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# Suppression of Lordotic Responsiveness in the Female Rat During Mesencephalic Electrical Stimulation[1]

GARY W. ARENDASH[2] AND ROGER A. GORSKI[3]

*Department of Anatomy and the Laboratory of Neuroendocrinology*
*Brain Research Institute, UCLA School of Medicine, Los Angeles, CA 90024*

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ARENDASH, G. A. AND R. A. GORSKI. *Suppression of lordotic responsivenss in the female rat during mesencephalic electrical stimulation.* PHARMACOL BIOCHEM BEHAV 19(2) 351–357, 1983.—The effects of biphasic electrical stimulation of the mesencephalic median (MRN) and dorsal raphe (DRN) nuclei, as well as the adjacent periaqueductal gray (PAG), on lordotic behavior were investigated in ovariectomized rats primed with three daily injections of estradiol benzoate (2 μg). Animals were tested between 4–8 hours after a progesterone (0.5 mg) injection on day four which normally facilitates high levels of receptivity during this period. Although stimulation of the MRN had no significant effect on lordosis, DRN activation at 100 Hz (0.5 msec pulse duration) or 10 Hz (2 msec pulse duration) caused a marked and immediate suppression (53% and 56%, respectively) in receptivity. This suppression does not appear to be due to activation of serotoninergic neurons originating in the DRN since pretreatment with an inhibitor of serotonin synthesis (parachlorophenylalamine, 320 mg/kg) essentially did not modify the suppression, thus providing no evidence in support of an inhibitory role for serotonin in lordotic behavior. Activation within the PAG adjacent to the DRN at 10 Hz (0.5 or 2 msec pulse duration) produced an immediate, dramatic decrease (81% and 80%, respectively) in receptivity. The suppressions induced by DRN and PAG stimulation appear most likely to be due to activation of a descending pathway inhibitory to the lordosis reflex at medullary or spinal cord levels.

Electrical stimulation  Raphe nuclei  Periaqueductal gray  Lordosis behavior  Rats

THE BRAIN monoamines, dopamine, norepinephrine, and serotonin (5-HT) have all been implicated in the neural control of rat sexual behavior [2,9]. Although a number of reports indicate an inhibitory role for brain serotoninergic pathways in the neural regulation of lordosis in female rats [2, 5, 8, 9, 21, 34, 35], a growing body of evidence argues against any such role [7, 30, 32, 33]. Evidence supportive of inhibitory 5-HT involvement in female sexual behavior comes from observations after a variety of pharmacological manipulations. Thus, lordotic behavior in minimally receptive, estrogen-primed rats has been reported to be facilitated after (1) the peripheral administration of the 5-HT synthesis inhibitor [16] parachlorophenylalanine (PCPA; [2, 9, 21, 35]); (2) the central or peripheral administration of the 5-HT receptor blockers, methysergide [5,34] or cinanserin [34,35]; and (3) the central administration of the 5-HT neurotoxin, 5,7-dihydroxytryptamine (5,7-DHT; [8]). These studies appear to indicate that a decrease in CNS serotoninergic transmission is capable of replacing progesterone in the facilitation of sexual behavior in such rats. Indeed, it has been proposed that a CNS serotoninergic system inhibits lordotic responsiveness tonically and that progesterone facilitates such responsiveness by decreasing neural transmission in this inhibitory system [20]. However, a number of investigators argue that the enhanced frequency of lordosis induced by PCPA treatment is due to indirect CNS actions of PCPA on non-serotoninergic neurons, resulting in the release of adrenal progesterone [2, 7, 30, 31]. Also, the facilitation of lordotic responses observed after intracerebral 5,7-DHT administration [8] has not been confirmed in a more recent study [32], casting further doubt on the putative inhibitory role of 5-HT in the regulation of female sexual behavior.

Nonetheless, several 5-HT agonists have been reported to suppress the high levels of receptivity normally seen in ovariectomized rats treated with both estrogen and progesterone [6,9], providing added support for a serotoninergic inhibitory influence on the frequency of lordosis. If such a pharmacologically-induced activation of brain 5-HT receptors can suppress receptivity, it should follow that electrical stimulation of CNS serotoninergic neurons would, through the release of endogenous 5-HT and the ensuing receptor activation, result in a similar suppression.

