Developmental programming: Imact of prenatal exposure to dexamethasone on gonadotropic cells in female rat offspring

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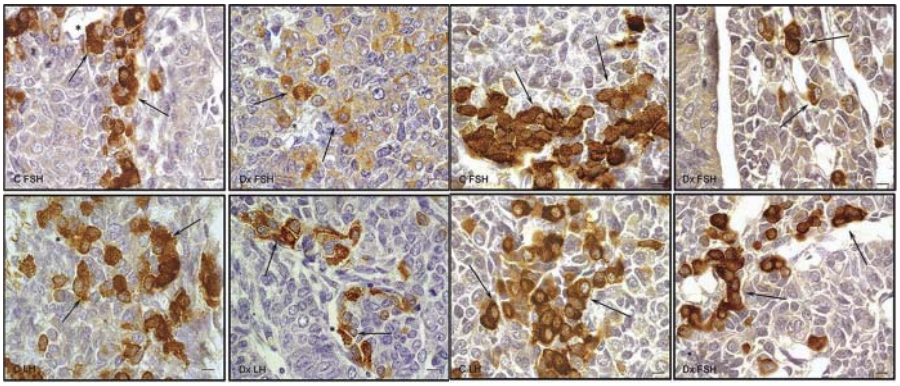
Introduction The concept of developmental programming implies a linkage between adverse environmental signals during prenatal development and low birth weight as a marker, along with a greater incidence of pathophysiological conditions in postnatal life [1]. Overexposure to glucocorticoids during critical times in fetal development leads to major phenotypic outcomes associated with low birth weight, such as cardiovascular, metabolic and neuroendocrine disorders [2], [3]. The synthetic glucocorticoid dexamethasone (Dx) is often used in obstetrical practice to treat a wide variety of inflammatory conditions or when the risk of preterm delivery exists. Glucocorticoids are also used in numerous experimental protocols to induce developmental programming [2], [4], [5], [6]. Reproductive system is recognized as an important target for developmental programming. Fetal period is critical for pituitary development. Exposure to a compound that affects pituitary cell proliferation and differentiation, such Dx, may alter developmetal trajectory of pituitary gland. The aim of this study was to investigate the effects of prenatal exposure to Dx on gonadotropic cells during the fetal, neonatal, infantile and peripubertal period.

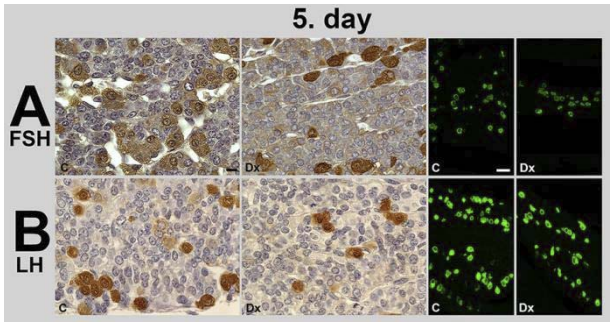
Details of experiment The gravid females were randomized into a control and an experimental group, each consisting of 10 animals. On day 16, 17 and 18 of pregnancy, experimental dams received 0.5 mg Dx s.c. /kg body weight. The control gravid females received the same volume of saline. Female offspring from control and experimental dams were sacrificed under ether narcosis on fetal day 19 and 21 and postnatally, on day 5 (neonatal period), day 16 (infantile period) and day 38 (peripubertal period). Randomization obviated any potential litter bias. The pituitary glands were excised and fixed in Bouin's solution for 48 h. After embedding in Histowax, each tissue block was serially sectioned at 3-μm thickness on a rotary microtome. Blood was collected from individual pups and sera were stored at –70 ° C until folliclestimulating hormone (FSH) and luteinizing hormone (LH) determination. Immunohistochemical, immunofluorescence (IFC), histological and stereological analysis were used in the study of gonadotrophic cells.

