EXPERIMENTAL BIOLOGY

Differences in Modification of Stress Mechanisms in Rat Pups Exposed to Continuous and Intermittent Maternal Deprivation

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During antenatal short-term intermittent maternal deprivation the content of epinephrine increased by 123% in the cortex and by 135% in the hypothalamus of 15-day-old rat pups, which is higher than during physiological development, while dopamine content, instead of increasing, decreased by 24% in the cortex and by 35% in the hypothalamus on day 15 of life. Shifts in norepinephrine and dopamine concentrations in the cortex were less pronounced in rat pups exposed to permanent maternal deprivation compared to intermittent deprivation, while the shifts in the hypothalamus were even more pronounced. Presumably, discoordination of the dopaminergic and sympathoadrenal systems in the course of development of the nervous system underlies behavioral disorders in rat pups under conditions of maternal deprivation.

Key Words: *maternal deprivation; behavioral reactions; catecholamines*

Maternal deprivation is a strong factor modifying the adolescent neuroendocrine system. Repeated 15-min (intermittent) maternal deprivation during the first 3 weeks of the postnatal period reduces the hypothalamo-cortico-adrenal response to dosed stress induced by low doses of adrenocorticotropic hormone or corticosterone [5], modifies the anatomy of nerves and synapses, cerebral function and metabolism [4]. Maternal deprivation leads to disorders in the adaptation potential of nervous activity and behavioral strategy and can manifest in inadequate behavior and reduced intellectual potential during maturing [6]. Shifts in the monoaminergic and opioid systems correlate with disorders in the adaptation potentialities of the nervous system [2]. A feedback between the glucocorticoid content and the types of psychoemotional reaction to stress and the capacity of glucocorticoids to inhibit NOS (NO synthase) by decreasing the reducing capacity of NADPH diaphorase in the neurons and neutrophils were demonstrated [6]. Here we compared the relationship between maternal deprivation and development of the sympathoadrenal and dopaminergic regulation of the brain in newborn rats.

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MATERIALS AND METHODS

The study was carried out on 128 newborn randombred albino rats of both sexes (the progeny of 26 females) in accordance with the European Communities Council Directive (24.11.86, 86/609/EEC) on handling of animals with laboratory purposes. Experiment protocol was confirmed by the local ethical committee. All pups were divided into 2 groups: control and experimental. The animals were kept in a vivarium and received full-value rations. Forty-two rat pups (21

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female and 21 male) were exposed to repeated maternal deprivation (separated from mothers in special cells) 3 times for 1 h daily starting from day 2 after birth, then for 6 h on days 6, 7, and 8, and for 12 h on days 12, 13, 14, 15, and 16. Twenty-eight rat pups (14 female and 14 male) were exposed to continuous maternal deprivation (separated from mothers on day 14 of life and transferred to formula feeding). Behavioral reactions and biochemical parameters in the hypothalamus and blood were studied on days 21 and 60 of the postnatal period.

On day 15 of postnatal development (age group 1) or on days 22-25 (age group 2) the open field test was carried out: the animal was placed in the center of the cage and its activity was visually evaluated for 2 min: vertical motor activity (VMA; number of rearing postures), horizontal motor activity (HMA; number of crossed squares), number of explored holes (complete plunging of the head into the hole), and grooming (muzzle touching by the forepaws while washing). It is usually considered that HMA reflects the motor component of the motor activity, VMA and plunging into holes reflect mainly the exploratory component, and grooming is an indicator of emotional strain of the animal during testing; modified Val'dman's coefficient, reflecting motor to exploratory activity ratio (HMA/VMA+holes) was estimated [1]. The content of biogenic amines (dopamine and norepinephrine) was measured in the cortex and hypothalamus by the standard methods using calibration curves plotted by the spectrofluorimetrical method. Fluorescence was measured at λ=485 nm and λ_{stim}=375 nm for norepinephrine and at λ=375 and λ_{stim}=325 nm for dopamine, respectively. The results were processed using STAT Soft software, the differences were considered significant at $p<0.05$.

