway testing took place under red light conditions during the dark portion of the rats' photoperiod. After conditioning, 77 male subjects were habituated to the empty runway apparatus for 10 min on two consecutive days. On the following day, all subjects were given a baseline test to measure their motivation to approach an empty, unscented goalbox. Individual trials were conducted using an identical procedure as in Experiment 1. Subjects were then assigned to one of four haloperidol dosage groups.

The next day, each subject was tested within the runway for his motivation to approach either the CS+ or CS −, as described in Experiment 1. On this "test day," all subjects ran for the same goalbox condition. Half of the subjects within each dosage condition ran for their CS+ and half for their CS −, making a total of eight independent groups. Forty-five minutes prior to this test, subjects within each group were pretreated with a vehicle injection or one of three doses of haloperidol, a dopamine-receptor antagonist. Subjects in Groups 1 and 2 were given ip vehicle injections of 0.002 M lactic acid. Subjects in Groups 3 and 4, 5 and 6, and 7 and 8 were given ip injections of 0.075, 0.15, and 0.30 mg/kg haloperidol respectively. All injections were given in a volume of 1 ml/kg. To clarify, half the subjects in each dosage condition were pretreated with a given dose of haloperidol and then exposed to the CS+ on test day; the other half received the same treatment but were exposed to the CS − .

3. Results

3.1. Experiment 1

When tested for their motivation to approach the CS+, unexpected noises disrupted the trials of two subjects. Thus, the run times of these two subjects, but only for the CS+ goalbox condition, were excluded from analysis. Fig. 1 shows the mean run time (+S.E.M.) for all 16 subjects running for the three goalbox conditions (no scent, CS+, and CS −). For the reason mentioned above, the mean for the CS+ condition only contains data from 14 subjects. A one-way repeated-measures ANOVA conducted on these data revealed a significant difference in run times across conditions, $F(2,26) = 4.860$, $P = .016$. Three post hoc two-tailed, paired-sample t tests compared the mean run times between each of the three conditions. There was no significant difference in subject run times between the no scent and CS − condition, $t(15) = -0.916$, $P = .374$. However, the mean run time difference between the no scent and CS+ condition was statistically significant, $t(13) = 2.206$, $P = .046$, as was the difference between the CS+ and CS − conditions, $t(13) = -2.732$, $P = .017$.

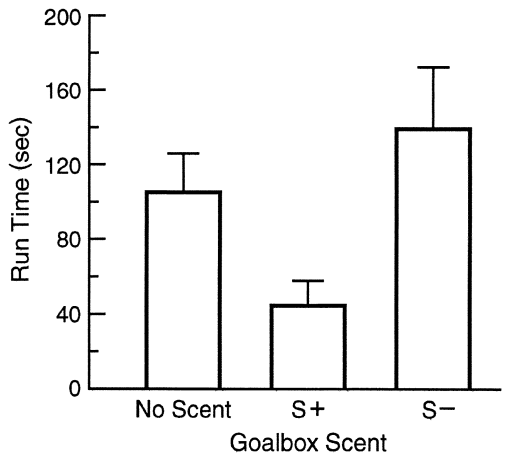

Fig. 1. Mean (+S.E.M.) run times for 16 male subjects tested for their motivation to approach an unscented goalbox (two trials), an S+ scented (one trial), and an S − scented goalbox (one trial). Subjects took significantly less time to enter an S+ scented goalbox versus an S − scented or unscented goalbox.

3.2. Experiment 2

Fig. 2, panels A–D, displays the mean (+S.E.M.) run times for subjects within each of the four dosage conditions. The data are presented such that for each group, the baseline run time (for an unscented goalbox) is paired with the subsequent test-day run time (for a scented goalbox). Thus, within each panel the data for two different groups of subjects are shown. A total of four 2 × 2 (Trial × Scent) ANOVAs were conducted on the data within each panel. For the vehicle condition, there was a significant interaction between trial and scent, $F(1,20) = 6.864$, $P = .017$, indicating that the change in subjects' behavior from baseline to test day was dependent upon the scent presented. Specifically, when the goalbox was scented with the CS+, subjects ran faster on test day compared to baseline, while subjects ran comparatively slower when the goalbox was scented with the CS −. There were no significant main effects or interactions in the data within panels B and C, corresponding to the 0.075 and 0.15 mg/kg dosage conditions respectively. However, there was a significant main effect of trial in the 0.30 mg/kg condition, $F(1,15) = 8.783$, $P = .010$. Subjects within both the CS+ and CS − groups demonstrated a relatively drastic increase in run times on test day, as compared to baseline, suggesting possible motor impairment due to the high dose of haloperidol given prior to testing.

