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Differential regulation of female sexual behaviour by dopamine agonists in the medial preoptic area

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ABSTRACT

The medial preoptic area (mPOA) is a brain region critical in the control of male sexual behaviour, and the neurotransmitter dopamine (DA) plays an important role within it. However, both the roles of DA and the mPOA in female sexual behaviour are not fully understood, with few studies producing consistent data. The present study examined the function of DA within the mPOA on the full cascade of female sexual behaviour. Ovariectomized female rats were bilaterally cannulated into the mPOA and partially hormonally primed with estradiol benzoate (EB). Different doses of a nonselective DA receptor agonist, and selective DA D1 and D2 receptor agonists (apomorphine, SKF 38393 and quinpirole, respectively) were infused bilaterally to the mPOA. Copulatory behaviour was then immediately tested over a period of 30 min in a bilevel chamber with a sexually experienced male. Precopulatory behaviours were increased in females following infusions of a low dose (0.25 μg) of apomorphine and both a low (0.05 μg) and a high dose (0.2 μg) of quinpirole. However, hops and/or darts were decreased following infusion of a low dose (0.05 μg) of SKF 38393. These results suggest that the ratio of DA D1/D2 activity within the mPOA of female rats is critical for the expression of precopulatory behaviours, and may work with other brain areas responsible for stimulating lordosis to control the timing of female sexual behaviour.

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1. Introduction

Female sexual behaviour is characterized by three phases of activity described as appetitive, precopulatory, and consummatory (Pfaus et al., 2003). Appetitive behaviours serve to bring a female in close proximity to a male, and include behaviours such as solicitations that signal the female's interest in copulation. Precopulatory behaviours act as a transition from appetitive to consummatory, and serve to trigger mounting behaviour by the male, which in turn elicits lordosis (Pfaff and Schwartz-Giblin, 1988; Pfaus, 1999; Pfaus et al., 2003). Consummatory sexual behaviours, such as lordosis, allow for copulation to take place, and are usually stereotyped, sexually differentiated, and species-specific (Pfaus et al., 2003). The most commonly studied precopulatory behaviours include solicitations, hops and/or darts, and pacing behaviour. Although precopulatory behaviours and lordosis occur frequently during a copulatory session, these two sets of behaviours are mutually exclusive and cannot occur simultaneously. Finally, as females receive a large number of intromissions during multiple copulatory series, solicitations cease, pacing increases, lordosis reflex intensities diminish, and females display more agonistic behaviour toward males (Bermant, 1961; Erskine, 1985; Krieger et al., 1976; McClintock and Adler, 1978; Peirce and Nuttall, 1961; Pfaus et al., 2000).

Precopulatory and consummatory aspects of female sexual behaviour are under the control of hypothalamic–limbic circuits, which contain receptors for the ovarian steroid hormones estrogen (E) and progesterone (P). Both hormones are necessary for the full display of female sexual behaviour (Beach, 1976; Pfaff and Schwartz-Giblin, 1988). For example, it is thought that E activates lordosis through binding in the ventromedial nucleus of the hypothalamus (VMH), while P further promotes lordosis within that area (Whalen, 1974), and also stimulates precopulatory behaviours within this and other regions of the brain, such as the medial preoptic area (mPOA) (MacLusky and McEwen, 1978), and the ventral tegmental area (VTA) (Frye, 2001; Frye and Walf, 2008).

Bilateral electrolytic lesions of the VMH inhibit lordosis (Pfaff, 1980), whereas lesions of the mPOA enhance lordosis (Clemens et al., 1976; Law and Meagher, 1958; Powers and Valenstein, 1972; Takeo et al., 1993) and electrical stimulation of the mPOA decreases lordosis (Moss et al., 1974; Napoli et al., 1972; Pfaff and Sakuma, 1979; Takeo et al., 1993). This suggests that the mPOA exerts an inhibitory influence on lordosis, possibly via direct outputs to the VMH (Chiba and Murata, 1985), although others have found results inconsistent with this (i.e. Bast et al., 1987; Gray et al., 1978; Numan, 1974; Singer, 1968). The potentiation of lordosis by mPOA lesion may also be context-specific. Whitney (1986) reported these effects depended on the testing situation: if females do not have the ability to pace

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copulatory contact, then lesions facilitate lordosis; whereas if females have the ability to escape the male, then lesions have no effect on lordosis. Excitotoxic lesions of the mPOA using ibotenic acid produced not only an increase in lordosis in females but also a dramatic reduction in precopulatory behaviours, decreasing the number of solicitations, hops and darts, and disrupting pacing (Hoshina et al., 1994). Guarraci and colleagues (2004) found a similar reduction in precopulatory behaviours following mPOA lesions, but the sexual receptivity of the female was not affected presumably because the females could pace the sexual interaction effectively in that study. Those data are consistent with the idea that the mPOA is critical for the expression of precopulatory behaviours, whereas its role in lordosis depends on the sexual context.

Dopamine (DA) released in the mPOA is critical for both appetitive and consummatory aspects of male sexual behaviour. DA input to the mPOA comes primarily from the zona incerta (Wagner et al., 1995), comprising the incertohypothalamic DA system that originates in the A13 cell group under the thalamus. Dopamine D1 receptors in the mPOA serve to facilitate the early stage of copulation through promotion of penile erection, while acting with D2 receptors synergistically to promote sexual motivation and decrease the latency to ejaculate (Moses et al., 1995). It was concluded that D2 receptors enhance sympathetically mediated ejaculatory mechanisms, while inhibiting the parasympathetically controlled erectile responses. Stimulation of both receptor subtypes, by apomorphine (APO) for example, primarily facilitates erection; however, shifting to D2 stimulation through higher levels of DA release during copulation, results in a switch toward ejaculation (Hull et al., 1989). Thus, different levels of extracellular DA, acting through the two receptor subtypes, control the timing of copulatory events.

