Stem cells for CNS repair: alternatives to the unlikely mechanism of cell replacement.

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The original idea to use stem cell transplant to replace lost neurons and oligodendrocytes in acute spinal cord and brain injuries has been re-defined during the recent years in view of the poor outcome in experimental models. Moreover, emerging topics concern the behavior (and/or the role) of endogenous neural stem (NSCs) and progenitor cells (NPCs) in pathological brains, and the paracrine properties of stem cells. In this talk the following points will be discussed:

1. Poor homing and engrafting of stem cells in the SNC. One critical point in transplantation in the mature CNS concerns the very rapid disappearance of most of the transplanted cells. This point will be discussed in light of the microglial reaction to xenograft (human neural stem cells in rat brain) and allograft (rat embryonic stem cells in the rat brain).
2. Paracrine properties of embryonic and somatic stem cells. In spite of the very poor homing, engrafting, and differentiation of different types of stem cells transplanted in pathological brains, some positive effects concerning the anatomy of the damage and the functional out-come are described in different models of brain and spinal cord lesion. Thus, the investigation of paracrine properties of these cells is of particular interest. We focused our attention on the mRNA expression profile for growth and neurotrophic factors (including NGF, BDNF, GDNF, CNTF, VEGF) in rat embryonic and neural stem cells, and human mesenchymal (from bone marrow, adipose tissue, dental pulp, amniotic membrane and umbilical cord) and neural stem cells, in order to establish potential neuroprotective properties of these cells.
3. 3D culturing of stem cells using artificial scaffolds. In view of the paracrine properties of stem cells, and in view of the very poor homing of transplanted cells in the central nervous system, we are working on the development of mixed scaffold/cell devices, to be able to keep an adequate number of appropriate cells in the lesion side. Rat embryonic and neural stem cells are cultured on on poly(L-lactic acid) electrospun nanofiber scaffolds and gel/sol 3D matrices (Cultrex and Hydrogel). Results concerning proliferation, differentiation and growth/neurotrophic factor mRNAs profile in these different 3D culture conditions will be discussed.