Stem cells and amyotrophic lateral sclerosis: the state of the art.

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Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder characterized by progressive motorneuronal loss. The available treatments provide symptomatic relief, none of them change the course of the disease. Stem cells represent the hope for therapies aimed at cell replacement and neuroprotection. Any experimental therapeutic approach to ALS is very difficult because some peculiarities of the disease, such as the unknown origin, the spatially diffusion of motor neuron loss, the paucity of animal models. Despite such daunting challenges, in experimental models a number of potential benefits of stem cells in ALS therapy have been demonstrated: by providing non-compromised supporting cells such as astrocytes, microglia or growth factor-excreting cells, onset can be delayed and survival increased.

Mesenchymal Stem Cells (MSCs) are multipotent stem cells that are very attractive in view of a possible cell therapy approach in neurodegenerative diseases because of their great plasticity and their ability to provide the host tissue with growth factors or modulate the host immune system. The administration of bone marrow-derived mesenchymal stem cells (BM-MSCs) has led to beneficial effects in animal models for several neurodegenerative diseases. Expanded MSCs can survive and migrate after transplantation in the lumbar spinal cord of SOD1G93A mice, where they prevent astrogliosis and microglial activation and delay ALS-related decrease in the number of motoneurons.

Encouraging data obtained with stem cells in animal models of neurodegenerative diseases led recently to the first clinical trials transplanting MSCs. We performed a Phase I trial in ALS for the assessment of the feasibility and toxicity of transplantation of autologous MSCs into the spinal cord. The trial was approved and monitored by the National Institute of Health and by the Ethics Committees. There was no immediate or delayed transplant related toxicity. Clinical, laboratory, and radiographic evaluations of the patients showed no serious transplant related adverse events also in the long term. Our study represents the first demonstration of the safety of MSC use after focal transplantation in the central nervous system. Therefore the results of our study represent an opening point for future studies in neurodegenerative diseases.