Although mPOA glutamate and GABA have clear roles in the sexual behaviour of female rats (for review, see McCarthy, 1995), the role of DA in this region remains unclear. Extracellular concentrations of DA increase in the mPOA of female rats as a function of hormone priming and copulatory stimulation. In ovariectomized (OVX) rats primed with low doses of EB (5 μg), DA release increases in the mPOA in response to progesterone (500 μg), and subsequently in response to perineal and vaginocervical stimulation during non-paced copulation with males (Matuszewich et al., 2000). The increase in DA did not occur if females were allowed to pace the copulatory contact, although significant increases in DA metabolites DOPAC and HVA were reported in that condition. Few studies to date have examined the neuropharmacology of DA in the mPOA on the sexual behaviour of female rats. APO microinjected into the mPOA was found to increase lordosis in female rats primed with low levels of E (Foreman and Moss, 1979), while no change in lordosis was found following infusions of SKF 38393, a DA D1 agonist, into the preoptic area for females primed solely with estradiol benzoate (EB; Apostolakis et al., 2006).

The present experiments investigated the effects of DA agonists infused into the mPOA of female rats on both appetitive and consummatory sexual behaviours. To determine whether DA receptor subtypes exert differential effects, effects of both nonspecific and selective D1 and D2 receptor agonists were examined following bilateral infusions to the mPOA of OVX rats maintained on partial hormone priming with EB alone. We hypothesized that DA agonists would increase female sexual behaviour from this hormone baseline, and that in line with the dual effects of the receptor subtypes seen in male sexual behaviour, D1 receptors would play a role in precopulatory behaviours, while D2 receptors would have an effect on lordosis.

2. Materials and methods

2.1. Subjects

Female Long-Evans rats, weighing 150–200 g, and male Long-Evans rats, weighing 200–250 g, all 6 weeks old, were obtained from Charles River Canada, Inc. (St- Constant, QC). Female rats were pair-housed in Plexiglas cages with wood-chip bedding until cannulation, after which they were housed individually. Males were housed in groups of four in large Plexiglas cages with wood-chip bedding. All rats were housed in the same colony room, maintained on a reversed 12-h light/dark cycle, with lights off at 0800. Regular rat chow and tap water was available ad libitum, and the room temperature was kept constant at 21 °C.

All animal procedures conformed to the guidelines of the Canadian Council for Animal Care and were approved by the Concordia University Animal Research Ethics Committee.

2.2. Surgery

2.2.1. Ovariectomy

Females were OVX bilaterally via a lumbar incision in order to prevent impregnation and allow for the control of hormone levels throughout testing. Females were anaesthetized with ketamine hydrochloride (100 mg/ml) and xylazine hydrochloride (20 mg/ml) mixed in a 4:3 ratio, respectively, and administered intraperitoneally at a dose of 1 ml/kg. Rats were given 1 week of recovery prior to behavioural training.

2.2.2. Cannula implantation

After becoming sexually experienced, females were anaesthetized using sodium pentobarbital (60 mg/ml) at a dose of 1 ml/kg. Using a stereotaxic instrument, rats were implanted with a stainless steel, 22 gauge, bilateral guide cannulae aimed 1 mm above the mPOA (AP −0.6, ML ±0.5, DV −7.0 mm from bregma, incision bar set at 0; Paxinos and Watson, 1998), with 28 gauge cannula blockers in place, cut 0.5 mm below the cannulae. Infusion cannulae, also 28-gauge, were cut 1 mm longer than the guide cannulae. All cannulae equipment was obtained from Plastics One (Roanoke, VA). Females were given seven days recovery time before any infusions or testing.

2.3. Hormone and drug administrations

During experimental trials, females were primed only with EB in order to avoid any ceiling effects. This was attained through subcutaneous injections of EB in a dosage of 10 μg per 0.1 ml of sesame oil 48 h before each experimental sex test.

Doses of each drug infused into the mPOA were: apomorphine ($n=8$): high: 1.0 μg; medium: 0.5 μg; low: 0.25 μg; SKF 38393 ($n=10$): high: 0.2 μg; medium: 0.1 μg; low: 0.05 μg; quinpirole ($n=11$): high: 0.2 μg; medium: 0.1 μg; low: 0.05 μg. Drugs were purchased from Sigma Chemical Co. (St. Louis, MO). All infusions were done at a rate of 0.5 μl/min per side for 1 min using an infusion pump (Harvard Apparatus, Pump 22), giving a total volume of 1 μl. Infusion cannulae were left in place for 1 min following infusion to allow for absorption, after which testing proceeded. Physiological saline was used as the vehicle for each drug in the experiment.

2.4. Behavioural training

All rats received four sessions of sexual experience prior to any experimental testing. Female rats were injected subcutaneously with EB (10 μg/0.1 ml of sesame oil) 48 h and P (500 μg/0.1 ml of sesame oil) 4 h before testing. Females were placed individually into a bilevel chamber (Pfaus, 1999) with a sexually vigorous male for a 30-min period of copulation. Copulatory training sessions were conducted at 4-day intervals to approximate the normal ovulatory cycle of the female. After the 4th training session, females were implanted with guide cannulae, and given 7 days of surgical recovery prior to drug testing.

