MORPHOLOGY AND PATHOMORPHOLOGY

Effect of Embryonal Nervous Tissue Transplantation on Morphofunctional Characteristics of *Locus Coeruleus* Neurons

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Transplantation of the nervous tissue into rat brain induces changes in the morphology, functional characteristics, and chromatin transcription activity in the *locus coeruleus* neurons, and in dynamic activity of recipients.

Key Words: *locus coeruleus; transplantation; neuron; transcription*

The mechanisms of damage-induced compensatory and repair processes in the central nervous system are a very important problem of modern biology and medicine. Under these conditions transplantation of embryonal nervous tissue is a method of choice [4-7,11]. Up to now, extensive experimental and some clinical experience on transplantation of the embryonal nervous tissue has been accumulated; however, much is unknown. In particular, it seems interesting to study the effect of nervous tissue transplantation on the parameters of the central nervous system.

The aim of the present study was to investigate the effect of transplantation of embryonal *locus coeruleus* (LC) formation on morphofunctional parameters of LC neurons and motor activity of recipients.

MATERIALS AND METHODS

Female Wistar rats weighing 180-200 g (n=30) were used as recipients; 18-day-old Wistar rat embryos served as donors. The rats were kept under standard vivarium conditions. Embryonal LC was transplanted into the third brain ventricle using the standard method [10]; cranial trepanation was performed in coordinates AP = 1.6, L = 0, H = 8 from the bregma [9]. Neurons of sham-operated animals served as the control; the development of the transplant was analyzed in comparison with an ontogenetically isochronous control.

Motor activity of experimental and control animals was assessed in the open field test 1 day before and 1 and 6 month after the operation [3,12]. Because of considerable individual differences in the motor activity of rats of the control and experimental groups, the animals with high and low motor activity (HMA and LMA, respectively) were arranged into two separate groups. Control and experimental animals were decapitated, and histological examination of brain sections was performed. The mean areas of perikaryons in the transplanted neurons was assessed morphometrically; chromatin transcription activity was evaluated by radioautography [8]. The data were processed statistically using the Wilcoxon test [2].

RESULTS

All rats but one survived and retain usual behavior. Histological examination revealed take of the graft in 75% of rats, in other cases the graft was not found. The graft was adjacent to the ventricle walls, filled 1/5-2/5 of the ventricle lumen, and was live.

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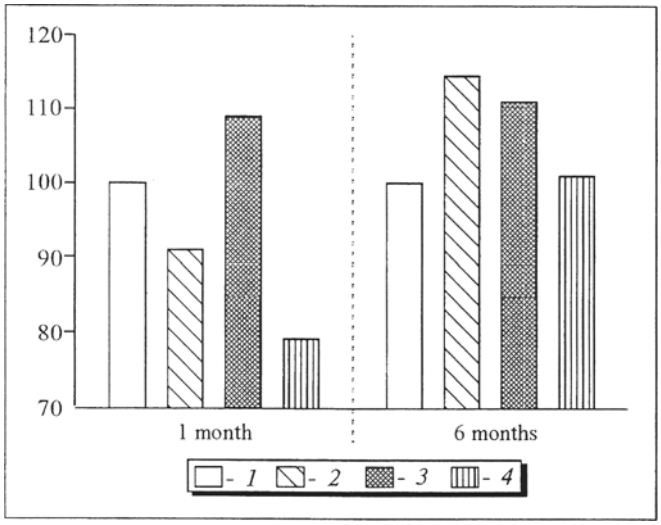

Fig. 1. Mean extranucleolar labeling in *locus coeruleus* neurocyte nuclei under conditions of transplantation. Here and in Fig. 2: *1*) control, sham-operated; *2*) control, ontogenetically isochronous; *3*) experiment, original *locus coeruleus*; *4*) experiment, graft. Ordinate: labeling (% of sham-operated control).

