Pituitary–Adrenal Function in Photic and Olfactory Deprived Rats[1] (36546)

J. Dunn, M. Bennett[2], and R. Peppler
(Introduced by Melvin Hess)
Department of Anatomy, Louisiana State University Medical Center, New Orleans, Louisiana 70112

Several recent studies have reported changes in the pituitary–gonadal axis following bilateral removal of the eyes and olfactory bulbs (1–4). Since it is generally accepted that a variety of neuroendocrine reflexes are dependent upon photic and olfactory stimuli, it seemed appropriate to determine whether photic and/or olfactory deprivation would also affect pituitary–adrenal function. Thus, the present study was undertaken to assess some aspects of pituitary–adrenal function in rats subjected to optic enucleation and/or olfactory bulb removal.

Materials and Methods. Animals used in these studies were adult (140–160 g), female, Sprague-Dawley (Charles-River, CD) rats, housed under conditions of controlled lighting (fluorescent illumination from 04:00 to 18:00) and temperature (25 ± 1°). Purina lab chow and tap water were available *ad libitum.* Olfactory bulbs were removed by dissection following partial removal of the overlying frontal bones. Blinding was produced by bilateral enucleation. Following surgery, rats were housed in individual cages and vaginal smears obtained 6 days a week.

Individual experiments were performed at intervals of 10 days, beginning 21 days after surgery. Plasma concentrations of corticosterone, measured fluorometrically (5), were used as an index of pituitary–adrenal function. Correction for residual fluorescence was not made. However, in this laboratory, fluorescence measured in plasma from adrenalectomized female rats is equivalent to approximately 6 μg corticosterone/100 ml plasma.

To examine the effects of blinding and/or anosmia on pituitary–adrenal function, nonstress and stress levels of plasma corticosterone were determined under a variety of temporal and stress conditions. The method used to assess nonstress and stress levels of pituitary–adrenal function was similar to that described by Zimmermann and Critchlow (6). Nonstress blood samples were obtained by removing rats from the animal quarters to an adjacent preparation room where they were rapidly anesthetized with ether or immobilized in the supine position. The external jugular vein was exposed and 1.0 to 1.5 ml of blood was collected in a heparinized syringe within 3 min of initial handling. Following 3 min exposure to ether vapor or immobilization, rats were placed in individual holding cages; 12 min later (15 min after onset of stress), rats were anesthetized with ether and a stress blood sample was taken from the jugular vein. Blood samples were immediately centrifuged and plasma was collected for determination of nonstress and stress levels of plasma corticosterone. The difference in corticosterone levels between first and second plasma samples was calculated for each rat and used as an index of the pituitary–adrenal response to ether or immobilization stress. All experiments began at 09:00 or 16:00.

To study the effects of negative feedback on pituitary–adrenal function, rats were injected subcutaneously with 100 μg/kg of dexamethasone-21-phosphate (dexamethasone) at noon, 4 hr prior to the collection of nonstress blood samples. The effects of dexamethasone on nonstress and ether stress

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[2] Present address: Departments of Neurosurgery and Pharmacology, University of Pittsburgh, School of Medicine, Pittsburgh, PA.

TABLE I. Effect of Blinding and/or Anosmia on Plasma Levels of Corticosterone.

	Corticosterone (μg/100 ml plasma)				
				Afternoon (4 p.m.)	
Group I	No. of rats	Morning (9 a.m.) Nonstress	No. of rats	Nonstress	Stress-increment immob.
Intact controls	9	23.3 ± 4.6[a]	8	42.2 ± 6.4	24.4 ± 4.9
Blind	8	20.8 ± 5.4	8	45.0 ± 9.2	29.9 ± 7.3
Anosmic	8	10.0 ± 3.0	8	43.8 ± 5.7	30.8 ± 5.3
Blind and anosmic	9	8.3 ± 2.3[b]	8	28.6 ± 8.0	33.5 ± 3.0

[a] Mean ± standard error.
[b] Indicates: $p < .05$ vs intact controls.

levels of plasma corticosterone were determined as described above. At autopsy, 5–6 months after surgery, adrenals were removed and weighed to the nearest milligram.

