BRAIN AND SPINAL CORD AFFECTED BY AMYOTROPHIC LATERAL SCLEROSIS

INDUCE DIFFERENT GROWTH FACTORS EXPRESSION PATTERNS IN NEURAL AND MESENCHYMAL RAT STEM CELLS

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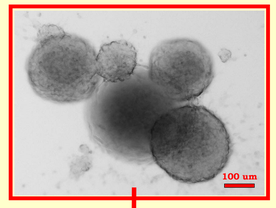
Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease characterized by selective loss of motor neurons and death caused by paralyses.

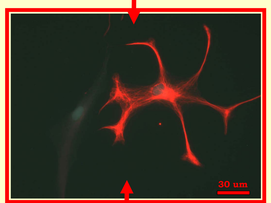
A modern therapeutic concept includes transplantation of stem cells with the aim to slow down progression of disease (Mitrecic et al, Anat Record 2009; Mitrecic et al, Cell Transp 2010).

Here we report that neural and mesenchymal stem cells stimulated by ALS-affected tissue response by specific increase or decrase in production of various growth factors.

Neural stem cells are obtained from the embryonic cortex (C) and ventral mesencephalon (M) of the 14 days old wt rat embryos.

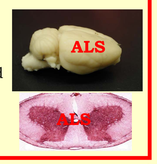


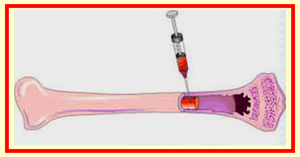
A neurosphere represent transitional globular heterogeneous accumulation containing multiplying neural stem cells.

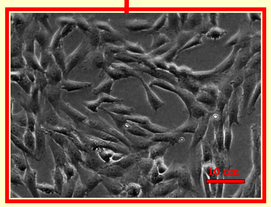


An example of appearance of MAP2 neural marker during differentiation of neural or mesenchymal stem cells.

The main aim of this work was to test the influence of protein extracts obtained from ALS-affected brain and spinal cord on WT neural and mesenchymal stem cells.

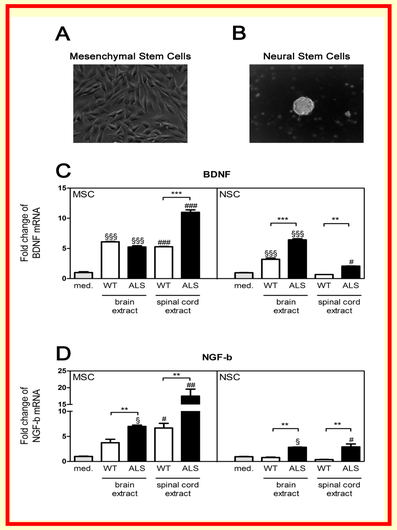




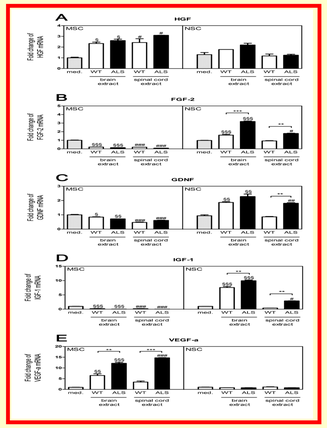


Mesenchymal stem cells obtained from rat bone marrow.

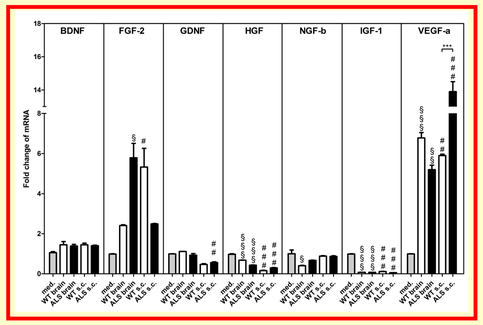
Stimulation of neural (NSC) and mesenchymal stem cells (MSC) with protein extracts from ALS - affected brain and spinal cord.



Nerve growth factor (NGF) and **brain-derived neurotrophic factor** (BDNF) were upregulated in both NSC and MSC cultures with ALS specific pattern.



Stimulation of fibroblasts with protein extracts from ALS - affected brain and spinal cord.



Fibroblast growth factor 2 (FGF2), **insulin-like growth factor** (IGF1) and **glial-derived neurotrophic factor** (GDNF) were upregulated in NSCs in an ALS-dependent manner, while the same factors were ALS-independently downregulated in MSCs.

Vascular endothelial factor (VEGF) upregulation was restricted to MSCs and fibroblasts.

Surprisingly, ALS spinal cord, but not the brain extract, upregulated BDNF in MSC and GDNF in NSC cultures.

Conclusions: a) inherent characteristics of different (stem) cell populations define their healing potential.

b) different response of stem cells obtained by their stimulation with either brain or spinal cord affected by ALS suggests differences in pathological process during the onset and progression of ALS in these two regions of the central nervous system.

Further reading:

*Mitrečić, D; Nicaise, C; Gajovic, S; Pochet, R. Distribution, differentiation and survival of intravenously administered neural stem cells in a rat model of amyotrophic lateral sclerosis. Cell Transplantation, 2010. in press.

*Nicaise, C; Mitrečić, D; Demetter, P; De Decker, B; Authelet, M; Boom, A; Pochet, R. Impaired blood-brain and blood-spinal cord barriers in mutant SOD1-linked ALS rat, Brain Research 2009; 1301:152-62.

*Mitrečić, D; Pochet, R; Gajović, S. Toward the treatments with neural stem cells: experiences from ALS. Anat Record. 2009; 292(12):1962-7.