[1]Supported by NSF grant BNS 78 20025 and NIH grant HD-01182.
[2]Current address: Department of Biology, University of South Florida, Tampa, FL 33620.
[3]Requests for reprints should be addressed to Dr. R. A. Gorski, Department of Anatomy, UCLA School of Medicine, Los Angeles, CA 90024.

The midbrain raphe region (especially the dorsal and median raphe nuclei) contains the cell bodies of major ascending 5-HT neuronal systems that send rostral projections to the hypothalamus and other forebrain areas [10,24]. In an effort to clarify the possible role of CNS serotoninergic neurons in the neural regulation of female sexual behavior, in the present study we investigated the potential for electrical stimulation in the region of the mesencephalic dorsal and median raphe nuclei to suppress the sexual activity of highly receptive steroid-treated rats. The possible role of serotonin in mediating any inhibitory responses elicited by raphe stimulation was also tested.

## METHOD

### *Animals and General Protocol*

Adult female Sprague-Dawley rats (Simonsen Laboratories, Gilroy, CA) were maintained in a reverse light room (lights on at 21:30 and off at 11:30) with Purina rat chow and tap water available ad lib. Animals were ovariectomized 2–3 weeks prior to mesencephalic electrical stimulation, and a stimulating electrode was implanted within the midbrain 5–7 days before stimulation. Animals were given 2 $\mu$g estradiol benzoate (SC) daily for the three days prior to testing, followed by 0.5 mg progesterone (SC) on the day of stimulation. This hormonal treatment results in a high frequency of lordosis 4–8 hr after the progesterone injection [4]. Thus, this formed the basis of the time frame in which the present stimulation study was conducted. Some dorsal raphe-implanted animals were injected with DL-parachlorophenylalanine methylester hydrochloride (PCPA; 320 mg/kg IP in about 1 ml of saline; Calbiochem, San Diego, CA), an inhibitor of serotonin synthesis [16], 71 hr prior to stimulation. This protocol results in a 55% depletion in brain serotonin levels [11].

### *Electrical Stimulation Procedures*

Five to seven days before stimulation, the animals were anesthetized with pentobarbital (Nembutal, 35 mg/kg IP), and bipolar concentric stainless steel electrodes were stereotaxically implanted into the dorsal raphe nucleus, median raphe nucleus, or periaqueductal gray of the midbrain using the atlas of Koenig and Klippel [17] as a guide. The center wire (0.012 mm dia.) and the barrel (27 gauge) were insulated from one another. Insulation was removed from 0.15 mm of the tip and 0.3 mm of the barrel, and these uninsulated areas were separated by a 0.4 mm band of epoxylite insulation. Stimulation was applied with a Grass S44 stimulator connected to SIU 5 stimulus isolation unit circuitry, which resulted in effective biphasic pulses being delivered to the animal. Four different sets of stimulation parameters were utilized: (1) 100 Hz, 0.5 msec pulse duration (pd); (2) 10 Hz, 0.5 msec pd; (3) 10 Hz, 2 msec pd; and (4) 2 Hz, 2 msec pd. Most rats were tested with 3 or often all 4 sets of stimulation parameters. All currents used were below threshold for eliciting behavioral effects possibly detrimental to lordosis and never exceeded 200 $\mu$A. Threshold levels which produced such behavioral effects (i.e., circling or turning behavior, escape behavior, or head twitching) were determined for all 4 sets of stimulation parameters during a very short pretest on the day before testing. Much milder, but noticeable, behavioral effects (such as random walking, hyperactivity, or sedateness) were tolerated since they do not affect the frequency of lordosis (see the Results section) and were to be expected from the results of previous electrical stimulation studies involving this brain region [13,18].

