Pharmacology Biochemistry & Behavior, Vol. 18, pp. 535–539, 1983. © Ankho International Inc. Printed in the U.S.A.

Facilitation of Estrogen-Induced Receptivity Through Metyrapone Administration in Ovariectomized Rats

DENYS DE CATANZARO, RANDOLPH P. KNIPPING AND STEPHEN W. WIGMORE

Department of Psychology, McMaster University, Hamilton, Ontario L8S 4K1, Canada

Received 27 February 1982

DE CATANZARO, D., R. P. KNIPPING AND S. W. WIGMORE. *Facilitation of estrogen-induced receptivity through metyrapone administration in ovariectomized rats.* PHARMACOL BIOCHEM BEHAV **18**(4) 535–539, 1983.—Previously it has been established that adrenalectomy facilitates lordosis in estrogen-primed ovariectomized female rats and that corticosterone administration restores lordosis to preadrenalectomy levels. The present study examined the effects of an inhibitor of the synthesis of corticosterone, metyrapone, upon lordosis in ovariectomized females. In Experiment 1, chronic administration of moderate doses of metyrapone was found to facilitate lordosis. In Experiment 2, a single metyrapone administration at various doses and time intervals before testing had a mild facilitatory effect on lordosis. Experiment 3 compared the effects of metyrapone on ovariectomized and adrenalectomized-ovariectomized females. The absence of a facilitatory effect in adrenalectomized females suggests that the drug's effect on lordosis is mediated by its established inhibitory effects on 11β-hydroxylation in the adrenal. These data are consistent with indications that corticosterone titer modulates female receptivity.

Metyrapone Corticosterone Lordosis Adrenalectomy Female sexual behavior Estrogen

THERE is growing evidence that activity of the pituitary-adrenal system can influence estrogen-induced sexual receptivity in female rodents. Several studies [9, 10, 11, 14, 15] have indicated that adrenalectomized-ovariectomized females show higher lordosis quotients in response to estrogen administration than do adrenally-intact ovariectomized females. Chronic peripheral corticosterone or dexamethasone administration, but not administration of progesterone or desoxycorticosterone, inhibits estrogen-induced lordosis in adrenalectomized-ovariectomized females [10,12]. Despite the fact that adrenalcorticotrophic hormone (ACTH) levels rise following adrenalectomy and are lowered by corticosterone administration [8,17] and evidence that peripheral ACTH administration can facilitate lordosis [10,11], the effects of corticosterone and adrenalectomy on lordosis do not appear to be mediated by ACTH [11]. However, under a variety of dosage regimens corticosterone level consistently influences female receptivity through some unknown mechanism [12].

The drug metyrapone is reported to be a potent inhibitor of adrenal synthesis of corticosterone, blocking action of the enzyme 11β-hydroxylase that produces this hormone from its precursor, 11-desoxycorticosterone [6, 13, 21, 31]. There appears to have been very little study of the behavioral effects of this substance. If corticosterone does indeed play a specific inhibitory role in the control of female sexual receptivity, it should be possible to facilitate lordosis by administering metyrapone to adrenally-intact females. Previously [12], the inference that corticosterone may have an inhibitory effect on lordosis was based primarily upon comparison of adrenalectomized-ovariectomized rats given various replacement doses of corticosterone. In the present study, ovariectomized but adrenally-intact animals were examined under varied acute and chronic regimens of metyrapone administration. This accordingly tests the generality of findings across physiological preparations, which should help to confirm or disconfirm a specific role of corticosterone in modulating female receptivity. The first two experiments demonstrate that metyrapone does indeed influence lordosis in manners consistent with such a modulatory role of corticosterone. The third experiment verifies the involvement of the adrenal gland in these effects of metyrapone by comparing its action in adrenalectomized-ovariectomized and ovariectomized females.

EXPERIMENT 1

In the first experiment, the effect of chronic administration of various doses of metyrapone was studied in ovariectomized females given either of two doses of estrogen. A chronic regimen was employed first because previous data have indicated that sustained variations in corticosterone titer most reliably influence estrogen-induced female receptivity [10,12]. The dose range was based upon dosages administered *in vivo* to adult rats in studies demonstrating alteration of adrenal functioning by this drug. For example, Malendowicz [22] administered 30 mg/animal daily for 5 days, demonstrating marked changes in adrenal histology, whereas Parvez and Parvez [24] administered 75 mg/animal daily for 1, 7, or 10 days, demonstrating a number of biochemical effects consistent with glucocorticoid suppression.

