# MORPHOLOGY AND PATHOMORPHOLOGY

# Directional Left-Sided Asymmetry of Adrenals in Experimentally Domesticated Animals

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Directional left-sided asymmetry of the adrenals was typical of black and silver foxes, American minks, and gray rats selected by their behavior. In domesticated, but to a greater extent, in aggressive animals, the weight of the left adrenal and the width of its medulla and cortex markedly surpassed the corresponding parameters of the right adrenal. In aggressive animals enlargement of the left adrenal cortex was associated with widening of the zona reticularis, while in domesticated animals with enlargement of the zona fasciculata.

**Key Words:** *asymmetry; adrenals; morphology; selection; behavior*

Asymmetry is the main principle of structural and functional organization of biological systems [2]. Asymmetry is typical of individuals, while symmetry is a statistical characteristic of fluctuating asymmetry in a population, when phenotypic expression of the parameter prevails at different sides of the body in various individuals. Asymmetry results from incomplete identity of microenvironmental conditions for the development of the left and right sides of the body [3]. However, several morphofunctional systems are characterized by directional contralateral differences. Much attention was given to asymmetry of cerebral hemispheres associated with various roles of structures in the left and right hemispheres in the regulation of physiological and behavioral characteristics [7,8]. Directional morphofunctional asymmetry is also typical of the peripheral compartment in the pituitary-adrenal system (adrenal cortex) [1,10,11]. The problem of asymmetry attracts our attention. We reproduce this process in experiments with black and silver foxes (*Vulpes vulpes*), American minks (*Mustela vison Schreb.*), and gray rats (*Rattus norvegicus*) to study the mechanisms underlying animals transformation during domestication. For many years we perform selection of these animals for domestication, as well as for the enhancement of aggressive and fear reactions to humans [13]. It should be emphasized that during selection for domestication expression of some morphological criteria (*e. g.*, monogenically determined mottles and individual craniological parameters) increases on the same side of the body in most individuals [12]. Therefore, fluctuating asymmetry of these parameters observed in behaviorally unselected populations is transformed into directional asymmetry under conditions of experimental domestication.

The question arises: whether directional asymmetry of these morphological parameters is a manifestation of common morphofunctional directional asymmetry that results from changes in neurohormonal regulation of the development during selection for domestication [13]? This selection is accompanied by the decrease in functional activity of the hypothalamic-pituitary-adrenal system (HPAS) at various levels [9] and morphological changes in the adrenal cortex [4,6]. On the other hand, activity of HPAS increases during selection for enhanced feral reactions [9]. It should be emphasized that attenuation of reactivity to stress in domesticated animals and enhancement of

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this reaction in animals selected for wildness are the main criteria for changes in HPAS activity. At the same time, relationships between stress reactivity and directional left-sided asymmetry of the adrenal cortex were reported [1,10,11]. The left adrenal is primarily involved in the reaction to stress. Probably, a greater weight of the left adrenal (compared to the right adrenal) plays an adaptive role [10].

The existence and type of adrenal asymmetry should be evaluated in behaviorally selected animals. Here we studied asymmetry in various morphofunctional parameters of the adrenals, including the weight and width of the cortex and its zones.

## MATERIALS AND METHODS

Experiments were performed on male and female black and silver foxes, American minks, and gray rats selected by behavioral parameters over several tens generations. Fur animals are bred at the Experimental Animal Farm (Institute of Cytology and Genetics). Gray rats are bred at the vivarium of the Institute of Cytology and Genetics. The control group of animals unselected for domestication or aggressiveness included only foxes. Changes in the directionality and level of asymmetry during postnatal ontogeny were determined in experiments on foxes. Over the first week of life the adrenals were taken from pups that could not be reared by mothers. The adrenals were also taken from culled adult 7-8-month-old foxes not involved in reproduction and selected from breeding animals, adult 5-6-month-old non-breeding minks, and 6-month-old rats that produced the offspring. Purified, but not fixed adrenal glands were weighted on a torsion balance with an accuracy of 0.5 mg. The type of asymmetry was estimated by the mean difference (Δ) between the weights of the right and left adrenals. The value significantly differing from zero indicated the existence of directional asymmetry. Fluctuating asymmetry corresponded to the mean difference that was close to zero [3]. The degree of asymmetry (coefficient of asymmetry) was calculated by the formula:

$$\frac{R\text{-}L}{R+L} \times 2,$$

where $R$ and $L$ are values of the parameter for the right and left sides, respectively.

Morphological characteristics of the adrenals were compared in female rats. The adrenals were fixed in Carnoy fluid. Paraffin slices (5-6 μ) were stained with hematoxylin and eosin. The width of the adrenal cortex and its zones was measured using an ocular micrometer (×150). Experiments were performed with 5 domesticated and 5 aggressive animals. For each animal we performed not less than 5 measurements in slices that corresponded to the maximum diameter of the adrenals. Thus, the mean width of the adrenal cortex and its zones in domesticated and aggressive animals was calculated by 25 measurements.

The differences between contralateral parameters were analyzed by Student's $t$ test.

