Interaction of Central and Peripheral Noradrenergic Structures in Rat Ontogeny

V. N. Yarygin, L. V. Bibaeva, and I. E. Malinina

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Morphology and morphometrical parameters of perikaryons and transcription activity of nuclear chromatin in neurons of cranial cervical sympathetic ganglion and in locus ceruleus are studied at different stages of ontogeny under conditions of desympathization and after selective damage to the locus ceruleus neurons induced by intracysternal injection of 6-hydroxydopamine. It is shown that the magnitude and direction of changes in neuronal ultrastructure and activity of protein-synthesizing apparatus varies during ontogeny and depends on the integral state of catecholaminergic neurons.

Key Words: *ontogeny; locus ceruleus; cranial cervical sympathetic ganglion*

Morphological, physiological and biochemical parameters of noradrenergic neurons in the brain and sympathetic ganglia are very similar [9]. Monosynaptic connections between neurons of cranial cervical sympathetic ganglion (CCSG) and locus ceruleus (LC) have not been identified [5,6], however, central and peripheral noradrenergic populations interact with each other facilitating adaptation of the organism to environmental factors. The existence of multisynaptic links between these structures also cannot be excluded. The aim of the present study was to confirm the existence of functional links and to study the effect of different experimental interventions on their appearance during ontogeny.

MATERIALS AND METHODS

Experiments were carried out on 47 female Wistar rats of different ages: juvenile (1-month-old), young (3-4-month-old), early reproductive (6-month-old), mature reproductive (12-month-old), and senescent (24-month-old) [1].

Desympathization was achieved through daily subcutaneous injections of guanethidine (15 mg/kg) from postnatal days 0 through 25. This procedure eliminated 70-80% adrenergic neurons in CCSG [4]. Selective chemical destruction of LC neurons was induced by intracysternal injection of 6-hydroxydopamine [2,10].

Light and electron microscopy and morphometry were performed; activity of endogenous RNA-polymerases in fixed cells was measured [8].

RESULTS

In normal rats, differentiation and formation of definitive phenotype of neurons is completed by the end of the first month after birth. At this time, rat CCSG and LC contain 27-25 and 1.7-1.5 thousand neurons, respectively [3,7]. The number of cells remains practically unchanged until senescence (24 month or elder), when, according to our previous findings, the number of neurons decreased by 20% both in LC and CCSG.

Guanethidine desympathization had no effect on the number of noradrenergic neurons in LC in all age groups. This fact confirmed the concept that guanethidine does not penetrate the blood-brain barrier. In CCSG, the applied scheme of treatment results in elimination of 70-80% noradrenergic neurons.

Intracysternal injections of 6-hydroxydopamine had no effect on the number of ganglionic neurons,

Russian State Medical University, Moscow

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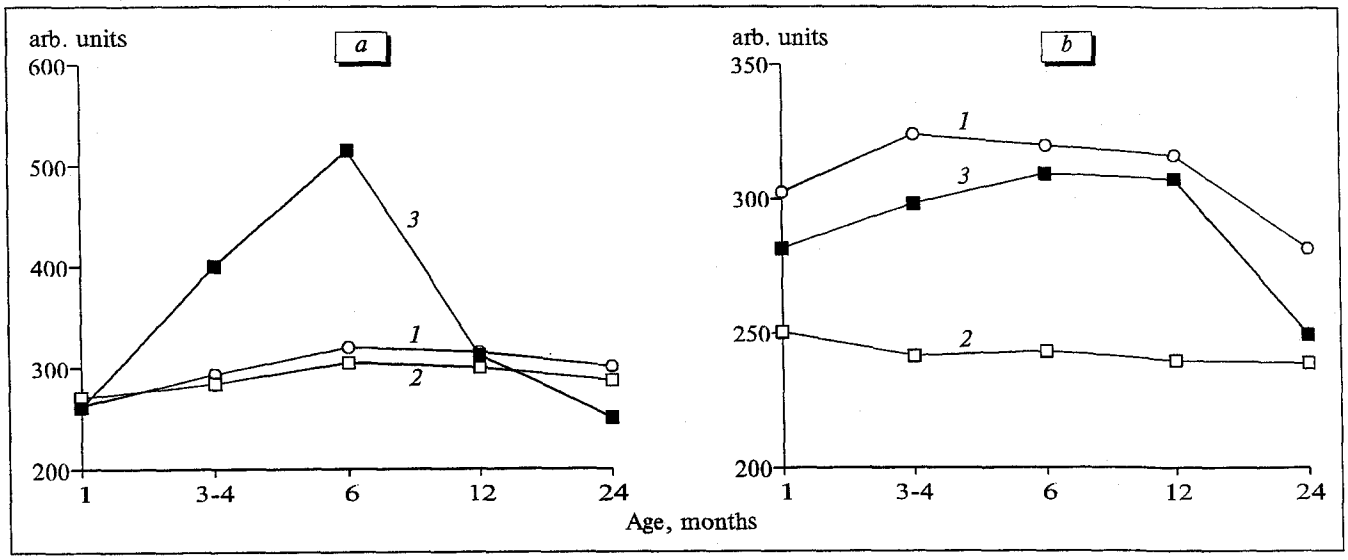