### *Behavioral Testing*

Tests for female sexual behavior started at approximately 13:00 hr, progesterone having been administered 4–8 hr earlier. The test animal's electrode assembly was connected to stimulator leads and the animal placed in a Plexiglas arena (45×45 cm) that was illuminated with a 25 W red bulb. The stimulator leads were suspended above the test animal via a spring-lever device to allow for free mobility. Two or three sexually experienced Long-Evans male rats had been placed in the testing arena at least 15 minutes before behavioral testing for adaptation. A 25-mount control period was obtained prior to each stimulation period, which also lasted for 25 mounts. A lordosis quotient (LQ) was computed for each animal's control and stimulation periods by dividing the number of lordotic responses by the number of mounts (i.e., 25) and multiplying by 100.

### *Statistical Analysis and Histology*

Differences in LQ between each stimulation period and the preceding control period were determined by the paired $t$ test. LQ values given in the text represent the mean±SE. All comparisons between means that are referred to as significant are at a probability of 0.05 or less. Since every animal was not tested in each condition, it was impossible to perform analysis of variance without losing data. Therefore, multiple paired $t$ tests were applied, but the critical significance level ($p<0.05$) was divided by the number of comparisons per experiment (usually four) to provide the most conservative estimate of statistical significance. At the conclusion of all behavioral testing, test animals were anesthetized with pentobarbital and perfused with 10 percent Formalin. Brains were subsequently removed, sectioned at 50 $\mu$m, and stained with thionin to localize the electrode tips.

## RESULTS

### *Median Raphe Stimulation*

Activation of the median raphe nuclus (MRN), irrespective of stimulus parameter, had no significant effect overall on the high levels of lordotic responsiveness normally seen in ovariectomized, estrogen-progesterone treated rats (Fig. 1). Only two of 12 animals stimulated with the MRN at 100 Hz, 0.5 msec pulse duration (pd) responded with at least a 25% decrease in LQ during stimulation, and only 3 out of 10 rats showed reduced receptivity during stimulation at 10 Hz, 2 msec pd. Figures 2 and 3 depict the electrode tip locations for MRN stimulation with these two sets of stimulation parameters. No animal stimulated with the remaining two sets of parameters (n=14) showed a decrease of 25% or more. Although MRN activation at 10 Hz, 0.5 or 2 msec pd did not produce any noticeable behavioral effects, stimulation at 100 Hz, 0.5 msec pd usually resulted in some hyperactivity, while stimulation at 2 Hz, 2 msec pd often produced sedateness. Both of these behavioral effects have been previously reported [18,27].

### *Dorsal Raphe Stimulation*

In sharp contrast to the inability of MRN activation to affect female receptivity, electrical stimulation within the dorsal raphe nucleus (DRN) resulted in an immediate and

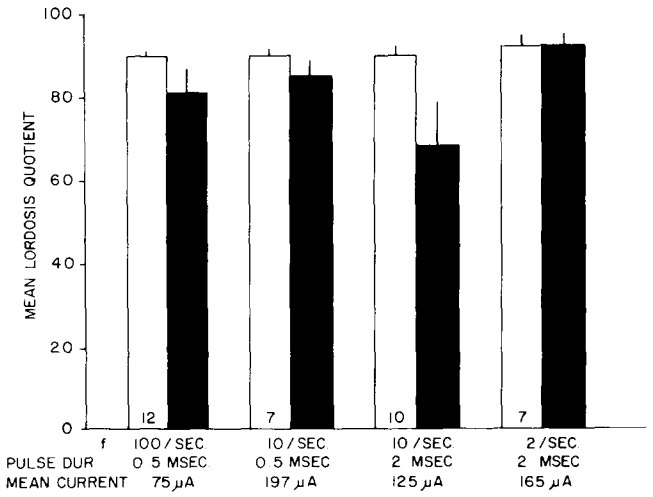


FIG. 1. Effects of median raphe electrical stimulation on mean lordosis quotients (LQ) ±SE. Open bars represent control LQ values while shaded bars indicate LQ levels during stimulation. Number of animals per group is indicated at the bottom of the control bars. f=frequency of stimulation. pulse dur=pulse duration. No significant differences noted.