METHOD

Sprague-Dawley female rats were obtained from Blue Spruce Farms, Altamont, New York at about 225 grams. These were housed in groups of two or three in triple wire-mesh cages in a room maintained at 21±1°C. About 2 weeks after their arrival all animals were bilaterally ovariectomized under 40 mg/kg sodium pentobarbitol (Somnitol, MTC Pharmaceuticals) supplemented with ether where necessary.

All animals were administered estradiol benzoate 7 days, 48 hr, and 24 hr before behavioral testing, with the first injection being about 1 week after surgery. Approximately half received 10 μg at each of these times whereas the remainder received 50 μg at each time. These estradiol injections were SC in 0.05 cc propylene glycol. Animals were also each given 5 daily injections of metyrapone (2-methyl-1,2-di-3-pyridyl-1-propanone, Sigma) beginning 48 hr after the first estradiol injection (5 days before behavioral testing). These were given in one of 5 doses, 0, 4, 12, 36, 108 mg/kg daily, to animals from both estrogen dose conditions, making a 2 (estrogen dose) × 5 (metyrapone dose) between-subjects experimental design. There were 12 animals in each treatment combination, except for the low estrogen dose 108 mg/kg metyrapone condition where there were 10 animals. The metyrapone injections were given IP in 2.64 ml/kg of 20% propylene glycol/80% physiological saline vehicle. Animals ranged from 240 to 325 g during the metyrapone injections.

Measurement of lordosis occurred in a dimly illuminated room separate from the animal colony and also maintained at 21±1°C. This involved presentation of females to stud male rats in Plexiglas arenas measuring 33×33×60 (height) cm. Stud males were given brief exposure to fully receptive females (each given 10 μg estradiol benzoate 48 hr and 500 μg progesterone 6 hr before presentation) just prior to sessions with experimental females. These males were employed during the dark phase of their reversed 12 hr light/12 hr dark cycle. Each female was placed with a male until ten mounts accompanied by pelvic thrusting had occurred. If a male did not mount, the female was placed in another arena containing a different male. The female's response to a mount was categorized as either a lordosis response, consisting of a full arching of the back [18,26], or no lordosis, consisting of any other response or no response. The experimenter measuring behavior was blind to each animal's treatment condition, with animals labelled by a second experimenter who transferred them to the observer. A lordosis quotient was calculated as the percentage of mounts resulting in a lordosis response.

RESULTS

Figure 1 presents mean lordosis quotients and standard errors of all conditions. At either dose of estrogen there was higher lordosis in the 12 mg/kg conditions than in all other conditions including the 0 mg/kg (vehicle control) conditions. This apparent facilitatory effect was not evident with higher doses; indeed, among the high estrogen dose animals, those given 108 mg/kg metyrapone showed lordosis quotients substantially lower than those of the vehicle control animals. A 2×5 analysis of variance was conducted on an arcsin transformation of the scores, which is appropriate for percentage data [19]. This analysis revealed significant main effects of estrogen dose, $F(1,108)=26.82$, $p<0.0001$, and of metyrapone dose, $F(4,108)=4.39$, $p<0.0025$, but no significant interaction. Multiple comparisons (Duncan's test) indicated that among high-estrogen animals, the 12 mg/kg group differed from the 0, 36, and 108 mg/kg groups; among low estrogen animals, the 12 mg/kg group differed from the 4 mg/kg group.

