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Ovariectomy-induced changes in the adrenal cortex of spontaneously hypertensive rats

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Summary. Many lines of evidence indicate that adrenocortical steroid hormones are involved in the development and maintenance of hypertension in spontaneously hypertensive rats (SHR). Twenty-eight days after ovariectomy a notable decrease in the sistolic blood pressure (BP) was found in SHR, along with a marked atrophy of their adrenal cortices. The hypothesis is advanced that the ovariectomy-induced lowering in BP in SHR may be, at least partly, mediated by the suppression of the adrenal secretory activity, due to the lack of circulating estrogens, which are well known to stimulate hypophyseal ACTH release.

Key words: Hypertensive rat, Ovariectomy, Adrenal cortex, Morphometry

Introduction

Compelling evidence has been accumulated indicating that in spontaneously hypertensive rats (SHR) the endocrine system plays a major role in the genetic expression of their spontaneously developing hypertension: hypophysectomy, adrenalectomy, thyroidectomy or gonadectomy, if performed prior to the development of hypertension, are able to prevent or notably retard the increase in blood pressure (Aoki, 1963; Aoki et al., 1963; Okamoto and Aoki, 1963; Iams and Wexler, 1977, 1979). Since sex hormones are well known to modulate the function of the hypothalamo-pituitary-adrenal axis (for review, see Kitay, 1968; Nussdorfer, 1986), it is conceivable that the effect of gonadectomy on the development and maintenance of hypertension in SHR may be mediated by adrenal cortex. The aim of the present study was to investigate the effect of ovariectomy on the adrenal cortex of SHR.

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Materials and methods

Adult female rats of SHR strain were obtained from the Department of Physiology, Academy of Medicine, Gdansk, Poland, due to the courtesy of Prof. Jozwa. They were maintained under standard conditions of lighting (14 h on: 10 h off) and temperature (22 ± 2°C), with free access to laboratory pellets and tap water. SHR were ovariectomized by dorsal approach, under ether anaesthesia. Other animals were sham-operated, and served as a control.

Systolic blood pressure (BP) was measured by tail-pletysmography (Physiograph 4; E&M. Instrument Co., Houston, Tx), just before the operation (initial) and sacrifice (final) (Molteni et al., 1969).

SHR were decapitated 28 days after surgery, and their adrenals, kidneys and heart were promptly removed and weighed. Adrenal glands were fixed in Bouin's solution, embedded in paraffin and serially cut at 5-6 μm. Sections were stained with hematoxylin-eosin, and employed for morphometric analysis.

Using a magnification of about x 100 and a square lattice test system of type A, the volume fractions of the individual adrenocortical zones (zona glomerulosa, ZG; zona fasciculata, ZF; zona reticularis, ZR) and of the zona medullaris and capsule were estimated by differential point counting (Weibel, 1979). The analysis was performed on every fifth serial section. The volume fractions of nuclei and cytoplasm of parenchymal cells and stroma, as well as the number of nuclear profiles of adrenocortical cells per unit area were estimated on a screen at X 3,000, using the multipurpose test system M42 (Weibel, 1979). The following parameters were evaluated: volume of adrenocortical zones, volume of adrenocortical cells, and number of adrenocortical cells in each zone. The detailed description of the morphometric methods employed and of subsequent calculations was given earlier (Malendowicz, 1987).

The data obtained from each animal were averaged per experimental group, and the standard error (SE) was calculated. The statistical comparison of the