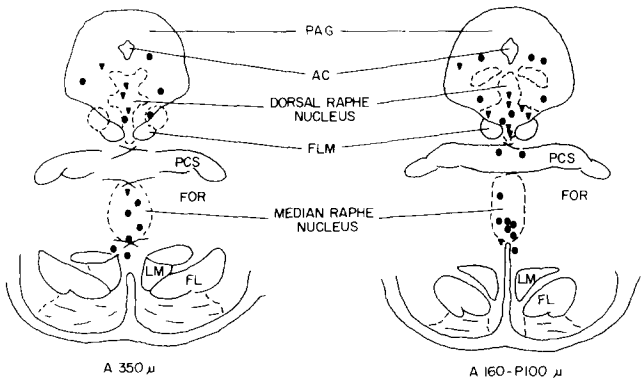


FIG. 2. Electrode tip locations within the midbrain at two anterior (A)-posterior (P) levels (A350 $\mu$ and A160–100 $\mu$ [18]); for stimulation at 100 Hz, 0.5 msec pulse duration and the effects of stimulation at these sites on lordotic behavior. ▼=inhibition: ≥25% suppression in LQ during stimulation; ●=no effect: <25% suppression during stimulation. Abbreviations: AC, cerebral aqueduct; FL, longitudinal fasciculus; FLM, medial longitudinal fasciculus; FOR, reticular formation; LM, medial lemniscus; PAG, periaqueductal gray; PCS, superior cerebellar peduncle.

significant suppression of the LQ when either 100 Hz, 0.5 msec pd or 10 Hz, 2 msec pd was used (Fig. 4; decreases of 53% and 56% were observed). Ten of 13 and nine of 11 animals, respectively, responded with at least a 25% decrease in receptivity during DRN stimulation with the above two sets of stimulation parameters. High control levels of lordotic responsiveness returned immediately following stimulation (LQ of 86.7±4.2 and 88.7±6.2 for the next 25 mounts, respectively). Electrode tip locations for all rats subjected to such DRN activation are shown in Figs. 2 and 3.

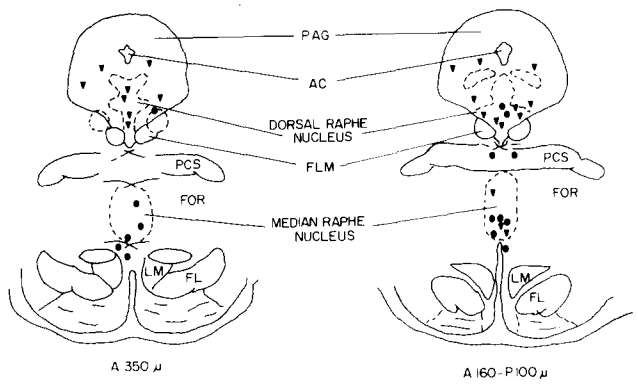


FIG. 3. Location of electrode tips in the midbrain for electrical stimulation at 10 Hz, 2 msec pulse duration and the effects of stimulation at these sites on lordotic behavior. Key and abbreviations as in Fig. 2.

The remaining two sets of stimulation parameters (10 Hz, 0.5 msec pd or 2 Hz, 2 msec pd) proved ineffective in suppressing the LQ. Although the current levels attained during DRN stimulation at 100 Hz, 0.5 msec pd were higher overall than those during MRN stimulation (125 vs. 75 $\mu$A, respectively), this does not mean that the MRN was receiving inadequate activation for observing any possible suppression in receptivity since both the DRN and MRN were stimulated at about the same current levels (134 and 125 $\mu$A, respectively) when 10 Hz, 2 msec pd was utilized—yet only the DRN-implanted animals responded with a significant decrease in LQ.

DRN activation at 100 Hz, 0.5 msec pd or 10 Hz, 2 msec pd was characterized by a general increase in activity and exploratory behavior. DRN stimulation at 2 Hz, 2 msec pd occasionally produced sedateness. These mild behavioral effects are similar to those reported previously during DRN activation [13].