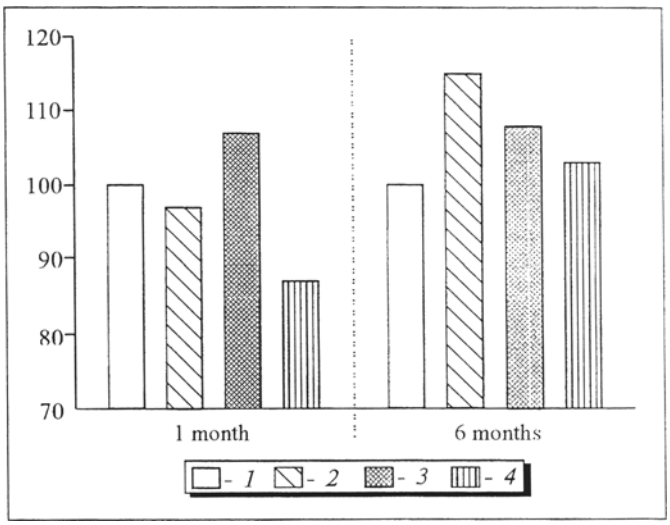

Fig. 2. Mean nucleolar labeling in *locus coeruleus* under conditions of transplantation.

One and six months postoperation the transplanted nerve tissue was characterized by the presence of morphological structures typical for normal LC. Morphological analysis revealed no considerable differences in the mean perikaryon area between transplanted and ontogenetically isochronous control neurons. The mean perikaryon area of the original LC neurons in recipient rats did not differ from that in controls.

Similar changes in the mean transcription activity of nucleoplasmic chromatin in original LC neurons were observed in the control (sham-operated) and experimental animals of both HMA and LMA groups: this parameter was increased by 9-11% throughout the experiment (1 and 6 months postoperation) (Fig. 1). A slight (7-8%) but significant increase in nucleolar transcription in neurons was also noted (Fig. 2). The dynamics of transcription of nuclear and nucleolar chromatin in transplanted neurons considerably differed from the correspondent parameters of original neurons: transcription activity of both nuclear and nucleolar chromatin in transplanted neurons one month postoperation was reduced by 30 and 20%, respectively, and by 5-10% six months postoperation (Figs. 1 and 2). Comparison of these parameters of transplanted neurons and LC neurons of ontogenetically isochronous control revealed a 12-18% decrease in the transcription activity of nucleolar and extranucleolar chromatin at all stages of the experiment (Figs. 1 and 2).

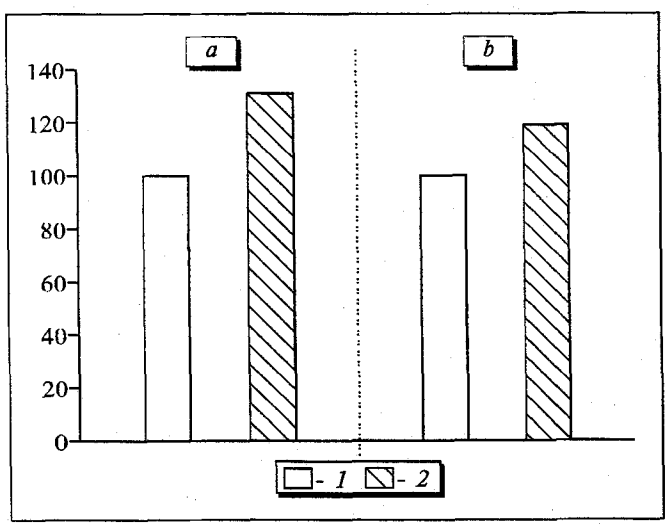

Fig. 3. Motor activity of rats under conditions of transplantation. Rats with low (*a*) and high (*b*) motor activity. *1*) sham-operated control; *2*) experiment. Ordinate: motor activity (% of sham-operated control).

Motor activity was enhanced in operated rats of both HMA and LMA groups at all stages of the experiment (Fig. 3). However, in HMA group this change was less pronounced than in LMA group (19 *vs.* 31%).

Thus, we have found that motor activity of the embryonal tissue recipients is changed; the transcription activity of nuclear chromatin in LC neurons and, consequently, their functional activity is increased; the graft is functionally active.

The so-called locomotor area of the midbrain practically correspond to LC location [1]. It can be assumed that changes in the motor activity of recipient rats are based on activation of both original and transplanted LC neurons accompanied by abundant release of norepinephrine in various structures, including the spinal cord segment. The elevated motor activity in animals, to whom LC neurons were trans-

planted, can be attributed to the presence of a functionally active transplant.

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