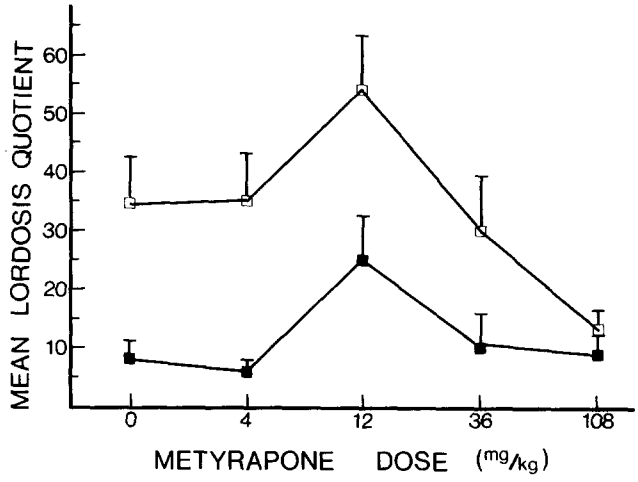

FIG. 1. Lordosis quotients (±SE) for ovariectomized females given one of two estrogen dose regimens (10 or 50 μg 7,2 and 1 days before testing) and one of 5 doses of metyrapone daily for five days prior to testing in Experiment 1. Closed squares represent animals given 10 μg estrogen; open squares represent those given 50 μg estrogen.

EXPERIMENT 2

Knowledge of temporal parameters of corticosterone elevation necessary to inhibit estrogen-induced receptivity may shed light on mechanisms underlying this effect. Previously [12], it was found that chronic corticosterone administration most reliably antagonized lordosis, whereas more acute administration was only effective when occurring prior to estrogen injections. The present experiment examined the effects of a single or acute administration of metyrapone in various temporal relationships to estrogen administration and behavioral measurement.

METHOD

Females were obtained, prepared, and maintained as in Experiment 1. All females received SC injections of estradiol benzoate, 50 μg at 7 days and 100 μg at 48 hr before behavioral testing. Females were also each given a single injection of one of four doses of metyrapone (0, 12, 36, 108 mg/kg), according to the procedures of Experiment 1, at one of three time intervals (24, 48, and 72 hr) prior to behavioral testing. Behavioral testing was conducted as in Experiment 1.

RESULTS

Table 1 presents the data from this experiment. Although lordosis quotients were well below full receptivity in all conditions, there was a trend toward higher levels of lordosis in animals receiving metyrapone than in those receiving only vehicle injections. There was no clear trend across metyrapone doses and times of administration. A 4 (metyrapone dose) by 3 (administration time) analysis of variance was conducted on the arcsin transformation of the

TABLE 1

MEAN (±SE) LORDOSIS QUOTIENTS FOR ESTROGEN-PRIMED OVARIECTOMIZED RATS WITH A SINGLE ADMINISTRATION OF METYRAPONE AT VARIOUS INTERVALS BEFORE TESTING

Hours before Testing	Dose (mg/kg)			
	0	12	36	108
24	9.0	6.0	6.2	24.0
	±5.4	± 4.0	± 4.9	± 9.1
n	10	10	8	10
48	5.0	23.3	17.0	14.4
	±3.4	±11.4	± 6.5	± 8.6
n	10	9	10	9
72	5.5	32.2	12.0	23.0
	±2.9	±13.9	± 6.6	± 5.5
n	9	9	10	10

scores, revealing a significant effect of metyrapone dose, $F(3,102)=2.75$, $p<0.0475$, but no significant effect of administration time nor any significant interaction. Subsequent multiple comparisons failed to identify the source of the significant effect, although data in Table 1 suggest that average lordosis quotients exceed those of vehicle conditions in all metyrapone conditions except those involving administration of lower doses at the 24 hr drug-test interval.

EXPERIMENT 3

It is possible that the facilitatory effects of metyrapone on lordosis observed with some chronic doses in Experiment 1 and with acute administration in Experiment 2 are due to a nonadrenal action of the drug. To investigate this possibility, the present experiment involved comparison of effects of metyrapone and vehicle control groups of both ovariectomized and adrenalectomized-ovariectomized females. In addition, two other variables were changed from previous experiments; metyrapone was obtained from a different supplier and chronic administration was accomplished through implanted osmotic pumps to ensure fairly constant release of the substance.

