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8-OH-DPAT Interacts With Sexual Experience and Testosterone to Affect Ejaculatory Response in Rats

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ROWLAND, D. L. AND E. J. HOUTSMULLER. *8-0H-DPAT interacts with sexual experience and testosterone to affect ejaculatory response in rats.* PHARMACOL BIOCHEM BEHAV **60**(1) 143–149, 1998.—Studies investigating the effect of 8-OH-DPAT (DPAT) on male sexual response have typically used subjects having variable sexual experience and levels of testosterone, factors known to independently influence male sexual behavior. This experiment examined the role of these two variables in the mediation of DPAT effects on sexual behavior. One hundred and six castrated males, half of whom received sexual experience, were tested with an effective dose of 8-OH-DPAT (0.1 mg/kg) or saline. In addition, males were tested under one of three regimens of testosterone. Results indicated that DPAT and testosterone exerted independent effects on ejaculatory measures, and along with sexual experience, showed interactive effects as well. When testosterone (T) levels were substantially below normal, DPAT showed no effect. When T reached threshold levels, the DPAT effect was limited to sexually experienced males. At high T levels, both experienced and naive males exhibited strong effects from DPAT. In contrast with ejaculatory measures, mounting and intromitting behaviors were relatively unaffected by DPAT. These results emphasize the importance of specifying both the animal's sexual history and its testosterone profile in studies investigating pharmacological effects on sexual response. © 1998 Elsevier Science Inc.

8-OH-DPAT Sexual experience Testosterone Rat 5-HT Serotonin Ejaculation Copulation Sexual behavior Intromission

A growing body of evidence supports the involvement of 5-HT_{1A} receptors in the regulation of sexual behavior in the male rat (1–3,18,21,27,28,35). Accordingly, the 5-HT_{1A} receptor agonist 8-hydroxy-2 (di-n-propylamino) tetralin, better known as DPAT, reportedly affects both sexual arousal and ejaculatory threshold in this species (1,3,16,19,20,30,31,37).

Studies investigating the effect of DPAT on ejaculatory parameters in male rats have typically used animals pretested for copulatory behavior, that is, animals with sexual experience [e.g., (19,20,35)]. The presumed rationale is that for DPAT to exhibit an effect, sexual responses must be reliably executed, thereby eliminating the subpopulation of persistent noncopulators and reducing variability within the sample. Although several studies suggest that sexual experience may be important to the facilitating effect of DPAT (19,31), a careful analysis of this factor that includes detailing of prior sexual histories has yet to be undertaken.

In addition, most investigations with DPAT have relied on intact (i.e., noncastrated) males in which levels of testosterone (T) are sufficiently high to activate sexual behavior. In studies using animals with subnormal levels of testosterone, the effect of DPAT is not so clear. For example, an initial report (1) indicated a facilitatory effect of DPAT on mounts, intromissions, and ejaculations in male rats 5 weeks postcastration, a time when T levels are presumably very low. More recently, Haensel et al. (20) argue that testosterone is, in fact, necessary for the stimulatory effects of DPAT on ejaculation, but that subnormal levels may be adequate.

The present study further investigated the conditions necessary for DPAT to facilitate sexual arousal and ejaculatory

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response in the male rat. The contributions of two factors known to interdependently affect sexual behavior, namely sexual experience and level of testosterone, were examined in the context of the DPAT effect on sexual behavior. Castrated rats, half of whom had received precastration sexual experience, were tested under an effective dose of 8-OH-DPAT (1–3,19,20,25,31). In addition, animals were tested under one of three regimens of SC testosterone, selected to produce blood titers of T ranging from sub to supranormal (11).

METHOD

Subjects

One hundred and six male Wistar rats, aged 60–70 days, were maintained on a reversed 14-L:10-D cycle (lights on at 0800 h) in a climate-controlled room (21–24°C) with food and water ad lib. Animals were housed by treatment (experienced vs. naive; testosterone regimen) in large cages, three to four to a cage.