### *Dorsal Raphe Stimulation after PCPA Treatment*

In order to test pharmacologically whether serotoninergic neurons were involved in mediating the suppression of lordotic behavior induced by DRN stimulation, one group of DRN-implanted animals was pretreated with PCPA. The substantial reduction in brain 5-HT levels expected to result from such treatment [11] did not attenuate the significant suppression of receptivity produced by DRN stimulation at 100 Hz, 0.5 msec pd or 10 Hz, 2 msec pd (Fig. 5; decreases of 43% and 78% were observed, respectively). Although only 4 of 8 DRN-implanted rats stimulated at 100 Hz, 0.5 msec pd exhibited a decrease of at least 25% in LQ, all seven animals stimulated at 10 Hz, 2 msec pd responded with decreases (≥25%) in LQ. Furthermore, four of these seven PCPA-treated rats showed a complete or near-complete absence of receptivity during DRN activation.

### *Periaqueductal Gray Stimulation*

A number of animals were implanted unilaterally with electrodes within the periaqueductal gray (PAG) since it was reasonable to suspect (from the results of the preceding section) that the ability of DRN activation to suppress lordotic behavior might be due to stimulus spread to adjacent PAG

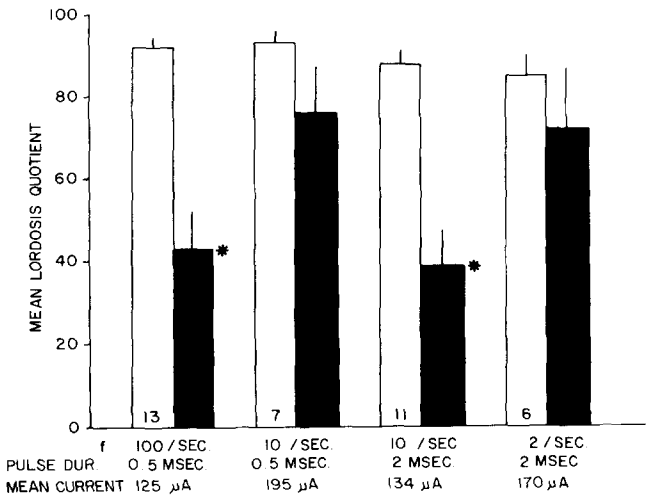


FIG. 4. Effects of activating the mesencephalic dorsal raphe nucleus on mean lordosis quotients (±SE). Key and abbreviations as in Fig. 1. *Significantly less ($p<0.001$) than respective control; $p<0.0125$ considered significant because of multiple (four) comparisons.

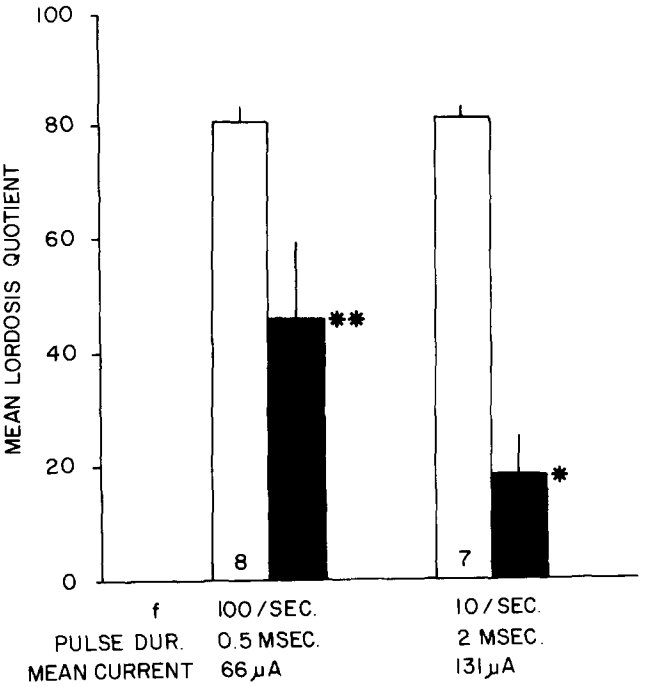


FIG. 5. Effects of electrical stimulation of the dorsal raphe nucleus on mean lordosis quotient (±SE) in female rats pretreated with parachlorophenylalanine 71 hr prior to stimulation. Key and abbreviations as in Fig. 1. *Significantly less ($p<0.001$) than control; $p<0.025$ considered significant because of multiple (two) comparisons. **Although $p<0.05$, this does not meet highly conservative significance criterion because of multiple (two) comparisons.

