
PHYSIOLOGY

Transgeneration Effects of Antenatal Acute Hypoxia during Early Organogenesis

T. Yu. Dunaeva, L. K. Trofimova, A. V. Graf,
M. V. Maslova, A. S. Maklakova,
Ya. V. Krushinskaya, and N. A. Sokolova

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We studied the effect of acute hypobaric hypoxia in early organogenesis on physiological and behavioral parameters of second-generation albino rats. Antenatal acute hypoxia was followed by physical and sexual retardation, increase in the mortality rate, and behavioral changes in second-generation animals (hypoactivity of males and females on day 22 of life and hyperactivity of males on day 57 of life). Second-generation animals exhibited no gender differences in body weight and horizontal and vertical locomotor activity.

Key Words: *antenatal acute hypobaric hypoxia; transgeneration effect; gender differences*

Antenatal hypoxia, the most common and severe complication of pregnancy, can be caused by various factors, including maternal smoking, viral infections, and gestoses. Antenatal hypoxia can result in spontaneous abortion, premature labor, and physical or mental disorders in children [3].

Little is known about the effect of acute hypoxia during the first trimester of pregnancy, which corresponds to the formation of systems and organs. Acute hypoxia during the early organogenesis (days 9-10 of pregnancy) has a complex effect on the offspring of rats: premature birth, impaired learning capacity, histological changes in brain structures, abnormal content of biogenic amines, and increased corticosteroid concentration in the blood. Female offspring is characterized by imbalance in biogenic amines and behavioral disorders, which

serve as the sign of masculinization [1]. Antenatal hypoxia affects not only the first, but also the second generation of mammals (*i.e.*, transgeneration effects are observed) [4,5]. Here we studied the effect of acute hypoxia during early organogenesis on the development of second-generation animals.

MATERIALS AND METHODS

Experiments were performed on male and female albino rat pups (46 females and 47 males) from 10 adult females. Two adult females were housed with one male. The onset of pregnancy was estimated from the presence of spermatozoa in vaginal smears. The day of detection of spermatozoa in vaginal smears was considered as day 1 of pregnancy.

The treatment group consisted of female rats exposed to acute hypobaric hypoxia (AHH) and 2 generations of offspring. The control group consisted of female rats not exposed to AHH and 2 generations of offspring.

Department of Human and Animal Physiology, Biological Faculty, M. V. Lomonosov Moscow State University, Russia. **Address for correspondence:** connie-phys@mail.ru. T. Yu. Dunaeva

TABLE 1. Effect of AHH during Early Organogenesis on Morphogenetic Parameters of Second-Generation Animals in the Early Postnatal Period

Period of postnatal development, days		Control group (n=38)	Treatment group (n=59)
Rat pups with separated auricles, %	4	35.1	9.3*
	5	100	85.2*
Rat pups with hair growth, %	12	30.8	45.2
	13	100	85.7*
Rat pups with open eyes, %	17	69.4	42.2*
	18	100	95.6

Note. Combined data on males and females. Here and in Table 2: * $p < 0.05$ compared to the control (Fisher's exact test).

AHH was modeled in an altitude chamber at 145 mm Hg (ascent to 11,500 m above sea level over 1 min) on days 9-10 of pregnancy. The lifespan of rats was recorded under these conditions (latency between the end of "elevation" and respiratory arrest or first agonal inspiration). If the lifespan did not exceed 5 min, the females were assigned to a group of specimens with low resistance to AHH.

On days 65-80 of life, the first-generation female offspring of low resistant rats were housed with intact males. Male and female offspring of the second generation were examined on days 2-57 of postnatal development. The following morphometric parameters were studied: separation of the auricles, hair growth, eye opening, and Kettle index (weight/height ratio, kg/m²). Behavioral characteristics of animals in the hole-board test were recorded on days 22 and 57 of postnatal development. Horizontal and vertical locomotor activity was studied over 4 min.

The results were analyzed by nonparametric tests (Mann—Whitney test and Fisher's exact test) using Excel and Statistica 6.0 software.

RESULTS

During early postnatal development (up to the 21st day of life), no gender differences were observed in both control and experimental groups. Hence, the data obtained in this period were combined. The results obtained on days 22 and 57 were analyzed separately for females and males in each group.

Second-generation animals of the experimental group demonstrated delayed separation of the auricles, hair growth, and eye opening (Table 1), which reflects physical retardation during the early postnatal ontogeny [2]. Opening of the vagina in females also occurred in the later period (Table 2), which reflects retardation of sexual development. Starting from day 22 of life, Kettle index in experimental females did not differ from the control, but

in experimental males it was significantly lower than in intact rats (up to day 57 of life, Fig. 1).