Sexual Experience

At approximately 90 days of age, males were divided into two groups: experienced (EXP) and naive (NAIVE). Animals in the naive group ($n = 54$) received no exposure to receptive females prior to DPAT testing and thus had no sexual experience. However, they did receive handling equivalent to that received by EXP males during the pretesting phase. Animals in the EXP group ($n = 52$) underwent a series of preexperimental tests with a receptive stimulus female (see details below) to provide sexual experience. These animals spent a minimum of three 45-min sessions with a receptive female to reach the preset criterion for ejaculatory experience of three ejaculations.

Drug Solutions

8-OH-DPAT, obtained from Sigma Chemical (St. Louis, MO), was dissolved in normal saline in a concentration of 0.1 mg/0.1 ml immediately prior to each test. Animals receiving DPAT were given 0.1 mg/kg of body weight. This dose was selected because it represents an epithreshold amount, and as such might be most likely to reveal interaction effects with T and sexual experience. Specifically, this dose has yielded mixed results in previous studies, with some groups reporting an effect (30,31) and others not (2,37). In our own pilot tests, this was the lowest dose at which a reliable decrease in ejaculatory latency was observed in noncastrated males.

Stimulus Wistar females were brought into heat with SC estradiol benzoate (50 μg/0.1 ml peanut oil) 48 h prior to testing, and intramuscular progesterone (500 μg/0.1 ml peanut oil) 17 h prior to testing (13,22,38). Testosterone was dissolved in peanut oil and administered subcutaneously (see details below).

Procedure

At approximately 110–120 days of age, males in both groups were castrated transcrotally under light ether anesthesia using standard laboratory procedures. Seven weeks following castration animals were begun on a daily regimen of testosterone propionate. The 7-week postcastration interval was chosen based on two observations: other studies investigating DPAT effects on ejaculation in castrated rats have used equivalent or shorter postcastration intervals (2,20); and analysis of T in five males at 50 days postcastration indicated undetectable levels (<0.20 nmol/l), indicating washout of endogenous T.

Three regimens of SC T administration were used, each chosen to produce a different range of circulating T. For the low dose (LOW: $n = 38$), males were given 4 consecutive days of 100 μg/0.1 ml peanut oil; for the medium dose (MED: $n = 37$), 8 consecutive days of 100 μg/0.1 ml peanut oil; and for the high dose (HIGH: $n = 31$), 14 consecutive days of 500 μg/0.1 ml peanut oil. These regimens were selected to produce blood titers of T ranging from subnormal to supranormal (11). Specifically, the two lower doses yield levels around the purported lower and upper limits of the threshold necessary for activation of normal sexual behavior, whereas the highest dose regimen produces T levels well into the normal range typically seen in the rat.

Sexual behavior testing with a receptive stimulus female began on the morning following the final day of T injection. During this test, half the animals in each group (EXP and NAIVE; HIGH, MED, and LOW T) were given 0.1 mg/kg DPAT ($n = 54$), the other half were given equivalent volumes of normal saline ($n = 52$).

Behavioral Testing

Testing of male sexual behavior was carried out between the first 30 to 180 min of the dark cycle in a red-light, sound-attenuated environment. Each male was placed in a large (38 × 48 cm) observation cage and injected 5 min later with either DPAT or saline. Twenty minutes after the injection, a receptive stimulus female was introduced. Using a testing strategy similar to other investigations of DPAT on sexual response (2,16,25,31), males were allowed to mate for either 45 min, or until the end of the second postejaculatory interval, whichever occurred first. The following measures relevant to male sexual response (6) were recorded: mount latency, intromission latency, ejaculation latency, mount frequency, intromission frequency, ejaculation frequency, mounts and intromissions to ejaculation, and postejaculatory interval. In addition, two indices were derived from these measures. First, to control for variation in testing length (22,37), the rate of mounting and intromitting (MIRATE) was calculated by dividing the total number of mounts and intromissions by the session length (in minutes). Second, to provide a measure of the number of mounts/intromissions needed to reach ejaculation, an index representing the ratio of the number of ejaculations to the total number of mounts and intromissions was calculated for each male. This "efficiency index" (EFFICIENCY) was preferred over the simpler "number of mounts/intromission to ejaculation" because it generated a single score for each male, no matter how many ejaculations it had, thereby eliminating the dependencies that result from multiple observations (ejaculations) from the same subject.