Females were primed with EB-alone (as above) and received four randomized drug tests at 4-day intervals, resulting in each experimental

rat receiving a low, medium, and high dose of one type of drug, as well as a vehicle trial, in a Latin squares randomized order. Females were placed into the chamber immediately following the drug infusion with a sexually vigorous male for a 30-min test, as in the training sessions. Following the last test, females were perfused intracardially, and their brains extracted to confirm cannulae placement.

All experimental testing sessions were captured onto DVD via camcorder, and later scored using a computerized event recorder (Cabilio, 1996). Frequencies of both female and male behaviours were scored. Male behaviours consisted of the number of mounts, intromissions and ejaculations. Female behaviours consisted of solicitations (characterized by a head-wise orientation to the male, followed by a 180 degree turn and runaway), hops and/or darts (characterized by either a hopping motion, or a burst of speed away from the male and sudden stop, without head-wise orientation; these could occur with or without each other), defensive behaviours (characterized by kicks, sideways takedowns, boxing postures, and prone positions in response to the male, as described by Barnett (1967)), level changes (going from one level of the chamber to the other), and magnitude of reflexive lordosis posture (ranging from 0, no lordosis posture, to 3, full lordosis posture, as in Hardy and Debold, 1971).

2.5. Perfusions and histology

Following completion of testing, animals were anaesthetized with sodium pentobarbital (120 mg/kg, ip), and perfused using PBS and 4% paraformaldehyde solutions. Following perfusion, the extracted brains were placed in the 4% paraformaldehyde solution overnight, and then transferred to a 30% sucrose solution until they were sliced. Coronal slicing was done at 30 microns, and cannulae placement was confirmed by a blind, third-party experimenter with placements marked in an atlas.

The criterion for exclusion from statistical analyses was set so that rats with both injector cannulae ending outside the boundaries of the mPOA were exempt from the study. The end result of this was that only animals that had correct unilateral or bilateral cannulations to the mPOA were included in the analyses. Cannulae placement data from subjects included in the statistical analyses are shown in Fig. 1.

2.6. Statistical analyses

A non-parametric equivalent of a one-sample repeated measures ANOVA, the Friedman test (Friedman, 1937), was performed on all sexual behaviours, both male and female, for each drug independently. A non-parametric test was used as the homogeneity assumption necessary for using an ANOVA was not satisfied, since partially-primed female rats show reduced (if not abolished) components of sexual behaviour. Analyses of behaviours included solicitations hops and/or darts (H/D), defensive behaviours, lordosis magnitudes 1–3, lordosis quotient (LQ; the number of lordosis postures taken divided by the number of mounts, intromission, and ejaculations), pacing (as indicated by level changes), mounts, intromissions, and ejaculations. In each case, the vehicle trial and the three drug infusion doses were compared. Any significant results were then further analyzed using a Wilcoxon signed-rank test to determine which two trials differed.

3. Results

3.1. General observations

No unusual behaviours (e.g., locomotor stimulation) were observed in animals following any of the doses of any of the DA agonists. Animals were easy to handle, and behaved normally before and after testing.

3.2. Effects of apomorphine

Fig. 2 shows the effects of infusions of saline or the three doses of apomorphine (APO) to the mPOA on the sexual behaviour of female rats. APO increased H/Ds and solicitations compared to the saline vehicle control but had no significant effect on pacing, lordosis, defensive responses, or measures of male sexual behaviour.

3.2.1. Solicitations

A trend of a main effect of dose of APO on the number of solicitations was found (Friedman test, $\chi^2=7.130$, $df=3$, $p<0.068$). Post hoc analyses revealed that the low dose of APO showed a trend toward an increase of SOL compared to the saline vehicle control and the high dose of APO.

3.2.2. Hops and/or darts

A significant main effect of dose was detected on the number of H/D displayed during the copulation test (Friedman test, $\chi^2=7.831$, $df=3$, $p<0.050$). Post hoc analyses revealed that the low dose of APO showed a significant increase of H/D compared to the saline vehicle control and a trend of an increase when compared to the high dose of APO.

3.3. Effects of SKF 38393

Fig. 3 shows the effects of infusions of saline or the three doses of SKF directly into the mPOA on the sexual behaviour of female rats. The low dose of SKF decreased H/Ds and reduced the number of ejaculations that males were able to experience with those females compared to the vehicle group; however, the medium and high dose did not produce this effect. No other effects on female or male sexual behaviours were detected.

3.3.1. Hops and/or darts

A significant main effect of dose was detected on the number of H/D displayed during the copulation test (Friedman test, $\chi^2=7.941$, $df=3$, $p<0.047$). Post hoc analyses revealed that the low dose of SKF showed a significant decrease of H/D compared to the saline vehicle control.

3.3.2. Ejaculations

A significant main effect of dose was detected on the number of male EJAC received during the copulation test (Friedman test, $\chi^2=8.357$, $df=3$, $p<0.039$). *Post hoc* analyses revealed a significant decrease in EJAC for the low dose of SKF compared to the saline vehicle control.