METHOD

Sprague-Dawley females were obtained and maintained as in the previous experiments. About half of those were bilaterally adrenalectomized, whereas all animals were ovariectomized through bilateral lumbar incisions. Adrenalectomized females were given continuous access to 0.9% saline solution in lieu of water immediately following surgery and throughout the course of the experiment. Estradiol benzoate was given to all females in SC doses of 50 μg at 7 days and 100 μg at 48 hr before behavioral testing, with the first estradiol injection occurring at least 2 weeks following surgery. Two days after this first injection, osmotic minipumps (Model 2001, Alza Corp, Palo Alto, CA) were implanted SC under ether anaesthetic in all animals. These were filled either with metyrapone (CIBA) in 20:80 propylene glycol: saline vehicle or with vehicle alone. The pump rate as specified by the manufacturer was 0.925 μl/hr, giving a metyrapone dose of 0.18 mg/μl continuously until the end of the experiment. Behavioral testing was conducted as in the previous experiments. There were 15 metyrapone treated and 12 vehicle-treated ovariectomized females and 12 metyrapone-treated and 11 vehicle-treated adrenalectomized-ovariectomized females in this behavioral test.

Because of the overall low level of responding in this first test, additional estrogen was subsequently given to about half of these same females and they were retested while the pumps were still infusing metyrapone or vehicle. This involved 100 μg estradiol benzoate injections at both 48 hr (immediately following the first test) and 24 hr prior to the second test. This additional procedure was effected with 8 metyrapone-treated and 7 vehicle-treated ovariectomized females and 6 metyrapone-treated and 6 vehicle-treated adrenalectomized-ovariectomized females.

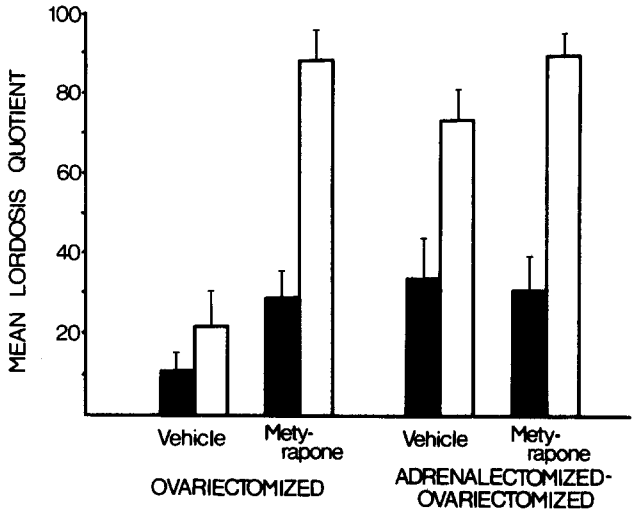

FIG. 2. Mean lordosis quotients (±SE) for adrenalectomized-ovariectomized and ovariectomized females receiving metyrapone or vehicle through subcutaneous osmotic minipumps in Experiment 3. The shaded bars represent scores from the first test whereas the open bars represent scores from the second test after additional estrogen administration.

RESULTS

Lordosis quotients for all animals at both tests are presented in Fig. 2. In both tests there apparently was heightened receptivity in metyrapone-treated as compared to vehicle-treated ovariectomized females. While adrenalectomized-ovariectomized females showed higher levels of responding than did ovariectomized females, there was no apparent effect of metyrapone among the adrenalectomized-ovariectomized animals. These data were analyzed statistically in three manners. A 2 (metyrapone/vehicle) × 2 (surgery) analysis of variance on data from all animals in the first test did not reveal significant effects. However, a 2×2×2 analysis of variance on all animals included in both tests, with the additional factor being the within-subjects repeated measure, revealed significant effects of surgery, $F(1,23)=11.76$, $p=0.0023$, of metyrapone, $F(1,23)=18.29$, $p=0.0003$, of the repeated test, $F(1,23)=78.18$, $p<0.0001$, of the surgery by metyrapone in-

teraction, $F(1,23)=7.02$, $p=0.0143$, and of the three way interaction, $F(1,23)=18.45$, $p=0.0003$. A 2×2 analysis of variance on data from the second test only revealed significant effects of surgery, $F(1,23)=14.63$, $p=0.0009$, of metyrapone, $F(1,23)=27.22$, $p<0.0001$, and of the surgery by metyrapone interaction, $F(1,23)=13.54$, $p=0.0012$. Multiple comparisons for this last analysis revealed that the ovariectomized vehicle-treated females showed lower receptivity than all other groups, which in turn did not significantly differ from one another.