regions. Indeed, PAG activation at 10 Hz (0.5 or 2 msec pd) produced an immediate and dramatic decrease (81% and 80%, respectively) in receptivity (Fig. 6). Nine of 10 animals stimulated with each of the above two sets of stimulus parameters responded with at least a 25% decrease in LQ; seven of these 9 showed a complete or near complete suppression of receptivity during PAG stimulation. As was the case for DRN activation, high levels of lordotic responses returned immediately following the end of stimulation (LQ of 88.3±4.2 and 95.5±1.9 for the next 25 mounts, respectively).

Although PAG activation at 100 Hz, 0.5 msec pd or 2 Hz, 2 msec pd did not significantly decrease the LQ (Fig. 6), the inability of the former of these to do so was probably the result of relatively low current thresholds for detrimental behavioral effects during PAG stimulation. At current levels above a mean of only 55 μA, such behavioral effects (i.e., escape behavior, ipsilateral circling, or immobility) were consistently noted, thus necessitating the use of lower current levels and probably inadequate PAG stimulation to suppress lordosis behavior. It should be noted that the two animals stimulated at 100 Hz, 0.5 msec pd that did show substantial decreases (64% and 100%) in receptivity during PAG activation were stimulated at 80 and 120 μA, respectively. Electrode tip locations for all animals stimulated within the PAG at 100 Hz, 0.5 msec pd and 10 Hz, 2 msec pd are depicted in Figs. 2 and 3.

In general, PAG activation at current levels below threshold for observation of detrimental behavioral effects produced either no noticeable effect or a decrease in motor activity. However, stimulation at 10 Hz (0.5 or 2 msec pd) within the dorsal half of the PAG induced tail elevation and occasional darting movements in most animals.

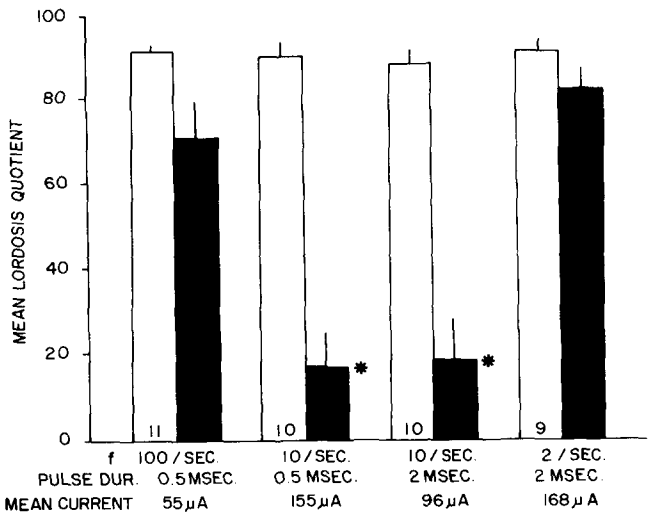


FIG. 6. Effects of electrical stimulation of the periaqueductal gray effects on mean lordosis quotients (±SE). Key and abbreviations as in Fig. 1. *Significantly less ($p<0.001$) than respective control; $p<0.0125$ considered significant because of multiple (four) comparisons.

## DISCUSSION

The experiments described in this study demonstrate that electrical stimulation of the mesencephalic DRN-PAG region in highly receptive estrogen-progesterone treated rats can

markedly suppress lordotic behavior as measured by the LQ. However, the decrease in receptivity induced by DRN stimulation does not appear to be mediated by serotoninergic neurons since blockade of serotonin synthesis with PCPA treatment prior to DRN stimulation did not attenuate the dramatic suppression of the LQ. This later finding argues against an inhibitory role for CNS serotoninergic systems in the neural regulation of lordotic behavior. Rather, the immediate and near complete suppression in receptivity elicited by activation of the adjacent PAG region indicates not only that mechanisms involved with lordotic behavior reside within the mesencephalic PAG, but that these PAG mechanisms appear to include an inhibitory component that can directly influence the reflex arc for lordosis.