Fig. 1. Size of perikaryons of neurons in the cranial cervical sympathetic ganglion (*a*) and locus ceruleus (*b*) in rats of different experimental group. *1*) control; *2*) injection of 6-hydroxydopamine; *3*) desympathization.

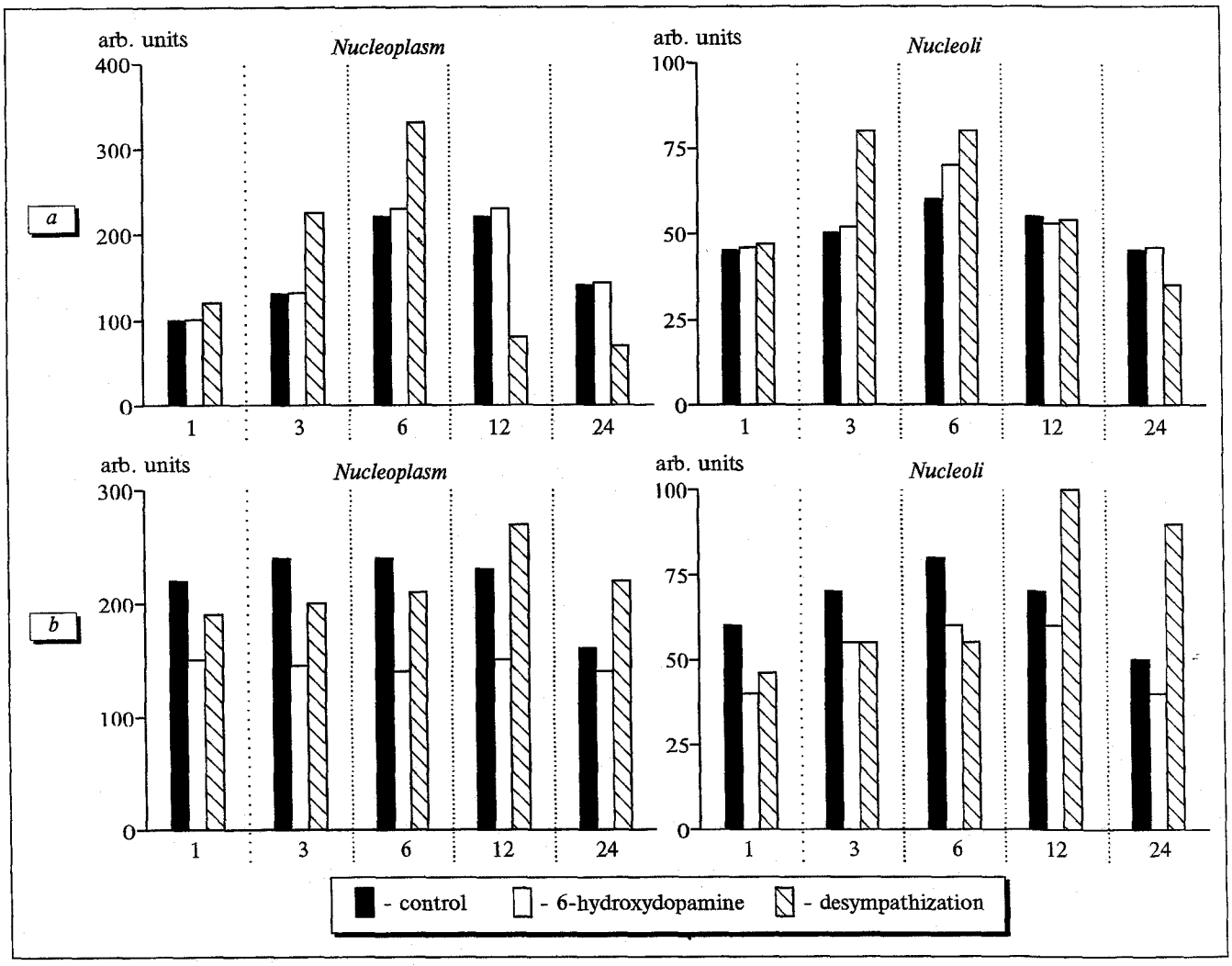

Fig. 2. Labeling of nucleoplasm and nucleoli of neurons in the cranial cervical sympathetic ganglion (*a*) and locus ceruleus (*b*) in rats of different experimental group.

but eliminate 20% neurons of LC 2-5 days after a single injection and 80% after a 2-month treatment.

In normal rats, the mean size of perikaryons in CCSG increased significantly from the 1st to 6th months after birth, and then slightly decreased to month 24, which is probably due to a reduced ratio of large neurons in senescent animals. It seems possible that aging is accompanied by elimination of this particular cell subpopulation. In LC, the age-related changes in the mean size of perikaryons were insignificant: only a tendency toward an increase in this parameter from month 1 to 6 and its decrease to month 24 was noted.

Under conditions of desympathization, in 1-month-old rats the mean size of perikaryons in CCSG remained unchanged, in 3-4 and 6-month-old rats this parameter rose, and in 12-month-old animals it decreased, whereas in LC the mean size of perikaryons in 1- and 3-4-month-old did not differ significantly. In desympathized 24-month-old rats, the mean size of perikaryons was significantly decreased in comparison with the control group.

In all age groups, 6-hydroxydopamine reduced the size of perikaryons in LC but had no effect on neurons in CCSG (Fig. 1).