GENERAL DISCUSSION

These results indicate that administration of metyrapone can facilitate lordosis behavior in estrogen-primed ovariectomized female rats. Such effects are clearly evident with moderate chronic doses of the drug and also may occur under regimens of acute administration. In the chronic case, the effect was observed both when the drug was administered through daily IP injections and when it was administered SC through an osmotic pump providing a relatively constant systemic infusion. High chronic doses appear to inhibit lordosis or at least to lack any facilitatory effect on the behavior. The increase in lordosis found with moderate chronic doses of metyrapone is evident in ovariectomized females but not in adrenalectomized-ovariectomized females. The facilitatory effect of metyrapone on estrogen-induced lordosis in adrenally-intact females occurs at a variety of estrogen doses.

A facilitation of lordosis by metyrapone is consistent with previous suggestions that corticosterone plays an inhibitory role in the control of female receptivity. Earlier studies [10, 11, 12] indicated that administration of exogenous corticosterone suppresses lordosis in adrenalectomized-ovariectomized females. It was inferred from such evidence that corticosterone titer modulates lordosis behavior, but the artificiality of the adrenalectomized-ovariectomized preparation may place limitations on inferences that can be drawn about the specificity of action of corticosterone. It accordingly is valuable to have convergent data from additional physiological preparations. The present study demonstrates that a drug blocking the synthesis of endogenous corticosterone increases female receptivity in adrenally-intact ovariectomized females. The doses and regimens of metyrapone administration that are effective in facilitating lordosis are very similar to those demonstrated elsewhere [21, 22, 23, 24] to reduce glucocorticoid synthesis. This may strengthen considerably the inference that corticosterone level influences female receptivity.

At the very least, it can be concluded that metyrapone's action on estrogen-induced lordosis is mediated by the adrenal. The absence of a facilitatory effect in adrenalectomized-ovariectomized females in Experiment 3 may rule out direct extra-adrenal mechanisms. It might be counterargued that, because the adrenalectomized-ovariectomized females showed a higher baseline level of receptivity than the ovariectomized females, consistent with previous findings [9, 10, 11, 14, 15], ceiling effects prevented a further increase in receptivity occurring through some extra-adrenal action. However, the level of receptivity in vehicle-treated adrenalectomized-ovariectomized females in either lordosis test of Experiment 3 was well below that of full receptivity, leaving considerable room for increases if metyrapone had had an effect on these females. The clearest explanation of these data is that the facilitatory effects of metyrapone are attributable to its effects on the adrenal.

The apparent inhibitory effect of high chronic doses of metyrapone on lordosis observed in Experiment 1 may be attributable to nonspecific or toxicological effects of such doses. In addition to its well-established action on 11β-hydroxylation, which markedly suppresses corticosterone synthesis [6, 13, 31], metyrapone also can block the conversion of desoxycorticosterone into 18-hydroxy-desoxycorticosterone by the rat adrenal [20] and interferes with the cleavage of cholesterol into pregnenolone in rat adrenal mitochondria [7]. These effects produce a number of shifts in the relative output of various glucocorticoids and mineralocorticoids synthesized by the adrenal, which in turn are likely to affect a variety of extra-adrenal metabolic processes. Evidence of extra-adrenal effects includes indications that metyrapone promotes hyperglycemia [5], stimulates the secretion of growth hormone [28], and has a direct stimulatory effect on pituitary ACTH secretion [16]. It also is conceivable that facilitatory effects of metyrapone on lordosis are attributable to adrenal action other than its blockage of corticosterone synthesis; for example, a shift in the output of adrenal androgens might be responsible. However, given that the most firmly established effect of metyrapone is its effect on 11β-hydroxylation and corticosterone synthesis, and previous evidence implicating corticosterone in the control of lordosis [10,12], it remains most parsimonious at this point to attribute the substance's effects on behavior to its action on corticosterone synthesis.