Mortality rate to day 57 of life was also higher in the experimental group.

Behavioral studies in the hole-board test showed that horizontal (Fig. 2, *a*) and vertical locomotor activities (Fig. 2, *b*) decrease by day 22 of life in both experimental males and females. However, in males vertical activity increased on day 57 of life (Fig. 2, *b*), while behavioral characteristics of females did not differ from the control at this term (Fig. 2).

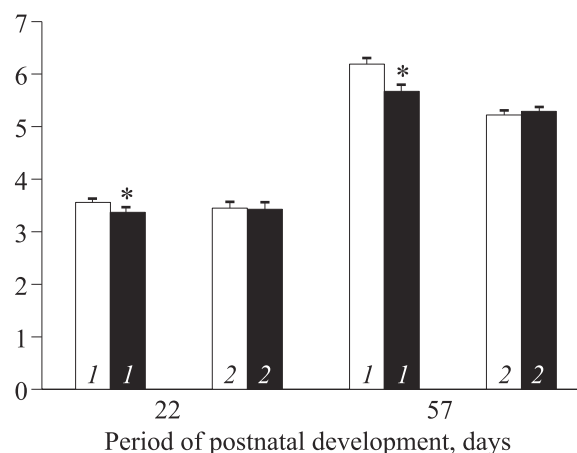


Fig. 1. Effect of AHH during early organogenesis on the Kettle index in second-generation rats. Here and in Fig. 2: males (1) and females (2). Light bars, control group; dark bars, treatment group. * $p < 0.05$ compared to the control.

TABLE 2. Effect of AHH during Early Organogenesis on the Kettle Index in Second-Generation Rats

Group	Period of postnatal development, days	
	40	45
Control group (n=15)	33.3%	93.3%
Treatment group (n=21)	4.8%	76.2%

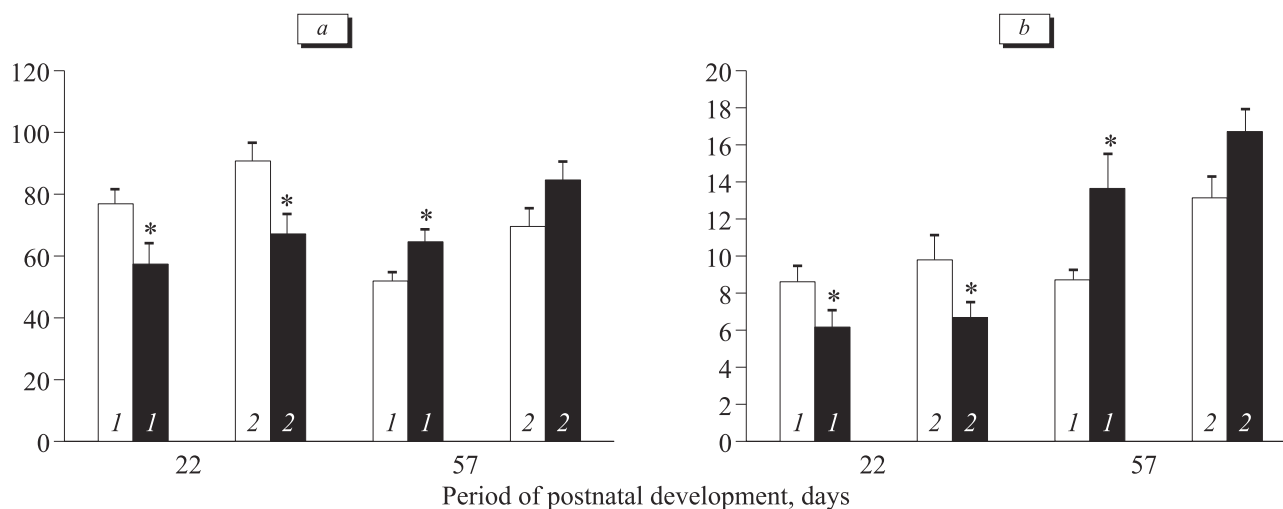


Fig. 2. Effect of AHH during early organogenesis on behavioral characteristics of second-generation rats in the hole-board test. Horizontal locomotor activity (a) and vertical locomotor activity (b).

Gender differences in body weight and horizontal and vertical locomotor activities between control males and females were revealed on day 57 of life, whereas no differences were found between males and females in the experimental group.

Our results indicate that AHH during early organogenesis has a modulatory effect on the development and behavioral characteristics of the first-generation and second-generation rats.

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