The results from previous studies investigating possible serotoninergic inhibitory influences on female receptivity have been inconsistent. Although PCPA has been reported to be capable of replacing progesterone in facilitating lordotic responsiveness in ovariectomized, estrogen-primed rats [9,21], other data indicate either no such behavioral enhancement after PCPA treatment [30], or an indirect PCPA-induced facilitation involving adrenal progesterone secretion [2,7]. Furthermore, the facilitation of lordotic behavior reported to occur in ovariectomized, estrogen-treated rats after central injection of the serotonin neurotoxin 5,7-DHT [8] could not be replicated in a later study [32], which found another serotonin neurotoxin, parachloroamphetamine (PCA), to be similarly ineffective for enhancing receptivity when administered centrally.

The present report provides additional evidence that CNS serotoninergic neurons may not be important for regulating female sexual behavior, at least in an inhibitory manner, because of (1) the inability of median raphe electrical stimulation to suppress the LQ, and (2) the inability of PCPA to attenuate the DRN-induced decrease in receptivity. Stimulation of the median or dorsal raphe nucleus presumably activated serotonin-containing fibers since the raphe region contains the cell bodies of serotoninergic neurons that project rostrally to the hypothalamus and other forebrain areas [10,24]. The use of four different sets of stimulation parameters in this study was designed to eliminate any parameter-based bias in the results. Indeed, the dorsal and median raphe nuclei were activated with stimulation parameters very similar to or identical to those previously reported to affect 5-HT and/or 5-hydroxyindoleacetic acid levels in the brain [1, 12, 13, 18], with 10 Hz, 0.5 or 2 msec pd being the most effective in this regard. Yet, no serotonin-mediated stimulation effects on receptivity were observed. This is in sharp contrast to an earlier report [3] that stimulation of the DRN inhibits the episodic pattern of pituitary luteinizing hormone (LH) release (presumably via suppression of LHRH release from the hypothalamus) present in ovariectomized rats. Furthermore, this inhibition was mediated by activation of serotoninergic neurons since pre-treatment with PCPA or metergoline (a serotonin receptor blocker) eliminated the DRN-induced inhibition of LH secretion [3].

We have subsequently attempted to enhance the lordotic responsiveness of minimally receptive estrogen-treated rats by administering metergoline (as in [3]) prior to testing (Arendash and Gorski, unpublished observations). However, no such behavioral enhancement was observed. We have also tested the ability of pharmacologically-induced receptor activation to suppress lordotic behavior in highly receptive estrogen, progesterone-treated rats through treatment with the 5-HT agonists, quipazine and cinanserin (Arendash and Gorski, unpublished observations). No such behavioral suppression was observed. Finally, we have investigated the effects of discrete lesions of the DRN and/or MRN on the lordotic behavior of minimally receptive, estrogen-treated rats (Arendash and Gorski, unpublished observations). If CNS serotoninergic neurons were providing a tonic inhibitory influence on lordotic responsiveness, enhanced receptivity would have been expected after raphe lesioning—no behavioral enhancement was observed. Therefore, the results from three experimental approaches (electrical stimulation, pharmacological manipulation, and lesioning) appear to indicate that brain 5-HT systems play a minimal, or no, inhibitory role in the neural regulation of female sexual behavior. These data, in addition to those obtained in earlier reports [7, 30, 32, 33], provide no evidence for the hypothesis that progesterone-facilitated lordotic behavior is mediated by a reduced activity of tonically inhibitory serotoninergic neurons [20]. Moreover, convincing evidence for 5-HT involvement in female receptivity has yet to be presented.

The present study demonstrates that electrical stimulation within the PAG, adjacent to the DRN, at 10 Hz (0.5 or 2 msec pd) induces a marked reduction in lordotic responsiveness. Indeed, it is possible that the suppression in receptivity observed during DRN activation was actually due to current spread into surrounding PAG regions. This notion is supported by the fact that PAG-induced lordotic suppressions (at 10 Hz) were generally more dramatic than those produced by similar DRN activation and were observable at lower current levels overall compared with DRN stimulation.