Testosterone Assay

Blood samples were obtained between 1200 and 1700 h from subgroups of animals selected in randomized blocks ($n \geq 4$) from each possible experimental condition (EXP vs. NAIVE; HIGH, MED, and LOW T; DPAT vs. saline). These samples were drawn on the day following final T administration via tail venipuncture while animals were under light anesthesia. Samples were collected into heparinized tubes, centrifuged for 30 min, and stored frozen until assayed within 7 days. Total testosterone was assayed using a commercially prepared kit (DPC, Los Angeles). Detection limit for this assay is 0.20 nmol/l, and crossreactivity with corticosteroids and other

androgens is minimal (3.3% or less). Interassay coefficient of variation was 9.8%, and the intraassay coefficient was 7.2%.

Data Analysis

Sexual response measures were analyzed using a three-way factorial ANOVA, with EXPERIENCE (EXP vs. NAIVE), dose of testosterone (TDOSE: LOW, MED, and HIGH), and DPAT (DPAT vs. saline) as the factors. Post hoc analyses were carried out with Newman–Keuls tests. All probabilities represent two-tailed tests of significance.

RESULTS

Number of Ejaculations (#EJAC)

The percentage of males in each experimental condition showing copulatory behavior appears in Table 1. Figure 1 and Table 2 indicate the manner in which DPAT, sexual experience, and testosterone affected number of ejaculations (a maximum of two ejaculations could be achieved by any male within the 45-min test session; results from the LOW T group are not shown because only one male, EXP and DPAT, ejaculated). Comparison of group means indicated more ejaculations for DPAT, $F(1, 94) = 7.38$, $p = 0.008$, and higher TDOSE animals, $F(2, 94) = 60.77$, $p < 0.001$, but no effect for EXPERIENCE, $F(1, 94) = 2.77$, $p = 0.100$. Significant interactions were found for DPAT × EXPERIENCE, $F(1, 94) = 4.06$, $p = 0.047$, and EXP × TDOSE, $F(2, 94) = 7.30$, $p = 0.001$. The DPAT × EXPERIENCE interaction reflects the high number of ejaculations that occurred under DPAT for the EXP group, an effect that was particularly pronounced under the MED T dose ($p < 0.05$). Under HIGH T, this difference all but disappeared relative to the other groups ($p > 0.05$). The EXP × TDOSE interaction indicated that sexual experience affected #EJAC differentially, with the greatest difference occurring under the MED T dose ($p < 0.05$).

Latency to Ejaculation (LATENCY)

The latency (in minutes) to the first ejaculation (5,10) in the session was compared across all groups (Table 3) for the MED and HIGH T conditions (only one LOW T male ejaculated). For this analysis, nonejaculating males were assigned a latency of 46 min, the maximum possible for the testing session (13). Significant effects occurred for both DPAT, $F(1, 60) = 10.53$, $p = 0.002$, and TDOSE, $F(1, 60) = 15.61$, $p < 0.001$, with decreased latencies for males under DPAT and higher levels of T. Interactions between DPAT and EXP, $F(1, 60) = 3.52$, $p = 0.065$, and EXP and TDOSE, $F(1, 60) = 10.49$, $p = 0.002$, were significant or marginally so. Post hoc analysis confirmed the shorter latency for experienced DPAT-treated animals compared with other groups ($p < 0.05$), but as with #EJAC, this difference was not significant under the high dose of T ($p > 0.05$).