Treatments were assigned, performed and data were analyzed according to a completely randomized design. Statistical probabilities were determined by analysis of variance or Student's *t* test.

Results. The effect of blinding and/or anosmia on nonstress levels of plasma corticosterone is summarized in Table I. As indicated, only rats subjected to both blinding and olfactory bulb removal had nonstress levels of corticosterone which differed from those of intact controls, and these differed ($p < .05$) from those of controls only in the a.m. All groups showed significant diurnal variation in nonstress levels of plasma corticosterone.

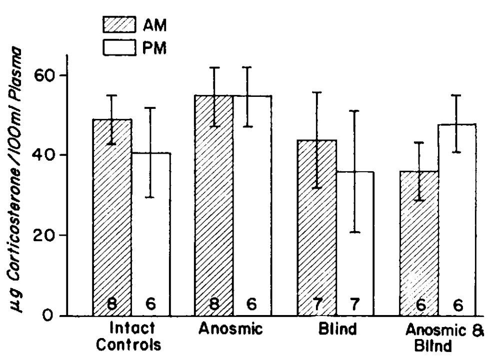

FIG. 1. Ether stress-induced increments in plasma levels of corticosterone. In this and the subsequent illustration the number of animals per treatment group is indicated at the base of the column; vertical lines indicate standard error.

The response of photic and/or olfactory deprived rats to immobilization and ether stress is summarized in Table I and Fig. 1, respectively. As indicated, sensory deprivation had no effect on the plasma corticosterone response to stress. Immobilization (Table I) and ether (Fig. 1) stress-induced increments in plasma corticosterone of experimentals were not different from those of intact controls.

The effect of dexamethasone on nonstress and stress levels of corticosterone is illustrated in Fig. 2. Experimentals as well as intact controls showed marked suppression of nonstress levels of plasma corticosterone and these levels were suppressed to the same extent in all groups. In contrast, differences were observed in stress-produced increments in plasma corticosterone. Blind and blind–anosmic rats failed to show a response to stress, whereas intact and anosmic rats showed significant ($p < .01$) increments in plasma corticosterone following ether stress (Fig. 2).

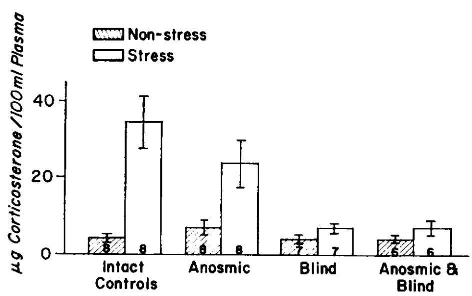

FIG. 2. Effect of dexamethasone (100 mg/kg) on morning (09:00) nonstress and stress (ether) levels of plasma corticosterone.

TABLE II. Effects of Blinding and/or Anosmia on Body and Adrenal Weights at Autopsy.

	No. of rats	Body wt (g)	Adrenals (mg)	Adrenals (mg/100 g)
Intact controls	8	247 ± 5[a]	68.1 ± 2.6	27.6 ± 1.3
Blind	8	240 ± 5	67.6 ± 3.0	28.6 ± 0.9
Anosmic	8	250 ± 7	71.2 ± 2.2	28.5 ± 0.8
Blind and anosmic	7	207 ± 5[b]	57.7 ± 3.1[b]	27.8 ± 0.9

[a] Mean ± standard error.
[b] Indicates: $p < .01$ vs intact control group.

Table II summarizes the effect of blinding and/or anosmia on body and adrenal weights. Whereas, neither blinding nor olfactory bulb removal affected body or adrenal weights, combined sensory deprivation (blind–anosmic rats) resulted in reduced body and adrenal weights ($p < .01$). However, relative adrenal weights (mg/100 g) of rats subjected to combined blinding and anosmia did not differ from those of controls.