3.4. Effects of quinpirole

Fig. 4 shows the effects of infusions of saline or the three doses of quinpirole (QUIN) to the mPOA on the sexual behaviour of female rats. QUIN increased the number of solicitations, but had no other effect on sexual behaviour.

3.4.1. Solicitations

A significant main effect of dose of QUIN on the number of solicitations was found (Friedman test, $\chi^2=10.273$, $df=3$, $p<0.016$). *Post hoc* analyses revealed that the low and high doses of QUIN significantly increased the number of solicitations compared to the saline vehicle control.

4. Discussion

The present study examined the effects of infusions of nonselective or selective DA receptor agonists into the mPOA on precopulatory and consummatory aspects of female sexual behaviour in OVX rats primed with EB alone. APO acts as a nonselective agonist at both D1 and D2 receptors. It produced a significant increase in H/Ds and a trend

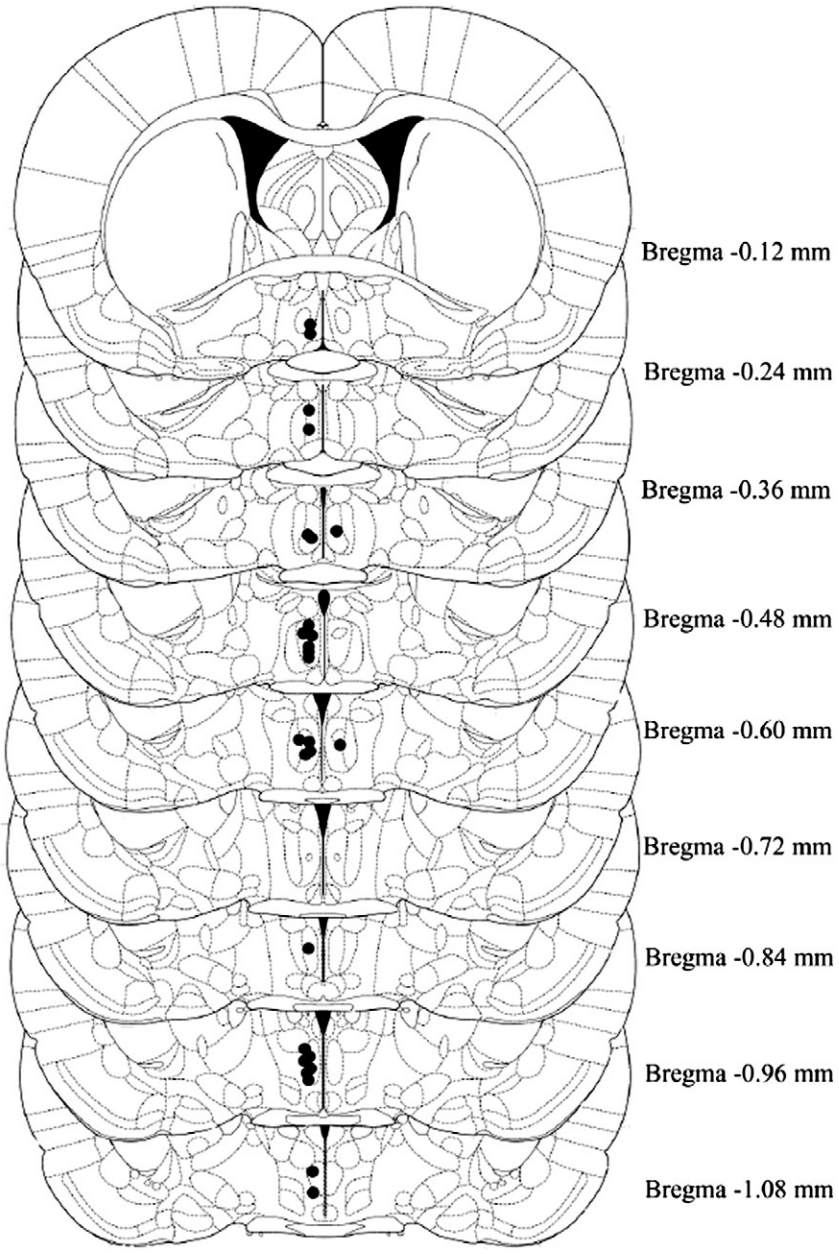

Fig. 1. Cannula placements in the present experiments according to the atlas of Paxinos and Watson (1998). Both bilateral (left side) and unilateral (right side) placements are depicted.

toward a significant increase in solicitations relative to control, without affecting other measures of female sexual behaviour. Selective agonist activity at D2 receptors with QUIN also increased H/Ds and solicitations, whereas selective agonist activity at D1 receptors with SKF reduced them. These effects indicate that DA in the mPOA is important for the control of precopulatory sexual behaviours in the female rat.

The present finding of a dual role of DA receptor activation in the mPOA on female sexual behaviour is reminiscent of effects found in males (e.g., D1 stimulation promotes erection whereas D2 stimulation promotes ejaculation; Hull et al., 1989). Based on those results, we hypothesized that the two DA receptor subtypes would play different, but complimentary, roles in promoting sexual behaviour in females: one subtype responsible for precopulatory behaviours, and one for consummatory behaviours. However, the current results indicate that each subtype plays contrasting roles in the control of precopulatory behaviours, and these behaviours are increased when both DA receptor subtypes are simultaneously stimulated. Females then seem to have different brain regions responsible for different aspects of their sexual behaviour; the mPOA is important in the display of precopulatory behaviours, indicating to the male that she is willing to copulate, while having no effect on the actual control of the processes behind the copulation itself. Much research in the past has indicated areas such as the VMH and VTA as being critical for the display of lordosis, and as such the specific DA receptor subtypes in the mPOA have control only over precopulatory behaviours. Because H/Ds and solicitations are two types of precopulatory behaviours, it is possible that instead of DA having specific effects on these particular behaviours, the manipulations by the selective receptor agonists had a general influence on precopulatory behaviours. This influence could be manifested through one or more types of behaviour, as it is possible that other types of precopulatory behaviours that were not measured (e.g., instrumental responses) may be affected through DA alteration.