Earlier studies have clearly implicated the mesencephalic PAG as an important link in a putative supraspinal reflex arc regulatory to lordotic behavior [19, 25, 26, 28, 29]. Somatosensory information, initiated by pelvic contact with the male rat, apparently ascends the spinal cord as a component of the spinoreticular (spinotectal) tract, which terminates, at least in part, on the lateral border of the PAG [15]. In this regard, an electrophysiological analysis has determined that many neurons in and around the PAG respond to somatosensory stimulation of the rear body area normally touched by males during a sexual encounter [19]. These neurons, either directly or indirectly, are thought to connect with descending motor pathways that activate lordotic musculature. Additionally, electrical stimulation in and around the PAG has been shown to produce rump and tail movements which resemble elements of the lordosis reflex [26]. The tail elevations induced by dorsal PAG stimulation in the present study appear to confirm this earlier observation.

Recently, Sakuma and Pfaff [28] reported that electrical stimulation in the PAG of minimally receptive, ovariectomized rats (primed only with estrogen) induced a significant facilitation of the lordosis reflex—exactly opposite to the PAG stimulation effects observed in the present report. In a companion study [29], the same authors found that bilateral lesions placed within the PAG induced a significant suppression in receptivity—a suppression we have not detected in a similar PAG lesion study (Arendash and Gorski, submitted for publication). Sakuma and Pfaff [29] also reported that PAG lesions abolish the facilitation of lordosis induced by stimulating the ventromedial nucleus of the hypothalamus, an important forebrain area regulatory to female receptivity. From these studies, they suggest that the PAG is at the top of a reflex loop composed of ascending somatosensory and descending motor components. They also suggest that the hypothalamus is not in this loop, but does provide tonic in-

fluences on it. The apparent inconsistency between the PAG stimulation effects of the present study and those of Sakuma and Pfaff may be explained on the basis of differences in hormonal priming procedures prior to stimulation—the latter authors used minimally receptive rats treated with estrogen only, while we used highly receptive estrogen-progesterone-treated animals. It should be remembered that the intact female rat usually shows a high LQ only on proestrus and that receptivity at this time is directly correlated with blood progesterone levels [14]. Therefore, treatment with both estrogen and progesterone, such as in the present study, may more closely mimic the physiological situation. Nonetheless, it is possible that our use of minimally receptive, estrogen-treated rats for PAG stimulation would have resulted in findings similar to those of Sakuma and Pfaff [28].

Several possibilities could explain the PAG- and DRN-induced suppression of the LQ observed in the present study. First, stimulation may activate a mesencephalic ascending neuronal pathway(s), such as the dorsal longitudinal fasciculus [15], inhibitory to female receptivity. However, the immediate nature of suppression at the onset of DRN or PAG stimulation would tend to make any mechanism involving sluggish forebrain behavioral circuitry unlikely. Second, stimulation may activate descending pathways originating in or passing through the DRN-PAG region which may inhibit the lordosis reflex arc at the level of the medulla or the spinal cord. In this regard, the medullary lateral vestibular nucleus and nucleus gigantocellularis appear to provide facilitatory input to the lordosis reflex [22,23], presumably through descending vestibulospinal and reticulospinal tracts, respectively. Perhaps the DRN and/or PAG stimulation of the present study resulted in either a direct or indirect suppression of lordosis-related neurons within these two medullary nuclei. A third possibility might involve a stimulation-induced interference with mesencephalic pathways facilitatory to lordotic behavior. However, our parameters of stimulation were similar to those used by Sakuma and Pfaff [28] to induce an enhancement in receptivity during PAG activation. Since it is difficult to conceive of how any facilitation or lordotic behavior can be observed if a significant interference component is being concurrently produced, this last-mentioned possibility may not be a likely one.

In summary, the results of the present study demonstrate that electrical stimulation of the mesencephalic dorsal raphe-periaqueductal gray region can suppress lordotic responsiveness in highly receptive, steroid-treated animals, perhaps through a direct effect on the reflex arc for lordosis. Furthermore, the dorsal raphe-induced suppression in female receptivity does not appear to be mediated by CNS serotoninergic systems, thus arguing against a major inhibitory role for brain 5-HT systems in the neural regulation of female sexual behavior.

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