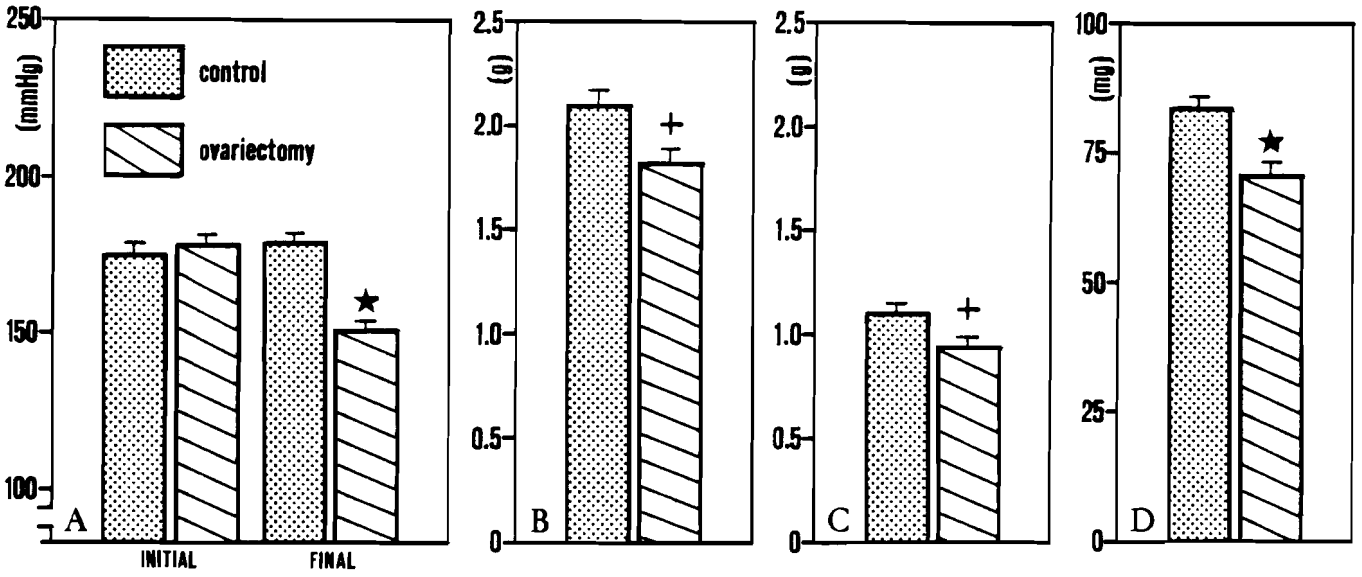

Fig. 1. Effect of ovariectomy on BP (A), kidney weight (B), heart weight (C) and adrenal weight (D) in SHR. Data are mean ± SE (n = 6). +, $P < 0.05$, and *, $P < 0.01$.

results was performed by Student's t-test.

Results

Ovariectomy caused a significant lowering in BP in SHR (-13%), as well as a net decrease in the kidney (-12%), heart (-10%) and adrenal weights (-14) (Fig. 1).

The ovariectomy-induced atrophy of the adrenal gland was coupled with marked decreases in the volumes of ZF and ZR (-13% and -18%), and in the average volume of the parenchymal cells in all zones (ZG, -25%; ZF, -33%; ZR, -25%). Ovariectomy did not change the number of ZF and ZR cells, while it notably increased that of ZG cells (43%) (Fig. 2).

Discussion

Several studies have suggested the involvement of the hypothalamo-pituitary-adrenal axis in the development of the hypertension in SHR (Aoki, 1963; Aoki et al., 1963; Okamoto and Aoki, 1963; Maruyama, 1969; Tabei et al., 1972; Tsuchiyama et al., 1972; Nickerson, 1976; Bartsch et al., 1978). SHR possess higher levels of circulating corticosterone and aldosterone (Iams and Wexler, 1979; Iams et al., 1979; Mantero et al., 1983), but ACTH blood and pituitary concentrations do not differ between normal and hypertensive rats (Häusler et al., 1984; Ardekani et al., 1989). Thus, the hypothesis has been advanced that adrenal glands of SHR are hyper-responsive to ACTH (Ardekani et al., 1989).