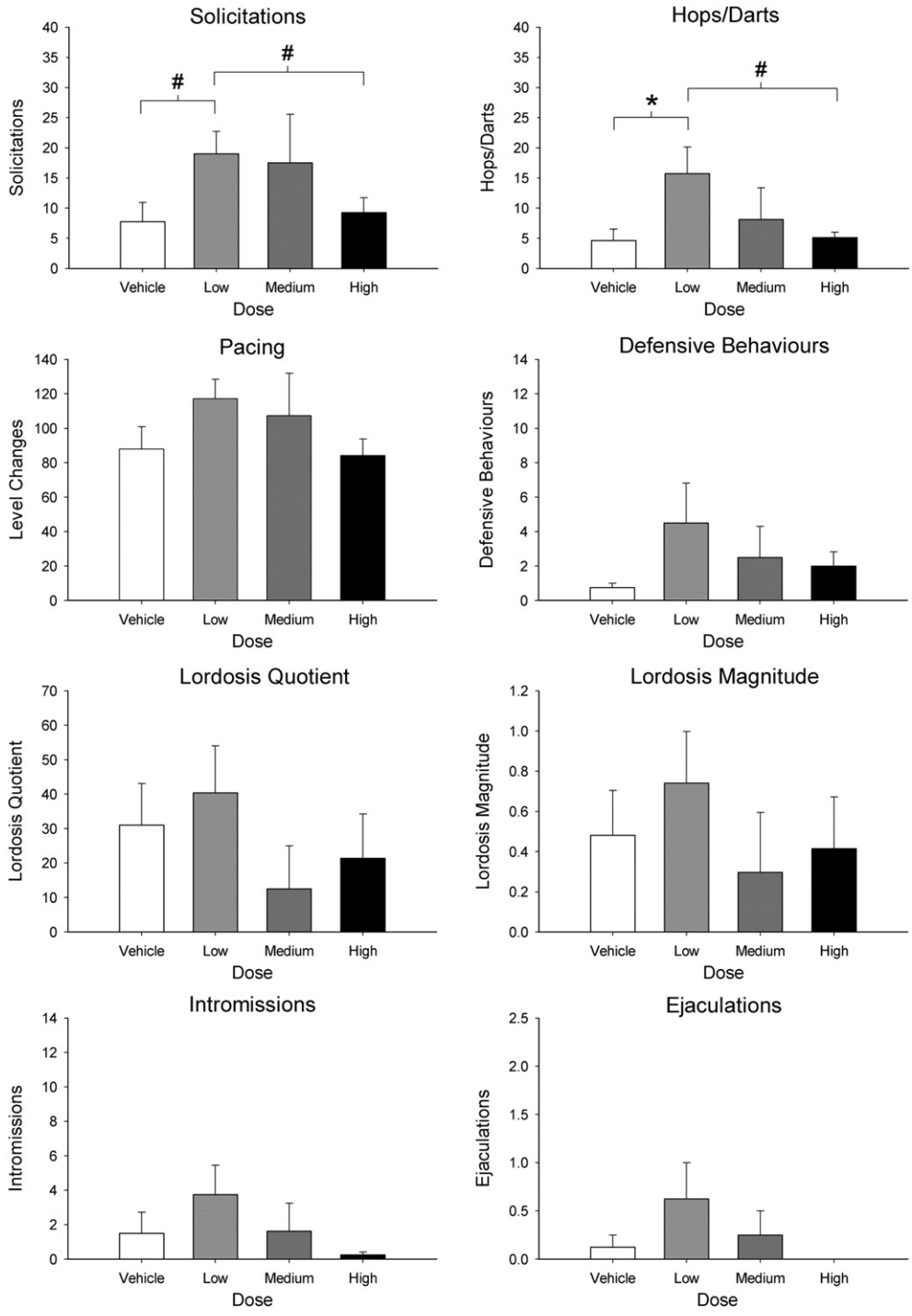

Fig. 2. The effect of three doses of apomorphine or saline vehicle infusions on the mean number of solicitations, hops and/or darts, level changes, defensive behaviours, mean lordosis quotient, mean lordosis magnitude, male intromissions and male ejaculations. Error bars represent the standard errors (* = $p<0.05$; # = $p<0.10$).