In CCSG neurons, changes in transcription activity of nuclear chromatin induced by desympathization were different in different age groups. For instance, in 1-month-old desympathized rats, the nucleoplasm chromatin activity was slightly but statistically significantly increased in comparison with the control, whereas no differences were noted in the index of labeled nucleoli. A more pronounced compensatory reaction to the reduction in the number of functionally active neurons was observed in 3-, 4-, and 6-month-old rats: index of labeling was significantly increased in nucleoplasm and nucleoli. Of special interest is the fact that in 12- and 24-month-old desympathized rats nucleoplasm labeling was reduced, while nucleolar transcription declined to the control level (Fig. 2, *a*).

In LC of 1-month-old rats, desympathization and injection of 6-hydroxydopamine significantly inhibited transcription activity of nuclear chromatin. This effect was also observed in mature 3-4- and 6-month-old animals. In 12- and 24-month-old desympathized rats, nuclear transcription activity considerably surpassed the control level. By contrast, injection of 6-hydroxydopamine reduced transcription activity (Fig. 2, *b*).

Thus, CCSG and LC responded to desympathization by opposite changes. Elevated chromatin transcription activity of CCSG neurons at certain ontogenetic stages (1, 3-4, and 6 months) was attended by reduced transcription activity of LC neurons, whereas later stages (12 and 24 months) were characterized by opposite shifts. This can be attributed to mutual compensation of LC and CCSG functions, the nucleoplasmin chromatin sites being more labile. These sites more rapidly and more markedly respond to changes in ontogeny than nucleolar sites.

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