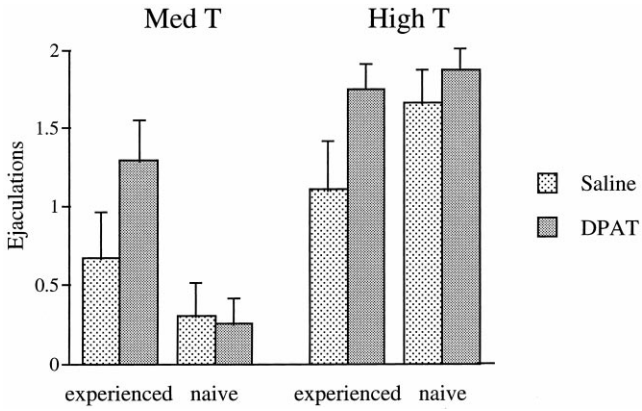

FIG. 1. Mean (±SE) number of ejaculations following injection of 8-0H-DPAT (0.1 mg/kg) or saline for sexually experienced and sexually naive male rats injected with testosterone 100 μg/8 days (MED T) or testosterone 500 μg/14 days (HIGH T). Under the MED T regimen, DPAT significantly increased the number of ejaculations in experienced but not naive animals. Sexual experience increased the number of ejaculations only under the MED T regimen.

Rate of Mounts and Intromissions (MIRATE)

Males that ejaculated twice were removed from the testing chamber at the end of the second postejaculatory interval, and therefore, test length varied for animals. To control for this variation, each animal's mounts and intromissions were divided by the length of its testing session to yield an overall index of sexual activity per minute of testing time (MIRATE). Comparison across conditions indicated significant DPAT, $F(1, 94) = 3.86$, $p = 0.052$, and TDOSE, $F(2, 94) = 7.31$, $p <$

TABLE 1

PERCENT OF COPULATING MALES IN EACH EXPERIMENTAL CONDITION

	LOW T			
	n	DPAT	*n*	Saline
EXP	10	77	9	89
NAIVE	10	55	9	89
	MED T			
	n	DPAT	*n*	Saline
EXP	10	88	9	100
NAIVE	8	89	10	80
	HIGH T			
	n	DPAT	*n*	Saline
EXP	8	100	8	100
NAIVE	8	100	7	100

TABLE 2

MEAN (±SE) NUMBER OF EJACULATIONS

	n	DPAT	*n*	Saline	Effects (*p*-Values)
EXP	27	1.07 (0.17)	25	0.64 (0.17)	Main Effects
NAIVE	27	0.63 (0.17)	27	0.48 (0.15)	DPAT: 0.008
					TDOSE: 0.001
					EXP: 0.100
LOW T	20	0.10 (0.07)	18	0.00 (0.00)	Interactions
MED T	18	0.83 (0.20)	19	0.47 (0.18)	D × T: 0.564
HIGH T	16	1.81 (0.10)	15	1.33 (0.21)	D × E: 0.047
					T × E: 0.001

TABLE 3
MEAN (±SE) LATENCY TO FIRST EJACULATION IN MIN FOR MED AND HIGH T CONDITIONS

	n	DPAT	*n*	Saline	Effects (*p*-Values)
EXP	18	21.5 (3.3)	18	36.2 (2.4)	Main effects
NAIVE	16	27.1 (4.4)	16	33.0 (4.1)	DPAT: 0.002
					TDOSE: 0.001
					EXP: 0.817
MED T	18	30.9 (3.8)	19	39.3 (2.6)	Interactions
HIGH T	16	16.5 (2.9)	15	28.8 (4.1)	D × T: 0.610
					D × E: 0.065
					T × E: 0.001
	Under MED T				
	n	DPAT	*n*	Saline	Post Hoc ($p < 0.05$)
EXP	10	23.4 (5.0)	9	37.7 (3.6)	Exp/DPAT <
NAIVE	8	40.5 (3.9)	10	40.8 (3.8)	all groups
	Under HIGH T				
	n	DPAT	*n*	Saline	
EXP	8	19.4 (4.1)	8	34.8 (4.8)	DPAT < Saline
NAIVE	8	13.7 (4.1)	7	19.9 (5.7)	