The contrasting roles of D1 and D2 receptor subtypes help to explain some of the inconsistencies reported in the literature regarding the role of both DA and the mPOA on female sexual behaviour. Early studies examining the role of the mPOA reported an enhancement of lordosis following lesions (Hoshina et al., 1994; Law and Meagher, 1958; Powers and Valenstein, 1972) *or* electrical stimulation (Moss et al., 1974; Napoli et al., 1972). Other studies reported decreases in precopulatory behaviour with inconsistent effects, if any, on lordosis (Guarraci et al., 2004; Whitney, 1986). Similarly, the function of DA has also been incompletely understood. Lordosis is diminished following systemic injections of several nonspecific DA agonists (i.e. Eliasson and Meyerson, 1976; Everitt et al., 1974; Everitt and Fuxe, 1977), and increased following nonspecific DA antagonists (i.e. Caggiula et al., 1979; Everitt, 1990). In contrast, LQs have been shown to increase following low doses of APO administered systemically (Hamburger-Bar and Rigter, 1975) or after infusions to the ventromedial hypothalamus (Mani et al., 1994). Foreman and Moss (1979) infused APO, flupenthixol, or haloperidol to the mPOA and found that APO increased lordosis only in rats primed with low levels of estrone, whereas flupenthixol and haloperidol lowered

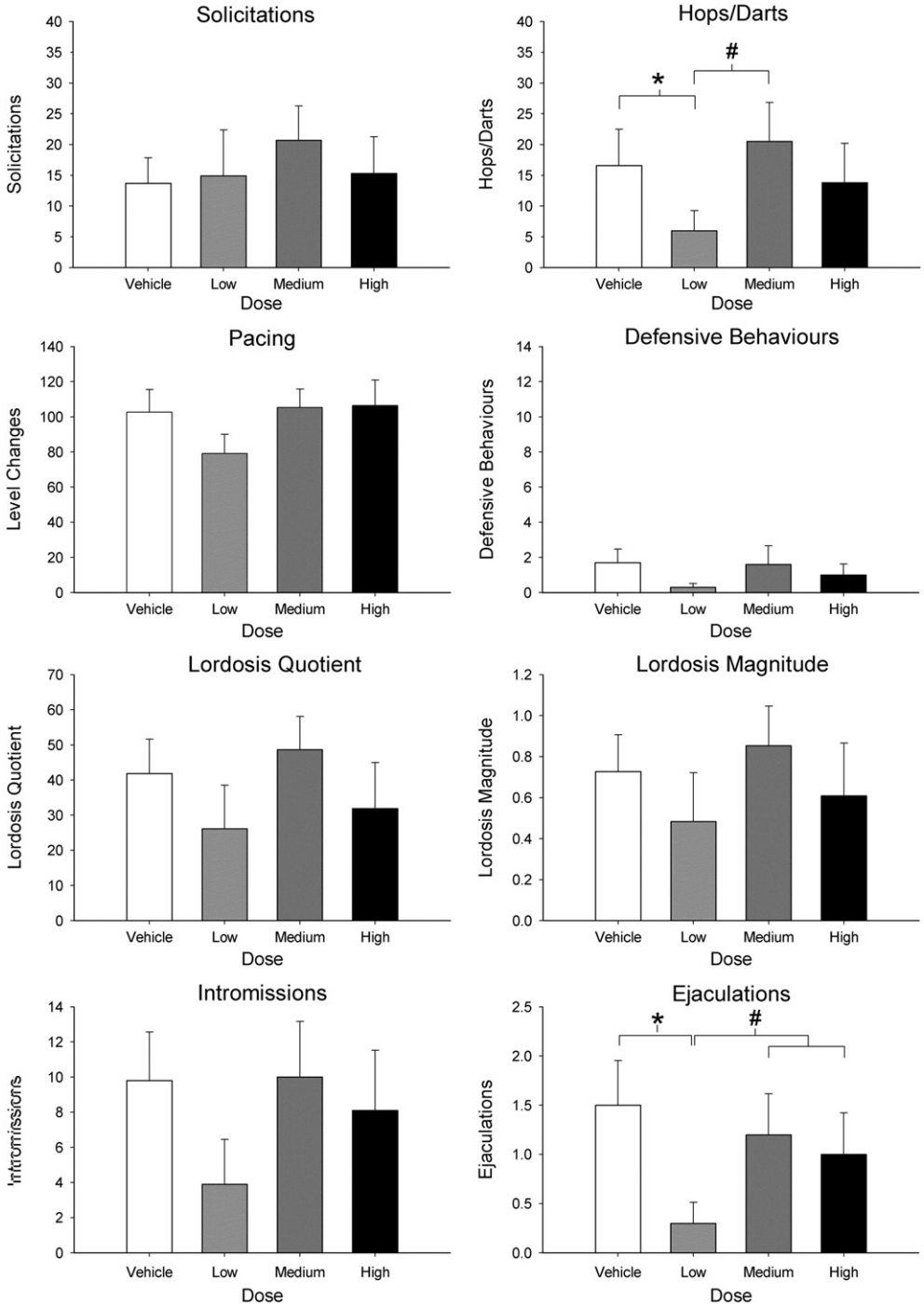

Fig. 3. The effect of three doses of SKF 38393 or saline vehicle infusions on the mean number of solicitations, hops and/or darts, level changes, defensive behaviours, mean lordosis quotient, mean lordosis magnitude, male intromissions and male ejaculations. Error bars represent the standard errors (* = $p<0.05$; # = $p<0.10$).

lordosis levels only in rats primed with high levels of estrone. They concluded that DA within those areas was critical for display of lordosis.

