Adrenal Relationships to Aggressiveness in Isolated Female Mice

Evidence of leucopenia[1-3], adrenal hyperplasia[3-6], increased plasma corticosterone[3-5] and involution of the thymus[3] have been reported in isolated mice and rats indicating increased adrenocortical activity. Isolation-stress also induced increased aggressiveness in male mice and rats[4-10]. Although many investigators have claimed that isolation-stress does not induce fighting behavior in female mice[4,7,11], others have demonstrated that prolonged periods of isolation will induce aggressiveness in female CFW mice[12-14]. It has been claimed that while an intact pituitary-gonadal axis is essential for the development and maintenance of aggression[4,5,11], the adrenals have been reported to have a modulating effect[4,5]. Investigations of adrenal catecholamine levels has indicated a relationship between increased sympathetic-adrenal activity and aggressive behavior[4,5,15,16]. Since most investigations have employed male mice in aggressive behavior and endocrine studies[4-6,15-19], the present study sought to clarify the adrenocortical and adrenal medullary involvements in isolation-induced aggression of female mice.

Ninety female albino mice (CFW) averaging 21 g were divided into 2 groups (46 isolated mice and 22 units of paired-control mice). All mice were weighed weekly during the 23 week study. To minimize diurnal effects, the various tests were performed between 09.00 h and 12.00 h noon. All animals were tested weekly for aggressive behavior in their home cages for 5 min periods. The target animals were naive, brown pigmented female mice. Open-field activity was determined after 5 and 12 weeks of isolation[2]. Total leucocytes (WBC) were assayed of tail-blood samples after 8 and 14 weeks. Decreases in total WBC counts have been used as a measure of adrenocortical activity[20]. At the end of the 23rd week, all animals were decapitated and heparinized plasma samples were assayed for corticosterone[21]. Adrenal and thymic weights were measured and the adrenals assayed for catecholamine [22].

Analyses indicated significant increases in the body weights of the isolated group compared to the paired-control mice from the 13th to the 23rd week. In accord with previous studies[1,2,12-14], analyses of open-field activity and total WBC counts respectively indicated significant increases in locomotor activity at week 12 and significant decreases in total WBC counts of the isolated mice at week 14. Relative organ weight evaluations and biochemical analyses indicated that the isolated animals had significantly heavier adrenals, displayed significant thymic involution and had significantly higher plasma corticosterone titers than the paired animals. No significant differences were observed in the total adrenal catecholamine levels. To sharply clarify and relate endocrine function (adrenocortical and adrenal-medullary) with aggressive behavior, a stringent selective basis was used to score and evaluate the highly aggressive as well as non-aggressive mice. The data of the intermediate aggressive animals were excluded from the calculations. To eliminate possible physiological effects due to aggression in the paired-nonfighter group, only paired animals were used wherein both cage mates were nonfighters. Reevaluation

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Effects of isolation and aggressiveness on body weights, organ weights and adrenal function

	n	Body wt. ($g \pm$ S.E.)	Thymus (mg/100 g $\pm$ S.E.)	Adrenals (mg/100 g $\pm$ S.E.)	Plasma corticosterone (μg/100 ml $\pm$ S.E.)	Adrenal catecholamine (mcg/100 mg $\pm$ S.E.)
I-F[a]	22	31.0 ± 0.5	116.1 ± 5.8	34.04 ± 1.12	11.41 ± 1.01	136.00 ± 7.34
I-NF	17	29.6 ± 0.6	98.9 ± 5.2	37.11 ± 0.94	15.42 ± 1.11	99.70 ± 7.70
P-NF	14	29.3 ± 0.4	133.0 ± 7.1	32.45 ± 1.22	9.74 ± 0.78	120.91 ± 8.29
Diff. I-F vs I-NF (%)		+4.7	+17.4	− 8.3	−31.5	+36.4
P value		0.08	0.04	0.05	0.01	< 0.01
Diff. I-F vs P-NF (%)		+5.8	−12.7	+ 4.9	+17.1	+12.5
P value		0.02	0.08	0.37	0.26	0.25
Diff. I-NF vs P-NF (%)		+3.8	−25.6	+14.4	+58.3	−17.5
P value		0.12	< 0.001	< 0.01	< 0.001	0.08

[a] I-F, isolated-fighters; I-NF, isolated-nonfighters; P-NF, paired-nonfighters.

of the isolated and control group data (Table) revealed that the isolated-nonfighter mice displayed the greatest increase in adrenal weights and plasma corticosterone levels and the greatest degree of thymic involution. The respective differences were statistically significant when compared to the isolated-fighter and the paired-nonfighter mice. Although the paired-nonfighter animals had smaller adrenal weights, lower plasma corticosterone levels, and larger thymic weights than the isolated-fighters, the differences were not statistically significant. In contrast, evaluation of the adrenal catecholamine levels revealed that in the isolated mice, the fighters had significantly higher catecholamine levels than the isolated-nonfighters. The paired-nonfighter animals had values intermediate between the two groups. Statistical analyses of the higher adrenal catecholamine levels in the paired-nonfighters when compared with the isolated-nonfighter group, although not significant yielded a low P value of 0.08.