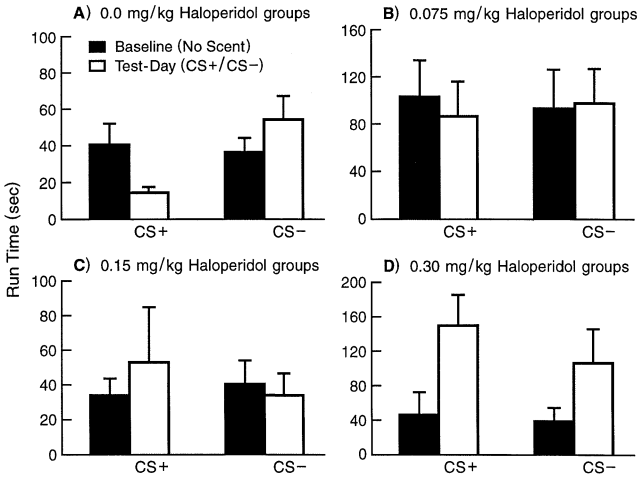

Fig. 2. Mean (+S.E.M.) run times for the eight groups of experimental subjects, under different dosage and stimulus conditions. Panels A–D depict data from subjects pretreated with 0.0, 0.075, 0.15, and 0.30 mg/kg haloperidol on test day, respectively. Black bars represent subject run times under baseline conditions (for an unscented goalbox) while white bars depict subject run times on test day, for one of the two conditioned scents (CS+/CS −). Within each panel, the two bars on the left correspond to data from subjects exposed to the CS+ on test day, while the two bars on the right are data from subjects exposed to the CS − on test day. Thus, each pair of bars represents data obtained from one group of animals.

4. Discussion

The results of both Experiments 1 and 2 indicate that male rats given five copulatory episodes in the presence of a distinct scent learned to associate it with sexual reward. In subsequent testing, subjects expressed a stronger motivation (as reflected by shorter run times) to approach the sexually conditioned scent in an operant runway over a scent previously paired with isolation or an unscented goalbox. This approach behavior occurred even though subjects perceived the olfactory cue in a different environment from the one that they were conditioned in, and even though they did not experience sexual reinforcement within the runway itself. Thus, this current methodology allows for the examination of the motivational impact of a secondary, conditioned incentive independent of other factors, including primary incentives and previously learned operant behaviors.

In addition, Experiment 2 provided evidence for a dopaminergic role in mediating these motivational effects. Vehicle-treated subjects displayed a pattern of responding similar to that seen in Experiment 1. When the goalbox was scented with the CS+ on test day, subjects expressed an increased motivation to approach it as reflected by faster run times. They were also slightly slower in approaching a CS − scented goalbox, similar to the runway behavior of subjects in Experiment 1. However, those subjects given the two lower doses of haloperidol (0.075 and 0.15 mg/kg) did not differentiate between an unscented goalbox and the CS+, signifying that the cue's incentive value had been abolished. Additionally, the run times of subjects given these same doses and presented with the CS − did not differ from baseline. We believe this pattern of results indicates that haloperidol caused a selective motivational deficit, and not a general loss of motor ability. In contrast, subjects given the highest dose of haloperidol (0.30 mg/kg) ran significantly slower for both the CS+ and CS − in comparison to baseline, and their ability to initiate movement and traverse the runway appeared severely compromised. It is likely then that this dose of haloperidol caused both a motivational *and* motoric impairment. It should be noted that the baseline run times of subjects across the four dosage conditions were not equivalent; specifically, subjects within the 0.075 mg/kg groups were slower to approach an unscented goalbox when compared to all other subject groups. However, this difference does not alter our interpretation of the obtained pattern of results. If anything, the higher baseline of the 0.075 mg/kg groups should have made it easier to see a decrease in test-day run times for a CS+ scented goalbox. This decrease was not observed, presumably due to the incentive-attenuating effects of haloperidol.

It is conceivable that the two lower doses of haloperidol differentially impaired subjects' faster running for the CS+ versus their slower running for the CS −. However, there are reasons to suspect that this explanation is inadequate. A number of studies have successfully dissociated the perform-

ance-debilitating effects of neuroleptics from their capacity to attenuate motivation (see Wise, 1982, for a review), and have shown that dopamine receptor antagonists do not necessarily compromise a rat's ability to respond normally on a single trial. In fact, prior research conducted in our laboratory has shown that haloperidol, within the dosage range adopted in the current study, does not affect the response-initiation latencies nor running speeds of subjects working in an operant runway for or food or heroin during relapse–reinstatement (McFarland and Ettenberg, 1995, 1998, 1999). Our own previous work has shown that while doses of 0.075 and 0.15 mg/kg haloperidol slow a subject's approach behavior for a goalbox containing an estrous female (Lopez and Ettenberg, 2001), the same two doses do not affect subject run times when the goalbox contains a nonestrous female or is empty, again suggesting that haloperidol's actions can be specifically motivational and not motoric. Interestingly, pilot studies preceding that work also showed that a 0.30 mg/kg dose of haloperidol slowed subject run times for all targets, including an empty goalbox. Thus, taken together with our previous findings, the current experiment's pattern of results indicates that haloperidol doses of 0.15 mg/kg and below are capable of specifically targeting motivational systems, while those of 0.30 mg/kg (and presumably higher) tend to inhibit voluntary movement.