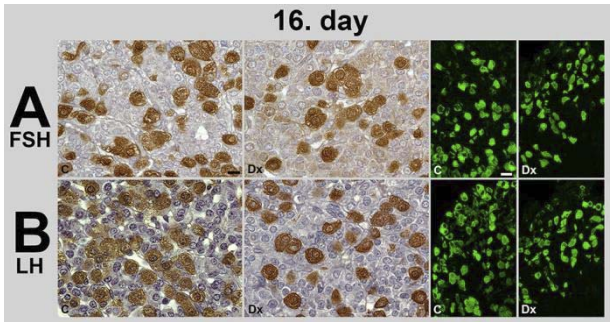
Results In 19-day old fetuses the pituitary gland already had definite histological organization. FSH and LH cells were strongly immunohistochemically stained and widespread throughout the pars distalis in small groups or as single cells. Histological characteristics of gonadotropic cells are preserved from fetal to peripubertal period of life. They were polygonal, oval or polyhedral in shape, with large, prominent often eccentrically located nuclei and a thin layer of surrounding cytoplasm. FSH and LH cells were in close contact with blood vessels. With maturation, from fetal to peripubertal period the number of gonadotrophic cells in the pituitary gland increased. Exposure to Dx during critical period in pituitary development decreased the number of gonadotrophic cells in fetuses. Since the number of gonadotrophic cells is mostly set during fetal life, reduction in number was longlasting and persists throughout neonatal, infant and peripubertal period (Fig. 1). Stereological analysis confirmed our histological observation (Fig. 2). Reduced serum concentrations of FSH and LH are likely due to the reduced number of gonadotrophic cells, as the

lack of a change in intensity of FSH and LH IFC signals suggests that the remaining gonadotropic cells were functional.



19. fetal day 21. fetal day





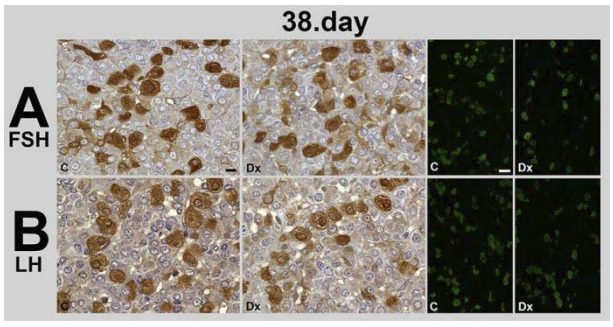


Figure 1. Gonadotropic cells in control and Dx exposed female offspring

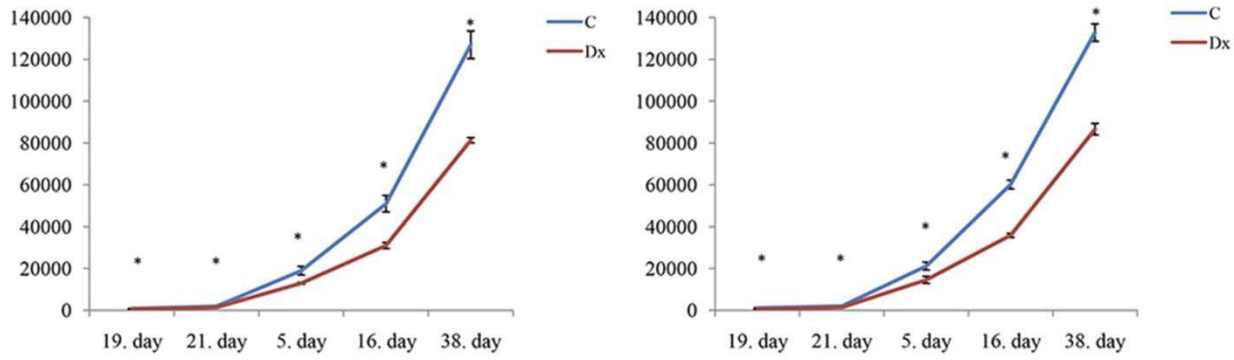


Figure 2.Total numbers of FSH and LH cells per pituitary gland in19- and 21-day old control and Dx exposed female fetuses and 5-16- and 38-day-old control and female offspring prenatally exposed to Dx. Results are given as means ± SD (n = 6)

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