Previously [12] it was suggested that the inhibitory effects of corticosterone on lordosis might be mediated by its effects on brain monoamine activity. This followed from pharmacological evidence that both dopaminergic [1, 2, 3, 15] and serotonergic [2, 15, 30, 32] activity reduces lordosis, taken with evidence that adrenalectomy facilitates and corticosterone inhibits the activity of monoamine oxidase (MAO), an enzyme that metabolizes and inactivates both dopamine and serotonin [25, 27, 29]. Accordingly, adrenalectomy may decrease and corticosterone increase serotonergic and dopaminergic activity, thereby respectively increasing and decreasing lordosis. Indeed, there is evidence that adrenalectomy reduces and corticosterone enhances central turnover of serotonin [4]. Consistent with both this hypothesis and data of the present study is a report that both acute and chronic administration of metyrapone substantially augments MAO activity, an effect believed to be mediated by its action on the adrenal [24]. Accordingly, one possibility is that the facilitatory effects of metyrapone on lordosis observed in the present study are mediated by effects on adrenal corticosteroids, which in turn modify central monoamine activity, which in turn affects lordosis level.

ACKNOWLEDGEMENTS

This research was supported by NSERC grant U0146 awarded to D. DE Catanzaro. The assistance of Bruce Gardner and Paul Moroz is gratefully acknowledged. Metyrapone for Experiment 3 was supplied courtesy of CIBA.