TABLE 4
COMBINED MOUNTS AND INTROMISSIONS PER MINUTE OF TESTING (MIRATE: MEAN ± SE) AFTER THE INITIATION OF THE FIRST MOUNT/INTROMISSION

	n	DPAT	*n*	Saline	Effects (*p*-Values)
EXP	27	0.86 (0.10)	25	1.06 (0.14)	Main effects
NAIVE	27	0.94 (0.19)	27	0.86 (0.12)	DPAT: 0.702
					TDOSE: 0.152
					EXP: 0.858
LOW T	20	0.64 (0.16)	18	0.85 (0.16)	Interactions
MED T	18	0.95 (0.13)	19	1.06 (0.18)	D × T: 0.535
HIGH T	16	1.16 (0.27)	19	0.97 (0.14)	D × E: 0.364
					T × E: 0.027

0.001, effects, as well as an EXP × TDOSE interaction, $F(1, 94) = 3.29$, $p = 0.041$.

DPAT animals appeared to be initially hindered in their sexual activity because of the stereotypic motor response associated with this drug (7,21). Thus, when the index of sexual activity per minute (MIRATE) was adjusted for the fact that saline-injected controls initiated sexual activity earlier in the session than DPAT animals [DPAT = 16.5 min vs. saline = 8.9 min; $F(1, 94) = 7.92$, $p = 0.006$, no differences between DPAT, $F(1, 94) = 0.15$, $p = 0.71$, and TDOSE, $F(2, 94) = 1.92$, $p = 0.15$, groups occurred (Table 4, Fig. 2). That is, for the time period during which animals were sexually active (beginning with the first mount or intromission), the rate of intromitting did not differ between groups.

Ratio of Ejaculations to Mounts and Intromissions (EFFICIENCY)

An index representing the ratio of the number of ejaculations to the total number of mounts and intromissions (EFFICIENCY) was calculated for each male. In general, the higher this index, the fewer the mounts/intromissions required for each ejaculation, and thus the greater the "efficiency" of the male's sexual response. Animals that mounted or intromitted but did not ejaculate would generate an index of 0.0. Males that failed to mount or intromit at least one time were excluded from analysis.

Consistent with other measures of ejaculatory response, significant DPAT, $F(1, 81) = 24.90$, $p < 0.001$, and TDOSE, $F(2, 81) = 50.12$, $p < 0.001$, effects occurred on this variable (Table 5) such that increasing efficiency was characteristic of males tested under DPAT and higher levels of T. In addition, significant interactions for DPAT × TDOSE, $F(1, 81) = 8.45$, $p < 0.001$, and TDOSE × EXP, $F(1, 81) = 6.17$, $p = 0.003$, occurred. Post hoc analysis indicated greater increases in efficiency to increasing doses of T for DPAT males than controls ($p < 0.05$), and higher efficiency in experienced DPAT males than in the other groups under both middle and high T doses ($p < 0.05$ for each comparison).

Postejaculatory interval (PEI)

Because PEI data were available for only 40 animals, data from the two higher doses of T were combined (the low dose of T was excluded, as no males in this condition yielded PEI data), and only DPAT and EXP effects were tested. A marginally significant effect was found for DPAT, $F(1, 36) = 3.41$, $p = 0.073$, as well as a significant DPAT × EXP interaction, $F(1, 36) = 2.98$, $p = 0.044$.

Testosterone

Mean T levels for the three injection regimens were as follows: LOW = 2.39 nmol/l (SEM = ±0.29; range = 1.04–3.60); MED = 5.00 nmol/l (SEM = ±0.32; range = 3.36–6.17); and HIGH = 11.90 nmol/l (SEM = ±0.85; range = 7.87–15.50).