The effects of agonists and antagonists selective for DA receptors also vary as a function of route of administration. For example, the selective D1 agonist SKF 38393 facilitated lordosis when infused to the ventromedial hypothalamus (Mani et al., 1994) but had no effect when injected systemically (Grierson et al., 1988). Systemic injection of medium doses of the D2 agonist LY 163502 increased lordosis, whereas high or low doses decreased it (Foreman and Hall, 1987). The D2 antagonist sulpiride also had dual effects when injected systemically, inhibiting lordosis in females primed with EB and P, but enhancing it in females primed with EB alone (Grierson et al., 1988). In contrast, the D2 agonist quinpirole had no effect on female sexual behaviour following infusion to the ventromedial hypothalamus (Mani et al., 1994), suggesting that the effect observed by Foreman and Hall (1987) may occur in other brain regions or peripherally.

What can explain the disparities regarding the purported role of both the mPOA and DA in female sexual behaviour? Melis and Argiolas (1995) have argued that differences in dose and in baseline levels of sexual receptivity may play a role in how DA and mPOA function to regulate female sexual behaviour. Low doses of DA agonists appear to increase lordosis in females with low receptivity,

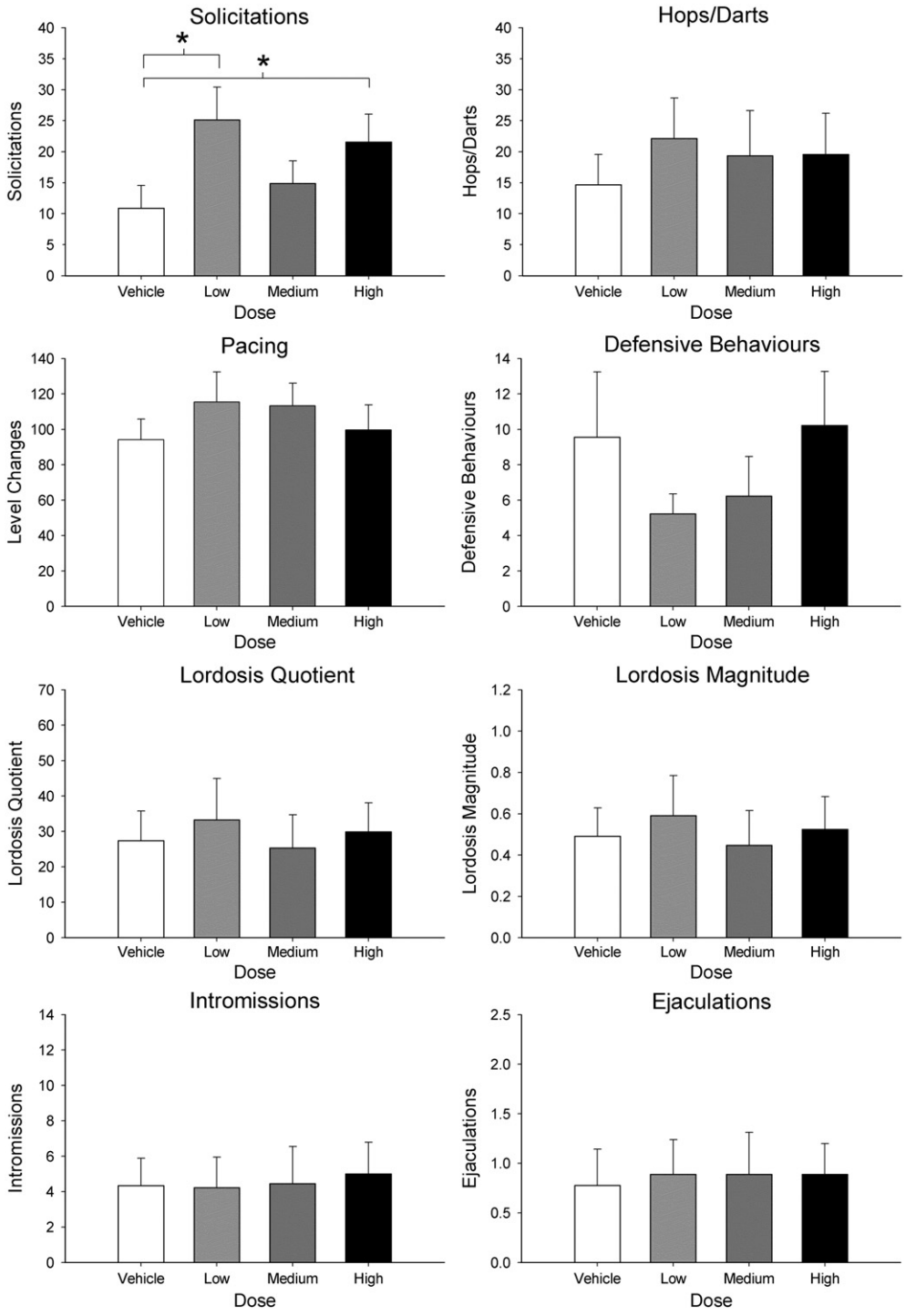

Fig. 4. The effect of three doses of quinpirole or saline vehicle infusions on the mean number of solicitations, hops and/or darts, level changes, defensive behaviours, mean lordosis quotient, mean lordosis magnitude, male intromissions and male ejaculations. Error bars represent the standard errors (* = $p<0.05$; # = $p<0.10$).

whereas high doses of the same drugs decrease lordosis in fully receptive females. Baseline sexual responding is critical because increases in sexual behaviours are easier to induce from low baseline levels (e.g., in OVX females primed with EB alone) whereas decreases are easier to observe from high baseline levels (e.g., in OVX females primed with EB and P). However, with regard to precopulatory behaviours, increases in solicitations have been demonstrated in both partially- and fully-primed females using systemic and central administration of melanocortin agonists, such as bremelanotide (Pfaus et al., 2004). Although it is impossible to increase maximal lordosis reflex responding, precopulatory behaviours like solicitations are frequency measures that are distributed throughout the copulatory session and can increase beyond maximal hormone priming.

