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Stem cells migration to the brain through cranial nerves endings

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Abstract

In the series of experiments Wistar rats(n=14) after intranasal implantation 35 thousand mesenchymal stem cells in 50 µl of buffer and modeling damage in sensorimotor there are no differences between ipsilateral and contralateral administration. In the series of experiments Wistar rats(n=18) after implantation in Meckel cavity of 35 thousand mesenchymal stem cells in 50 µl of buffer and modeling damage in cerebellar cortex it was shown that ipsilateral administration more efficient than contralateral administration.

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Introduction

Taking into account the ability of stem cells to migrate to damaged area (1, 2) as well as the presence of perineural tracing along central projections of cranial nerves (3) can define a *hypothesis* of stem cells targeted migration after introduction into receptive fields of olfactory and trigeminal nerves to different brain areas of anterior and posterior cranial fossae.

Material and Methods

Mesenchymal stem cells (MSC) were isolated from adipose tissue of female rats and cultivated for 9 days for cell mass gain. The cells were stained with PKH67 Green Fluorescent Cell Linker at the operation day. The final concentration of cells was 700 thousand cells per 1 ml. Five groups of animals were formed: unilateral injury of sensorimotor zone with intranasal administration of MSC (n=8); bilateral injury in sensorimotor zone with intranasal administration of MSC (n=6); unilateral cerebellar injury with ipsilateral administration of MSC into Meckel cavity (n=6); unilateral cerebellar injury and contralateral administration of MSC into Meckel cavity (n=6); bilateral cerebellar injury and unilateral administration of MSC into Meckel cavity (n=6). Brain tissue aspiration was performed in sensorimotor zone (2.5 mm lateral from midline, 2.5 caudal to Bregma and 2.5 mm from brain surface) or at the level of cerebellar cortex (2.0 mm lateral from midline, 1.5 caudal to Lambda and 2.5 mm from brain surface). 50 µl of cell suspension was injected under nasal mucosa of rats or into Meckel cavity in 10 min after local destruction of brain regions. Longitudinal sections of brain were made using cryostat in 10 days after the operation and studied using fluorescent microscope.

Results and Discussion

It was found that intranasally administered MSC migrated generally to anterior cranial fossa. MSC from Meckel cavity – to posterior cranial fossa. There are no differences between the number of cells in damaged sensorimotor areas of left and right cerebral hemispheres after intranasally injection (**Fig.1**).

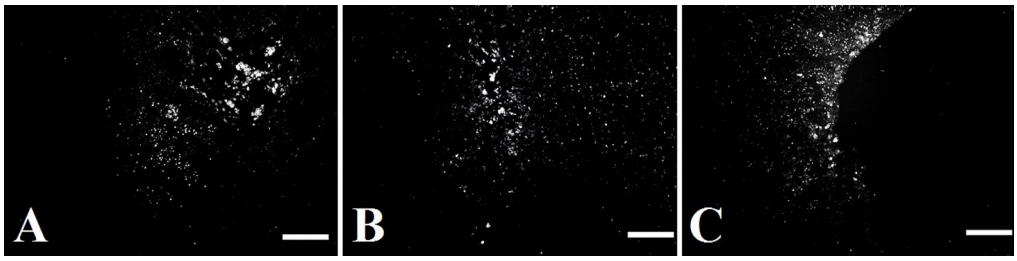

Figure 1. Fluorescent cells in 10 days after unilateral destruction of sensorimotor zone in right hemisphere (A), and after bilateral destruction of sensorimotor zone in left (B) and right (C) hemispheres. Scale bar 200 μm.

It was found that injection of MSC into Meckel cavity accompanied by priority of ipsilateral migration. Bilateral injury also showed the same priority of ipsilateral tracing compared to contralateral one (**Fig.2**).

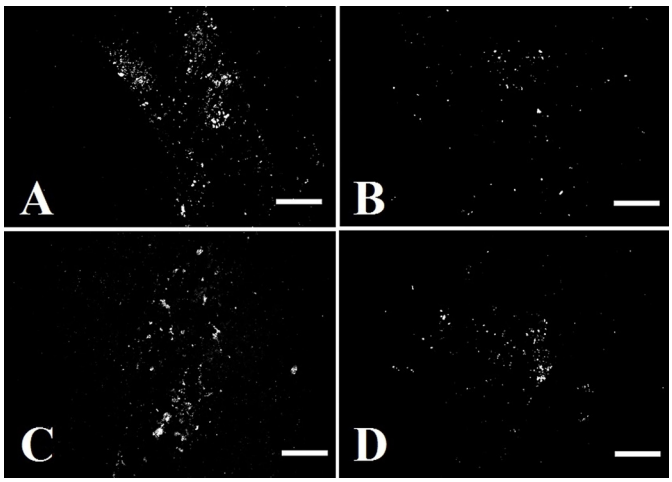

Figure 2. Fluorescent cells in 10 days after unilateral destruction of cerebellar cortex region and ipsilateral administration of MSC into Meckel cavity (A), after unilateral destruction of cerebellar cortex region and contralateral administration of MSC into Meckel cavity (B), after bilateral destruction of cerebellar cortex region in right (C) and left (D) hemispheres. Scale bar 200 μm.

Conclusions

The hypothesis of using of stem cells natural migration from receptive fields of olfactory and trigeminal nerves to anterior or posterior cranial fossae was proven. Intranasally administered stem cells were spread out mainly in anterior cranial fossa, while the cells implanted into Meckel cavity – in the tissues of posterior one.

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