## RESULTS

In fox pups the weight of the left adrenal surpassed that of the right adrenal over the first week of life (Table 1). These differences were observed in male and female animals of 3 populations. In control and, particularly, in aggressive animals these differences between the weights of contralateral adrenals tended to be more pronounced than in domesticated foxes. In aggressive animals the difference varied from 9 to 27% of the mean weight of the adrenal (0.18±0.09). In control and aggressive females left-sided asymmetry in the weight of the adrenals observed in the first days of life was preserved during maturity. In other foxes these differences became insignificant. HPAS in foxes [9] and other animals [5] continues to develop over the first months of postnatal ontogeny. It should be emphasized that domesticated and aggressive foxes are characterized by different ontogenetic dynamics of these processes (*e.g.*, dynamics of reaching the concentration of peripheral blood corticosteroids observed in adult animals). Moreover, this level in domesticated animals is much lower than in aggressive foxes in various periods of life. Probably, the development of any system is accompanied by changes in the type and degree of morphofunctional asymmetry in constituent structures. It cannot be ex-

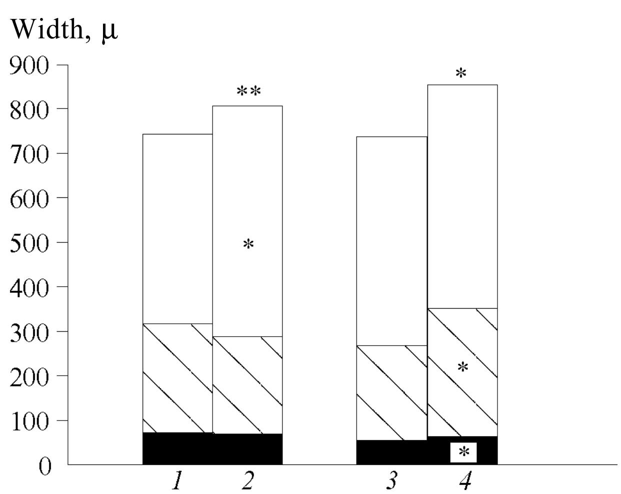


**Fig. 1.** Total width of the adrenal cortex and its zones in female domesticated (*1*, *2*) and aggressive rats (*3*, *4*). Light portion: zona fasciculata. Shaded portion: zona reticularis. Dark portion: medulla. Right (*1*, *3*) and left adrenals (*2*, *4*). *$p$<0.001 and **$p$<0.05 compared to the right adrenal.

**TABLE 1.** Asymmetry in Weight of Adrenals ($M\pm m$)

| Animals | Domesticated | | Control | | Aggressive | |
|---|---|---|---|---|---|---|
| | females | males | females | males | females | males |
| Foxes | | | | | | |
| 1-7 days | | | | | | |
| Δ, mg | -0.89±0.27** (78) | -0.76±0.23* (93) | -1.34±0.43** (42) | -0.90±0.36** (56) | -1.54±0.69*** (11) | -0.87±0.36*** (14) |
| CA | -0.07±0.02 | -0.07±0.02 | -0.09±0.04 | -0.07±0.03 | -0.18±0.09 | -0.08±0.03 |
| 7-8 months | | | | | | |
| Δ, mg | -5.22±3.02 (59) | -0.57±3.59 (81) | -12.69±4.56** (48) | -6.79±4.33 (73) | -19.96±4.99* (56) | -2.37±4.46 (76) |
| CA | -0.02±0.01 | -0.001±0.02 | -0.05±0.02 | -0.03±0.02 | -0.09±0.02 | -0.01±0.02 |
| Minks, 5-6 months | | | | | | |
| Δ, mg | -4.06±1.60*** (15) | -18.67±3.22* (15) | — | — | -5.83±1.61** (12) | -10.00±2.30* (22) |
| CA | -0.11±0.05 | -0.19±0.03 | — | — | -0.16±0.04 | -0.11±0.02 |
| Gray rats, 6 months | | | | | | |
| Δ, mg | -0.96±0.51*** (41) | -2.20±0.33* (27) | — | — | -1.03±0.52*** (44) | -1.59±0.35* (42) |
| CA | -0.01±0.03 | -0.12±0.02 | — | — | -0.02±0.023 | -0.09±0.02 |

**Note.** *$p<0.001$, **$p<0.01$, and ***$p<0.05$: differences between contralateral adrenals. The number of animals is shown in brackets. CA: coefficient of asymmetry.

cluded that various types and rates of HPAS development, as well as different hormonal status during this period, produce various effects on the type and degree of asymmetry in adult animals.

After attaining maturity pronounced left-sided asymmetry in the weight of the adrenals was observed only in control and aggressive female foxes. In adult minks the weight of the left adrenal was much higher than that of the right adrenal independently on the age and behavioral characteristics of animals. These differences in males were more pronounced than in females. The differences between aggressive males and females tended to be significant ($p$~0.1). Significant differences were observed between domesticated males and females ($p$=0.001). These differences were also typical of gray rats. In domesticated and aggressive males contralateral differences were more pronounced than in female rats. In gray rats directional left-sided asymmetry in the weight of the adrenals was also observed at the morphological level. In animals selected for domestication and wildness the width of the left adrenal medulla markedly surpassed that of the right adrenal medulla (domesticated animals: Δ=99.00±24.08 μ, $p<0.001$; aggressive animals: Δ=100.00±20.77 μ, $p<0.001$). Moreover, these differences were revealed in the adrenal cortex (Fig. 1). Although domesticated and aggressive rats were characterized by the same directionality of asymmetry in the weight of whole adrenals and widths of the medulla and cortex, the type of asymmetry for individual zones of the cortex was different. In domesticated rats the width of the zona fasciculata (source of glucocorticoids) in the left adrenal was much higher than in the right adrenal. Moreover, in aggressive females the width of the zona reticularis (source of sex steroids) in the left adrenal markedly surpassed that in the right adrenal. The mechanisms of these differences remain unclear. The existence of contralateral differences is of considerable interest.

Our results show that all studied animals are characterized by directional asymmetry in the weight of the adrenals. Selection by behavioral characteristics modulates this asymmetry, which depends on the age, sex, and species of animals.

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