DISCUSSION

This experiment further specifies the conditions under which the well-known stimulatory effects of DPAT on ejacu-

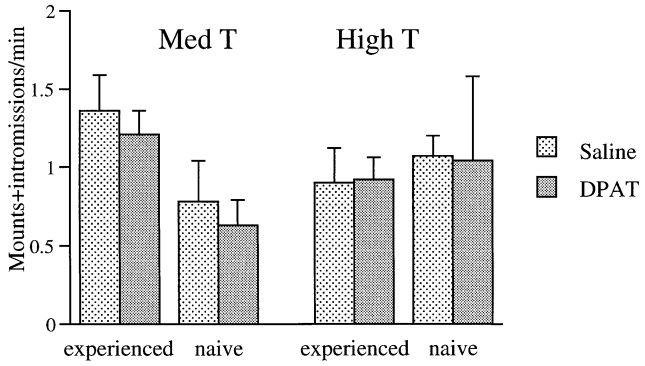

FIG. 2. Mean (±SE) number of mounts and intromissions per minute (MIRATE) following injection of 8–0H-DPAT (0.1 mg/kg) or saline are represented for sexually experienced and sexually naive male rats injected with testosterone 100 μg/8 days (MED T) or testosterone 500 μg/14 days (HIGH T). No differences between groups were observed.

TABLE 5
MEAN RATIO (±SE) OF EJACULATIONS TO NUMBER OF MOUNTS AND INTROMISSIONS (EFFICIENCY)*

	n	DPAT	*n*	Saline	Effects (*p*-Values)
EXP	25	0.053 (.011)	24	0.014 (0.016)	Main effects
NAIVE	20	0.054 (.004)	24	0.021 (0.008)	DPAT: 0.001
					TDOSE: 0.001
					EXP: 0.290
LOW T	13	0.005 (.004)	16	0.000 (0.000)	Interactions
MED T	16	0.030 (.009)	17	0.011 (0.014)	D × T: 0.001
HIGH T	16	0.117 (.014)	15	0.044 (0.011)	D × E: 0.109
					T × E: 0.003
	Under MED T				
	n	DPAT	*n*	Saline	Post Hoc ($p < 0.05$)
EXP	10	0.043 (.014)	9	0.013 (0.006)	EXP > NAIVE
NAIVE	8	0.008 (.005)	8	0.009 (0.007)	DPAT > Saline
					DPAT/EXP > all groups
	Under HIGH T				
	n	DPAT	*n*	Saline	
EXP	8	0.105 (.022)	8	0.025 (0.007)	DPAT > Saline
NAIVE	8	0.129 (.019)	7	0.073 (0.020)	

*All subjects are included for overall DPAT by EXPERIENCE and DPAT by TDOSE interactions, but when broken down by TDOSE, the LOW T condition is not presented.

latory behavior are likely to occur. Using a low effective dose of DPAT, measures of ejaculatory response but not intromitting behavior were significantly enhanced. However, this effect depended on both the T level and sexual experience of the male.

Specifically, our results further define the role of testosterone in the effect of DPAT on ejaculatory frequency and latency. We found that levels of T in the range of 2.4 nmol/l were not adequate for DPAT to stimulate sexual behavior and/or lower ejaculation latency. However, this T level represents the lower limit of its activating effect [e.g., (11)], and accordingly, level of sexual activity in these subjects was low compared to that seen under the higher T doses. When testosterone reached 5.0 nmol/l, although subnormal relative to intact controls, the effect of DPAT was clear, at least in sexually experienced males. At still higher levels of T, the effect of DPAT was maintained, but the advantage of sexual experience was eliminated.