In comparing the total isolated vs paired female data, the alterations in behavior, open-field activity, WBC counts and organ weights agree with previous reports of increased excitability, aggressiveness and adrenocortical activity due to isolation[1–3, 12, 13]. While evaluation of the total population of isolated (n = 46) vs paired mice (n = 44) showed no significant differences in the respective adrenal catecholamine levels, analyses of the data based on fighting behavior indicated that the significantly higher levels in adrenal catecholamine concentrations of the isolated-fighter mice were apparently counterbalanced by the isolated-nonfighter group. The intermediate although higher catecholamine values observed in the paired-nonfighter vs isolated-nonfighter groups (P 0.08) would suggest that animal interaction present in paired populations stimulated adrenal medullary activity to a certain degree even though it was not accompanied by aggression. It is of interest that the catecholamine levels of the total population of paired mice (n = 44), which included even aggressive animals, were significantly higher than the concentrations observed in the isolated-nonfighter group (P 0.01). The present findings with female mice consequently agree in general with previous studies involving males which indicated that isolated fighters had higher sympathetic-adrenal activity than isolated-nonfighter mice[4, 5, 15, 16]. In contrast, measures of adrenocortical activity (adrenal weights, thymic involution, and plasma corticosterone) indicated that isolated nonfighters had significantly higher pituitary-adrenal activity than either the isolated-fighters or the paired-nonfighters and suggested that heightened adrenocortical activity was not directly related to agression. Recent reports have indicated that increased aggressiveness due to isolation was associated with low ACTH titers and reduced aggressiveness with high plasma ACTH[23–25]. The present investigation indicates that isolation induced aggression in female mice was directly related to increased sympathetic-adrenal activity. Conversely, no direct relationship was noted between adrenocortical activity and aggressiveness.

Résumé. Lorsque des souris femelles soumises à l'isolement sont groupées selon leur tempérament belliqueux et non-belliqueux, on observe une augmentation de l'activité médullossurrénalienne chez les animaux isolés belliqueux. Au contraire, les souris isolées non-belliqueuses ont montré des taux de catécholamines inférieurs et une secrétion cortico-surrénale nettement augmentée.

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Effect of Oestradiol on Ovarian Progesterone and 20α Hydroxypregn-4-en-3-one Secretion During Pseudogestation in the Rat

Having demonstrated that the ovarian secretion of progesterone in the pseudopregnant rat follows a nychthemeral rhythm[1], we proceeded to examine and analyse the effects induced by different doses of oestradiol during the various phases of this circadian secretory cycle, in an attempt to elucidate the role of oestrogens in the overall regulation of luteal function under different endocrine conditions.

Materials and methods. Adult female rats (Ivanovas, Kisslegg, Germany) weighing 200–250 g, that had been kept under standard laboratory conditions in respect of temperature, humidity and lighting (light from 06.00 until 20.00 h daily), were mated with vasectomized males on the evening of pro-oestrus. The onset of pseudogestation was confirmed by the presence of a vaginal plug on the following morning (subsequently verified by vaginal smears). The rats were then divided into groups of 10 (5 in each cage) and treated daily from the 1st until the 6th day of pseudogestation with various doses of 17β-oestradiol, dissolved in sesame oil and administered s.c. Controls received the solvent only. Where appropriate, 20α-hydroxypregn-4-en-3-one (20α-OH-P) levels were measured by a fluorimetric method.

On the 7th day, between 08.00 and 12.00 or 15.00 and 17.00 h, a cannula was inserted in the renal vein near the left ovarian vein according to the method described by FAJER and BARRACLOUGH[2]. Blood samples (0.5 ml collected in 3–5 min) taken from each animal were subjected to chromatography, and the progesterone content of the eluate was measured by a slightly modified version of the protein-binding assay of NEILL et al.[3].

Results. The Figure shows the variations in progesterone secretion in relation to the doses of oestradiol on the 7th day of pseudogestation in intact rats. The administration of oestradiol in doses of 0.01, 0.03 or 0.1 μg/kg daily for the first six days of pseudogestation resulted in a statistically significant decrease in the progesterone content of the ovarian venous blood cannulated on the 7th day, between 08.00 and 12.00 h (Figure), i.e.

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