RESULTS

In control rat pups norepinephrine content in the cortex and hypothalamus increased by 35 and 62% on day 15 and by 28 and 33% more on day 21. On day 60 norepinephrine content remained the same as on day 21 (Table 1).

Dopamine content on day 15 increased by 31% in the cortex and decreased by 27% in the hypothalamus, after which it virtually did not change until day 60 of postnatal development.

Antenatal short-term intermittent maternal deprivation notably modulated the balance of biogenic amine in the CNS of the newborn rats. On day 15 norepinephrine content increased by 123% in the cortex and by 135% in the hypothalamus, which was greater than during normal development (Table 1). On day 21 the contents of these amines remained at the same level and on day 60 dropped both in the cortex and hypothalamus.

By contrast, dopamine content in control rats on day 15 decreased (but not increased) by 24% in the cortex and by 35% in the hypothalamus. The content of dopamine was not restored by day 60 of life.

In animals exposed to permanent maternal deprivation the shifts in norepinephrine and dopamine content in the cortex were less pronounced than in those exposed to intermittent deprivation, contrary to the hypothalamus, where these shifts were more pronounced (Table 1).

TABLE 1. Norepinephrine and Dopamine Contents in Brain Compartments of Newborn Rats under Conditions of Maternal Deprivation ($M \pm m$)

Group		Norepinephrine, μg/g wet tissue		Dopamine, μg/g wet tissue	
		cortex	hypothalamus	cortex	hypothalamus
Day 1	control	0.085±0.005	0.12±0.02	0.19±0.01	0.44±0.04
Day 15	control	0.13±0.03	0.23±0.02	0.25±0.02	0.37±0.03
	intermittent maternal deprivation	0.20±0.02*	0.28±0.02*	0.28±0.02*	0.29±0.02*
Day 21	control	0.19±0.02	0.34±0.02	0.30±0.02	0.39±0.02
	maternal deprivation				
	intermittent	0.24±0.02*	0.28±0.03*	0.28±0.03	0.28±0.02*
	permanent	0.195±0.008*+	0.23±0.02*+	0.23±0.02*+	0.25±0.02*
Day 60	control	0.23±0.03	0.32±0.03	0.32±0.03	0.40±0.03
	maternal deprivation				
	intermittent	0.28±0.02*	0.30±0.02	0.30±0.02	0.30±0.02*+
	permanent	0.26±0.03	0.21±0.03*+	0.21±0.03*+	0.26±0.03*

Note. $p<0.05$ *compared to respective control, +compared to intermittent maternal deprivation.

The increase of norepinephrine content, usually associated with increased anxiety, excitability, and decrease in dopamine content, attests to essential changes in the development of the cerebral biogenic amine system during the early postnatal period under conditions of maternal deprivation; these shifts were more pronounced in case of intermittent deprivation. These shifts were paralleled by disorders in the behavioral regulation manifesting in increased VMA, particularly on day 60 of life in animals exposed to intermittent maternal deprivation and as early as on day 21 in those exposed to permanent deprivation. Changes in HMA were less pronounced.

The effects of maternal deprivation on the behavioral reactions in animals of all ages manifested in alteration of the initial trend in the dynamics of Val'dman coefficient: in controls it increased on day 15 and tended to decrease on day 21, while in animals exposed to intermittent deprivation it decreased during both periods and in those exposed to permanent deprivation the coefficient decreased on day 21. Moreover, maternal deprivation modulated the level of emotional strain in newborn rats: by day 15 the level of emotional strain appreciably increased, while HMA decreased in rat pups exposed to permanent deprivation.

Thus, behavioral disorders in the progeny under conditions of maternal deprivation are caused by discordination of the dopaminergic and sympathoadrenal systems during the development of the nervous system in newborns.

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