Our results indicate that minimal levels of T are critical to the expression of ejaculatory response and, further, that a low, effective dose of DPAT is not sufficient to compensate for the inhibiting effect of low T on ejaculation. These findings contrast with those of other researchers who report that DPAT affects ejaculation under much lower T levels than we found (1,20). The interactions among DPAT, experience, and testosterone provide possible insight into this issue. It appears that regarding the DPAT effect, sexual experience and testosterone level tend to offset one another, that is, experience may compensate for the limiting effect of low T, and vice versa. Haensel et al. (20), for example, observed stimulatory effects of DPAT under presumably much lower T than in our experiment, but their males had had extensive sexual experience prior to testing. Ahlenius et al. (1) observed a DPAT effect in naive, castrated males, but only when males were treated with doses of DPAT five times those used in our study. In our experiment, a low dose of DPAT was offset by sexual experience; and the advantage of sexual experience was offset by high T levels. Thus, at normally high levels, T is sufficient for sexual response, and sexual experience imparts no added advantage. However, under lower T levels, sexual experience plays a significant role in the DPAT effect.

Interactions among DPAT, T, and sexual histories may help explain the failure of some studies to find a DPAT effect at the dose used in this study. While others (19,31) have reported strong DPAT effects in animals with varying sexual histories, those results may apply primarily to rats with normally high levels of T. Specifically, Haensel et al. (19) reported DPAT-stimulated ejaculation in both initially sexually active (ejaculators) and initially sexually inactive males (nonejaculators). Although this apparent discrepancy between studies may be attributed to the higher DPAT dose used by Haensel et al., it may also reflect the different ways in which sexual histories were specified in the two studies. In that study, groups were established on the basis of sexual responding during a single short test after an unspecified amount of sexual experience, and DPAT was administered only after animals in both groups underwent further extensive testing. In contrast, in the present study ejaculatory experience was experimentally controlled and documented, and differences in this experience were found critical to the DPAT effect, at least under moderate T levels.

In a more comparable study, Mos et al. (31) reported strong DPAT effects for both naive and moderately experienced males, but not for extensively experienced males. Although our findings generally support theirs, several exceptions occur. Unlike their naive males, ours showed minimal DPAT effects unless T levels were high. Procedural differences may account for some variation between studies. For one, in their study sexual experience was not quantitatively defined in terms of sexual response, thereby preventing direct comparison with our groups. Furthermore, Mos et al. tested males repeatedly such that "naive" males appeared to accumulate substantial experience over successive sessions, perhaps rendering them equivalent to our sexually experienced males. Alternatively, the males used by Mos et al. may have had T levels within the range of our high T group, where DPAT had little differential effect on experienced vs. nonexperienced males. So, although we add qualification to Mos et al.'s (30) conclusion regarding the specific role of varying levels of sexual experience in DPAT effects on sexual behavior, we concur with their general conclusion that baseline levels of sexual experience may be critical in detecting prosexual effects of drugs like DPAT. Although further work specifying the particular component of sexual experience that facilitates the DPAT effect has yet to be undertaken, such findings emphasize the importance of specifying in detail both the sexual history and testosterone profile of subjects used in studies testing the effects of serotonergic-modulating drugs on sexual response.

Ideas regarding the interdependence of factors affecting sexual response are, of course, not new. It has long been known

that male rats with extensive sexual experience are more resistant to procedures affecting testosterone (e.g., castration) that normally disrupt sexual behavior (12,24). Although the neural mechanisms mediating such effects remain to be elucidated, recent studies on male sexual behavior offer partial explanation. DPAT is thought to act through serotonergic spinal (26,27,36) and/or diencephalic nuclei (5,10,13,14,16) involved in consummatory or reflexive aspects of male sexual response (15,32, 33). Many of these same nuclei appear to be androgen sensitive (4,8,9). Androgens, therefore, may act to prime neural response to DPAT's stimulating effect by inducing changes in receptor characteristics or cell responsivity in these regions (23,29). In a manner paralleling androgenic effects on the CNS, experience also may exert a priming effect in some of these same neural areas (34). Recent evidence showing that the effects of sexual experience can be blocked with drugs such as cyclohexamide and the NMDA antagonist MK-801 (17) suggest that sexual experience plays a clear role in modulating neural response. The variable effects of DPAT on ejaculatory response may well reflect such differences in CNS priming resulting from sexual experience and/or the level of circulating testosterone.

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