The present study clearly demonstrates that ovariectomy notably decreases BP in SHR, and this drop is accompanied by conspicuous changes in the structure of the adrenal cortex. Gonadal hormones exert either hypertensive or hypotensive effects in rats by regulating, among other, the vascular tone (Altura, 1972). This may be one of the mechanisms whereby estrogens modify BP in SHR. However, estrogens also exert a potent effect on the hypothalamo-pituitary-adrenal axis (for review, see Kitay, 1968): they are able to enhance ACTH release and corticosterone secretion, and to stimulate adrenal growth (Maléndowicz et al., 1986; Lesniewska et al., 1990). In the present study, removal of the ovaries results in a significant decrease in the weight of adrenals in SHR, an effect depending on the lowering of the volumes of ZF and ZR and on the decrease in the average volume of all adrenocortical cells. These changes indicate a depressed stimulation of the adrenal gland by ACTH and a lowered secretory activity of the glands (for review, see Nussdorfer, 1986).

In light of these findings it seems conceivable to suggest that the mechanism underlying the ovariectomy-induced decrease in BP in SHR may, at least partly, involve the inhibition of the adrenocortical secretory activity.

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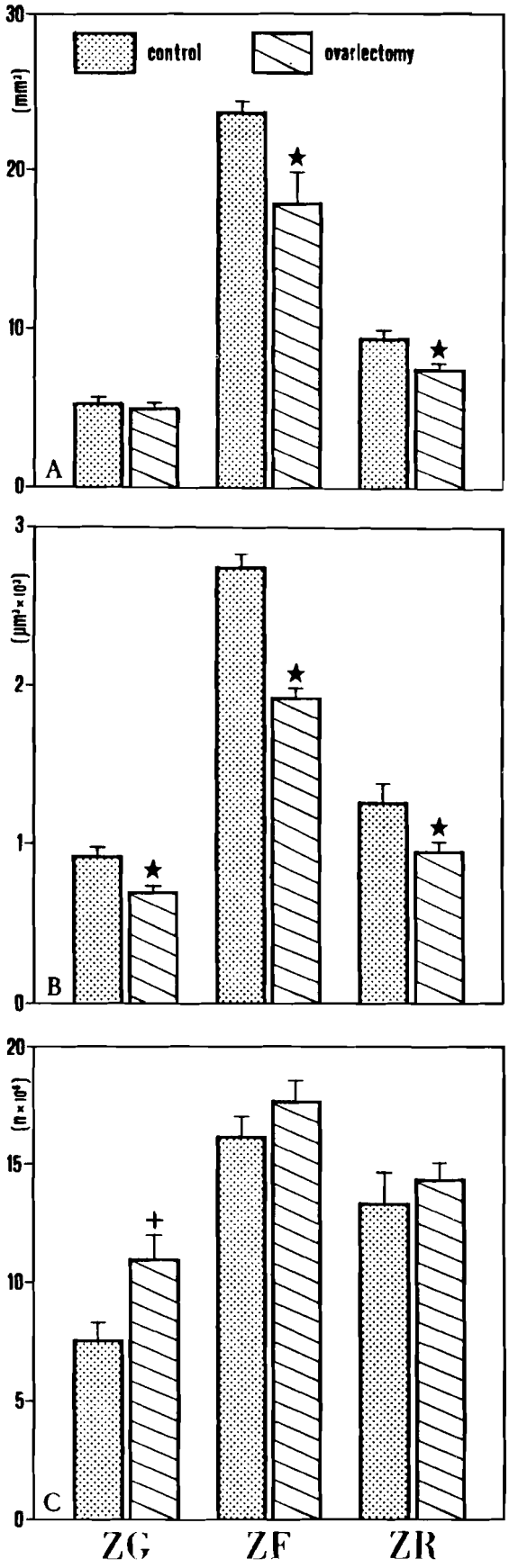

Fig. 2. Effect of ovariectomy on the volume of adrenocortical zones (A), the average volume of adrenocortical cells (B) and the number of adrenocortical cells per zone (C) in SHR. Data are mean ± SE (n = 6). +, $P < 0.05$, and *, $P < 0.01$.

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