Another potential explanation of the dual nature of DA receptor function in the mPOA (and perhaps elsewhere) stems from the work of Hull and colleagues indicating that the ratio of DA receptor subtype activation in this region is critical for the display of male sexual behaviour. Hull et al. (1989) suggested that stimulation of D1 receptors (or both receptor subtypes, as with a nonspecific agonist such as APO) facilitates erection via parasympathetic outflow, whereas shifting the stimulation ratio to D2 receptors results in a switch to sympathetic outflow and the facilitation of ejaculation. The

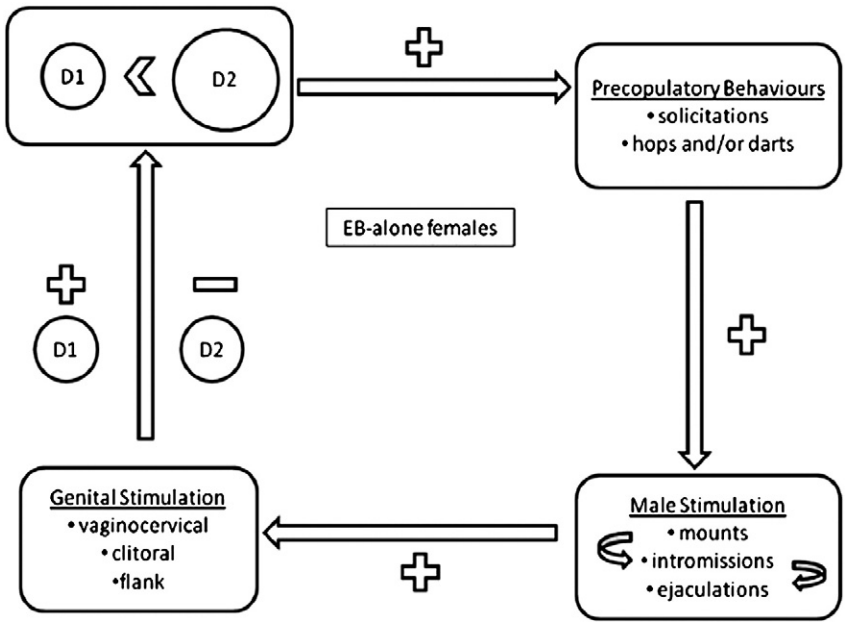

Fig. 5. Model for the effect of the ratio of dopamine subtypes in female sexual behaviour.

ratio of receptor activation was viewed as controlling the rate of copulation, determining whether males could obtain and sustain erections (D1) and potentially delay ejaculation, or ejaculate rapidly (D2). The current results suggest a similar ratio may control the timing of female sexual behaviour. Because lordosis postures and precopulatory behaviours such as solicitations cannot be performed at the same time, mechanisms are required to time and order them in an optimal pattern. Whereas in males, the ratio in DA receptor activity acts to effectively shut down a copulatory session through the promotion of ejaculation, in females it could be that shifts in DA activity between D1 and D2 receptors in the mPOA communicate with other brain areas responsible for lordosis (e.g., VMH) in determining which behaviours, lordosis or precopulatory, are being displayed at certain times throughout the copulatory session. Alternatively, the mPOA may modulate activity in the VTA, which in turn alters DA transmission in the nucleus accumbens (NAc). The mPOA sends efferent projections to the VTA (Conrad and Pfaff, 1976; Edwards and Einhorn, 1986; Fahrbach et al., 1986; Phillipson, 1979), and we note that DA release patterns as revealed by both microdialysis and voltammetry in the mPOA and NAc are identical during copulation in male rats (Blackburn et al., 1992) and female rats (Matuszewich et al., 2000; Pfaus et al., 1995). Bilateral infusion of the DA receptor antagonist haloperidol to the mPOA or NAc dose-dependently reduces appetitive sexual behaviours in males (Pfaus and Phillips, 1991), whereas infusion to the mPOA further disrupts copulation. Thus, the activation of specific DA receptor subtypes in the mPOA may be a common substrate for activating appetitive behaviours in both male and female rats (Pfaus, 2009).

As in males, the ratio of DA receptor subtype activity in the mPOA may be important in the timing of behavioural expression during copulation, controlling precopulatory behaviours in order to influence the amount of genital stimulation females receive from males (Fig. 5). The idea that the mPOA, in conjunction with the VMH, is important in the timing of female sexual behaviour (including pacing, lordosis and solicitations) has been suggested previously (Pfaus et al., 2007). Engaging in solicitations allows females to initiate sexual activity with males and helps to control the rate of copulation, which contributes strongly to reproductive success (Erskine, 1989). Evidence for this stems from findings that precopulatory behaviours determine what kind of stimulation females receive from the male, and when this stimulation will occur (Erskine, 1989; McClintock and Adler, 1978). Solicitations decrease as the male stimuli increases in intensity throughout the copulatory session (Bermant, 1961; Erskine, 1985; Pfaus, 1999). Switching the ratio of predominant DA receptor activity from D2 to D1 during copulation may result in a progressive decrease in precopulatory behaviours.

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