

Effect of Deoxycorticosterone Acetate Administration to Pregnant Rats on the Brain of Their Offspring

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Effects of deoxycorticosterone acetate injected to rats on gestation days 18 and 20 on morphometric indexes of the brain and RNA concentration in neurons of neocortical layer V in 1-day-old offspring were studied. The brain in 1-day-old prenatally treated rats was more developed than in the offspring of intact and control females.

Key Words: brain; development; deoxycorticosterone; pregnancy

Steroid hormones produce considerable effects on the brain development [2,4,5,10-13]. It was shown that adrenalectomy accelerated brain growth in rats, and that this effect can be blocked with corticosterone [14]. At the same time, blood concentration of various corticosteroids in women varies during pregnancy. The content of glucocorticoids varies insignificantly, while the concentration of the main mineralocorticoid aldosterone changes by more than 10 times [2,14]. It should be emphasized that these variations in corticosteroid concentration are characterized by individual and region-specific differences even under normal conditions [1, 14]. The question arises of how the levels of these hormones affect brain development in the offspring. Our previous studies revealed a significant positive correlation between zona glomerulosa activity in the adrenal cortex in pregnant rats and the weight of the brain in their 21-day-old fetuses [6]. Taking into account that this zone is the source of mineralocorticoids, here we studied the effects of deoxycorticosterone acetate (DOCA), an agent with mineralocorticoid activity, on some indexes of prenatal brain development. Previous studies showed that DOCA injected to pregnant rats stimulates the development of macroglial cells in the neocortex of newborn animals [7].

MATERIALS AND METHODS

The offspring ($n=55$) of 7 rats weighing 230-280 g and intramuscularly injected with 0.05 ml 0.5% DOCA on days 18 and 20 of pregnancy was examined. The offspring of intact females ($n=18$) and 3 rats treated with an equivalent volume of peach oil on days 18 and 20 of pregnancy ($n=24$) served as the control. The rats were kept in a vivarium with food and water *ad libitum*. The offspring aging 1 day was decapitated, and the body weight and weight of the brain were measured. Slices (7 μ) of the anterioparietal lobe stained with gallocyanine were examined, the widths of the cortex and molecular layer and the mean number of neurons in layers II and V per standard field of view were determined by using a MOV-15 ocular micrometer. The concentration of RNA in the cytoplasm of layer V neurons was estimated cytospectrophotometrically on a Lyumam-12 microscope at 550 nm. For morpho- and cytophotometric analysis, the samples were taken from 4 animals of each litter (DOCA-treated rats, $n=28$; intact control rats, $n=8$; and peach oil-treated control rats, $n=12$). The results were analyzed using Statistica 5 software.

RESULTS

The offspring of DOCA-treated rats had a greater body weight than the animals prenatally treated with peach

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TABLE 1. Effects of DOCA Administration to Pregnant Rats on the Brain of 1-Day-Old Offspring ($M \pm m$)

Parameter	Control		DOCA
	intact	peach oil	
Body weight, g	4808 \pm 101 (4200-5750)	4279 \pm 72 (3800-4950)	4999 \pm 75* (3300-6300)
Brain weight, mg	206.0 \pm 2.5 (180-223)	193.0 \pm 15.6 (165-226)	233 \pm 3** (180-280)
mg/g body weight	43.00 \pm 0.58 (43-58)	45.00 \pm 0.55 (40.2-54.7)	47.0 \pm 0.5** (40.5-59.9)
Width, μ cortex	488.0 \pm 12.5 (440-561)	493.0 \pm 15.6 (429-586)	559.0 \pm 9.4** (455-697)
molecular layer	48.0 \pm 3.5 (35-66)	51 \pm 2 (41-59)	63.0 \pm 1.5** (53-81)
Neurons per microscopic field			
layer II	45.0 \pm 0.4 (44-47)	45.0 \pm 1.2 (39-51)	46.0 \pm 0.7 (39-52)
layer V	31.0 \pm 0.7 (28-34)	28.0 \pm 0.9 (22-31)	23.0 \pm 0.3** (21-27)
RNA concentration in the cytoplasm of layer V neurons	0.1090 \pm 0.0067 (0.086-0.143)	0.0880 \pm 0.0059 (0.051-0.114)	0.1230 \pm 0.0057* (0.077-0.187)

Note. Significant differences: *compared to control rats treated with peach oil; **compared to intact control rats. Extreme values are shown in parentheses.

oil, but did not differ in this parameter from the offspring of intact control rats. The absolute and relative weights of the brain and the widths of the cortex and molecular layer in the offspring of DOCA-treated rats were greater than in control animals of both groups, while the neuron density in the cortical layer V of the anterior parietal lobe in treated rats was lower than in the control. RNA concentration in the cytoplasm of layer V neurons in DOCA-treated rats was higher than in the control (Table 1).

These data indicate that injection of DOCA to rats during late gestation accelerates brain growth, development of the neocortex, and differentiation of neurons. This effect is probably related to anabolic properties of mineralocorticoids or direct effects of DOCA on cells of the developing brain carrying receptors for these hormones [5,11]. It can be also suggested that the influence of DOCA on the brain of rat offspring is mediated by its effects on steroidogenesis in maternal adrenal glands and on the formation and functioning of the adrenal glands in fetuses [2]. These findings agree with our previous data [6] and reports on better development of macroglial cells in 1-day-old rats prenatally treated with DOCA [7].

The data reported here indicate the possibility of stimulating embryonal organogenesis of the brain. Our findings extend the notion of the regulation of brain development, while previous studies mainly concern factors impairing (decelerating) this process. Furthermore, these results are of considerable importance in

view of great variability of aldosterone secretion during normal pregnancy and decreased production of the hormone under conditions of preeclampsia [3,8,14].

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