Discussion. In contrast to the changes reported for the pituitary–ovarian system, in the present study, adrenocortical activity was not markedly affected by photic and/or olfactory deprivation. Morning and afternoon nonstress levels of corticosterone of blind and anosmic animals did not differ from those of controls. Only rats subjected to combined sensory deprivation (blind–anosmic) had nonstress levels of corticosterone different from those of controls, and these were significant only in the a.m. Even so, both a.m. and p.m. nonstress levels in blind–anosmic rats were within the range of corticosterone values routinely observed in this laboratory for intact female rats.

In agreement with the studies of Zimmermann and Critchlow (7), dexamethasone completely suppressed nonstress levels of corticosterone in all groups, and this suppression was compatible with a normal stress response in control and anosmic animals. In contrast, blind and blind–anosmic rats given dexamethasone failed to show a plasma corticosterone response to the 3 min ether stress. However, in the absence of dexamethasone the stress response of blind and blind–anosmic rats appeared intact as evidenced by the finding that neither ether nor immobilization stress increments of blind or blind–anosmic preparations differed from those of controls.

The explanation for the low nonstress corticosterone levels observed in blind–anosmic rats and the failure of blind and blind–anosmic dexamethasone-treated rats to respond to stress is not presently known. Ablation of the optic and olfactory nerves may have influenced directly the hypothalamo–pituitary–adrenal axis. Alternatively, the low nonstress corticosterone levels and the absence of a stress response may reflect changes in the neuroendocrine reflexes regulating ovarian function since recent studies (1–4) have demonstrated marked changes in pituitary–ovarian function following photic and olfactory deprivation. Reduced ovarian weights (3), absence of compensatory hypertrophy (4) and a decrease in the cornification index (3) have been reported for rats subjected to blinding and anosmia. Since there exists considerable evidence to support an interrelationship of estrogen and pituitary–adrenal function, it is possible that the low nonstress levels in blind–anosmic rats and the absence of a stress response in blind and blind–anosmic dexamethasone-treated rats reflect decreased levels of estrogen. Normal cyclic variations in ovarian function are closely correlated with fluctutations in plasma levels of corticosterone (8, 9) and elevations in estrogen levels, whether produced by injection or by ovarian secretion during the estrous cycle, interferes with feedback suppression of ACTH secretion (10). Consistent with the possibility that sensory deprivation may result in a reduction in circulating levels of estrogen are data in this laboratory which indicates that the number of ovarian

Graafian follicles (larger than 352 μ) is greatly reduced in blind–anosmic rats (unpublished observation). Blind rats show numbers intermediate to those of intact control and blind–anosmic rats. Additionally blind–anosmic rats in the present study showed a decrease in the percentage of vaginal smears containing cornified cells. Collectively, these data suggest that photic and olfactory deprivation produced changes in the hypothalamo–pituitary–ovarian axis which secondarily influenced the pituitary–adrenal system via changes in circulating estrogen.

Summary. The effect of photic and/or olfactory deprivation on pituitary–adrenal function was determined in female rats subjected to bilateral optic enucleation and/or olfactory bulb removal. Morning (09:00) and afternoon (16:00) nonstress levels of corticosterone of sensory-deprived rats appeared normal, and in all cases nonstress levels were completely suppressed with dexamethasone (100 μg/kg). Stress mechanisms of blind and/or anosmic rats, in the absence of dexamethasone, were intact. Stress-induced increments in plasma corticosterone of experimentals did not differ from those of intact controls. However, in the presence of dexamethasone, blind and blind-anosmic rats failed to show a plasma corticosterone response to ether stress. These data suggest that pituitary–adrenal function, unlike pituitary–ovarian function, is not markedly affected by photic and/or olfactory deprivation. Absence of the stress response in blind and blind–anosmic dexamethasone-treated rats may reflect changes in ovarian function and not alterations in the pituitary–adrenal axis.

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