These results, in general, support the large body of evidence implicating dopamine as a biochemical signal of motivationally significant stimuli (Blackburn et al., 1987, 1989, 1992; Kiyatkin, 1995; Mogenson et al., 1980; Phillips et al., 1991; Salamone, 1994; Schultz, 1998; Schultz et al., 1997). This dopaminergic signal can occur in response to the perception of primary incentives such as estrous female cues, even within a sexually naïve male (for reviews, see Mitchell and Gratton, 1994; Phillips et al., 1991; for specific studies, see Louilot et al., 1991; Wenkstern et al., 1993). The dopamine response may also become conditioned, tied to the perception of a stimulus that predicts the presence of a primary goal (Schultz, 1998; Schultz et al., 1997). West et al. (1992) noted that sexually conditioned incentives increase the firing rate (percentage and magnitude) of cells within the nucleus accumbens, hypothesizing that this effect may be mediated by mesolimbic dopamine activation. Collectively, these studies suggest that both primary and secondary sexual incentives influence motivational systems associated with the initiation of copulatory behavior via mesolimbic dopaminergic pathways.

Unfortunately, the results of the current experiments do not allow one to determine whether dopamine receptor antagonism exerts a direct inhibitory influence on sexual motivation, or rather causes deficits in other psychological arenas that affect motivational capacity. For example, it is possible that systemic haloperidol pretreatment compromised the attentional capacities of the male subjects, such that they were unable to respond normally to the conditioned incentive (Clark et al., 1987; Matthysee, 1978; Ragozzino, 2000). Similarly, it is possible that dopamine receptor antagonism caused a nonspecific reduction in the salience of available environmental stimuli (Horvitz, 2000). More detailed experimentation is necessary to dissociate these possibilities.

It should also be mentioned that the results reported here run somewhat counter to other data from our laboratory, in which haloperidol did not reduce subjects' motivation to approach an olfactory discriminative stimulus (S+) predictive of either heroin or food reward (McFarland and Ettenberg, 1995, 1997, 1998). A number of methodological differences between those studies and the current one may explain the discrepancy in results. Most significantly, in the prior experiments, subjects were trained to traverse a runway through repeated trials of partial reinforcement. The discriminative stimuli placed within the runway (almond or orange extract) predicted the presence or absence of the goalbox reward. Motivational testing, therefore, took place within the same apparatus that conditioning was concurrently occurring. Thus, subjects' motivation to approach the goalbox was mediated not only by the presence of secondary incentives (including the S+), but also the establishment of a stimulus–response association (and/or action–outcome association; Dickinson and Balleine, 1994). In addition, because reinforcement occurred within the runway, the many contextual cues available (i.e., the apparatus itself) most likely became salient secondary incentives over repeated testing. In contrast, subjects within the current experiments never received sexual reinforcement within the runway, and thus their motivation to approach the goalbox was based purely on the incentive value of the CS+ or CS − . One might expect that haloperidol would have less of a behavioral effect in the presence of multiple motivational inputs, including a strong S–R habit.

Another possibility emerges from the recent work of Shultz and colleagues (Schultz, 1998; Schultz et al., 1997) who have demonstrated that dopaminergic neurons respond to unexpected, but not expected, incentives. Perhaps then in the previous work by McFarland and Ettenberg (1995, 1997, 1998), the subjects' increasing expectation of heroin or food reward upon presentation of the S+ led to an eventual decline in dopaminergic mediation of the incentive-motivational processes underlying their approach behavior. In contrast, in the current experiments, the CS+ may have been an unexpected incentive in the context of the runway, and thus stimulated dopaminergic pathways. Haloperidol pretreatment annulled this response and prevented motivational activation.

Motivational states function to choose and initiate behavioral sequences that increase the probability of achieving a particular goal state, given current environmental circumstances. The ability to form motivationally specific stimulus–outcome associations allows individual organisms to accommodate their behavior to local conditions (that vary between members of a species) in an attempt to efficiently satisfy recurring physiological needs and maximize survival and reproductive success. More specifically, such condition-

ing processes might allow males to recall, seek, and identify locations where female conspecifics regularly gather, and where copulation is more likely to occur. In addition, sexual predictive signals may facilitate behavioral interactions between males and females, and potentially stimulate critical aspects of reproductive physiology (Domjan et al., 1998; Graham and Desjardins, 1980). For example, male Japanese quail release a greater volume of semen and greater numbers of spermatozoa over controls when allowed to copulate in the presence of a sexually conditioned, secondary incentive (Domjan et al., 1998). Regardless of functionality, it is clear that sexual reward is a powerful mediator of incentive formation and enhancement, and that both the establishment and expression of such associations are, at least in part, mediated by dopaminergic release (Lopez and Ettenberg, 2000).

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