REFERENCES

1. Ahlenius, S., J. Engel, H. Eriksson and P. Sodersten. Effects of tetrabenazine on lordosis behaviour and on brain monoamines in the female rat. *J Neural Transm* **33:** 155–162, 1972.
2. Ahlenius, S., J. Engel, H. Eriksson, K. Modigh and P. Sodersten. Importance of central catecholamines in the mediation of lordosis behaviour in ovariectomized rats treated with estrogen and inhibitors of monoamine synthesis. *J Neural Transm* **33:** 247–255, 1972.
3. Ahlenius, S., J. Engel, H. Eriksson, K. Modigh and P. Sodersten. Involvement of monoamines in the mediation of lordosis behavior. In: *Sexual Behavior: Pharmacology and Biochemistry*, edited by M. Sandler and G. L. Gessa. New York: Raven Press, 1975, pp. 137–145.
4. Azmitia, E. C., S. Algeri and E. Costa. In vivo conversion of ^{3}H-L-tryptophan into ^{3}H-serotonin in brain areas of adrenalectomized rats. *Science* **169:** 201–203, 1970.
5. Bruno, O. D., P. Metzger and I. J. Malaisse. Inhibitory effect of metyrapone on glucose utilization by brain and muscle and on insulin release by the pancreas. *Acta Endocrinol (Copenh)* **70:** 710–718, 1972.
6. Chart, J. J., H. Shepard, M. J. Allen, W. L. Bencze and R. Gaunt. New amphenone analogs as adrenocortical inhibitors. *Experientia* **14:** 151–153, 1958.
7. Cheng, S. C., B. W. Harding and A. Carballeira. Effects of metyrapone on pregnenolone biosynthesis and on cholesterol-cytochrome P-450 interaction in the adrenal. *Endocrinology* **94:** 1451–1458, 1974.
8. Cox, G. S., J. R. Hodges and J. Vernikos. The effect of adrenalectomy on the circulating level of adrenocorticotrophic hormone in the rat. *J Endocrinol* **17:** 177–188, 1958.
9. Davidson, J. M., C. H. Rodgers, E. R. Smith and G. J. Bloch. Stimulation of female sexual behavior in adrenalectomized rats with estrogen alone. *Endocrinology* **82:** 193–195, 1968.
10. de Catanzaro, D. and B. B. Gorzalka. Effects of dexamethasone, corticosterone, and ACTH on lordosis in ovariectomized and adrenalectomized-ovariectomized rats. *Pharmacol Biochem Behav* **12:** 201–206, 1980.
11. de Catanzaro, D., D. S. Gray and B. B. Gorzalka. Effects of acute central and peripheral ACTH$^{1-24}$ administration on lordosis behavior. *Physiol Behav* **26:** 207–213, 1981.
12. de Catanzaro, D., R. P. Knipping and B. B. Gorzalka. Antagonism of estrogen-induced lordosis by corticosterone in adrenalectomized-ovariectomized female rats and mice. *Pharmacol Biochem Behav* **15:** 761–766, 1981.
13. Dominguez, O. V. and L. T. Samuels. Mechanism of adrenal steroid 11β-hydroxylase on methopyrapone (metopirone). *Endocrinology* **73:** 304–309, 1963.
14. Eriksson, H. and P. Sodersten. A failure to facilitate lordosis behavior in adrenalectomized and gonadectomized estrogen-primed rats with monoamine-synthesis inhibitors. *Horm Behav* **4:** 89–97, 1973.
15. Everitt, B. H., K. Fuxe, T. Hökfelt and G. Jonsson. Studies on the role of monoamines in the hormonal regulation of sexual receptivity in the female rat. In: *Sexual Behavior: Pharmacology and Biochemistry*, edited by M. Sandler and G. L. Gessa. New York: Raven Press, 1975, pp. 147–159.
16. Ganong, W. F. and E. M. Gold. Changes in blood ACTH levels following administration of SU-4885 to adrenalectomized dogs. *Physiologist (Bethesda)* **3:** 63, 1960.
17. Gemzell, C. A., D. C. van Dyke, C. A. Tobias and M. M. Evans. Increase in the formation and secretion of ACTH following adrenalectomy. *Endocrinology* **49:** 325–336, 1951.
18. Gorzalka, B. B. and G. J. Mogenson. Sexual behavior, In: *The Neurobiology of Behavior: An Introduction*, edited by G. J. Mogenson. Hillsdale, NJ: Lawrence Erlbaum Associates, 1977, pp. 151–186.
19. Kirk, R. E. *Experimental Design: Procedures for the Behavioral Sciences*. Belmont, CA: Brooks/Cole, 1968.
20. Kraulis, I. and M. K. Birmingham. Inhibition of the biosynthesis of 18-hydroxy-11-deoxycorticosterone by SU-4885. *Can J Biochem* **43:** 1471–1476, 1965.
21. Liddle, G. W., D. Island, E. M. Lance and A. P. Harris. Alterations of adrenal steroid patterns in man resulting from treatment with a chemical inhibitor of 11β-hydroxylation. *J Clin Endocrinol Metab* **18:** 906–912, 1958.
22. Malendowicz, L. K. Comparative studies on the effects of aminoglutethimide, metopirone, ACTH and hydrocortisone on the adrenal cortex of adult male rats. II. Histological and histochemical studies. *Endokrinologie* **61:** 75–93, 1973.
23. Milkovic, K., R. Romic, J. Paunovic and S. Milkovic. Failure of the metopirone (Su4885) suppressed fetal adrenal glands to maintain corticosterone concentration of adrenalectomized pregnant rats. *Endocrinology* **96:** 1297–1299, 1975.
24. Parvez, H. and S. Parvez. The effects of metopirone and adrenalectomy on the regulation of the enzymes monoamine oxidose and catecol-O-methyl transferase in different brain regions. *J Neurochem* **20:** 1011–1020, 1973.
25. Parvez, H. and S. Parvez. The regulation of monoamine oxidase activity by adrenal cortical steroids. *Acta Endocrinol* **73:** 509–517, 1973.
26. Pfaff, D. W. *Estrogens and Brain Function*. New York: Springer Verlag, 1980.
27. Rastogi, R. B. and R. L. Singhal. Evidence for the role of adrenocortical hormones in the regulation of noradrenaline and dopamine metabolism in certain brain areas. *Br J Pharmacol* **62:** 131–136, 1978.
28. Takahara, J., N. Ogawa and T. Ofuji. Extra-adrenal action of metyrapone upon human growth hormone secretion in man. *Endocrinol Jpn* **19:** 197–201, 1972.
29. Veals, J. W., C. A. Korduba and S. Symchowicz. Effect of dexamethasone on monoamine oxidase inhibition by iproniazid in rat brain. *Eur J Pharmacol* **41:** 291–299, 1977.
30. Ward, I. L., W. R. Crowley, F. P. Zemlan and D. L. Margules. Monoaminergic mediation of female sexual behavior. *J Comp Physiol Psychol* **88:** 53–61, 1975.
31. Williamson, D. G. and V. J. O'Donnell. Mechanism of metopirone inhibition of a soluble adrenal steroid 11β-hydroxylase. *Can J Biochem* **45:** 153–163, 1967.
32. Zemlan, F. P., I. L. Ward, W. R. Crowley and D. L. Margules. Activation of lordotic responding in female rats by suppression of serotonergic activity. *Science* **179:** 1010–1011, 1973.