Intracerebroventricular transplantation of neural stem cells in an experimental model of amyotrophic lateral sclerosis

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Human Neural Stem Cells (hNSCs) treatment for neurodegenerative and neuroinflammatory diseases might exert antagonizing effects on inflammation and neurodegeneration. We showed that hNSCs transplantation in the spinal cord of SOD1^{G93A} rats can delay disease progression, motor functions deterioration and significantly extends animals survival. These clinical improvements were associated with a reduction of ALS histopathological markers and motor neurons preservation in the transplanted areas.
Moreover, we demonstrated that the procedure is feasible in ALS patients. The patient cohort was too small to draw final conclusions, however we observed a significant transitory decline of the ALS-FRS-r score progression for up to 4 months, in accordance with another comparable trial (NCT01348451).
To improve the hNSCs efficacy, a conceivable hypothesis is to increase cell dosage. This objective has been tackled by increasing the number of spinal cord injections (NCT01730716), however, this approach is limited due to the backbone destabilization consequent to the surgery.
Here, we are evaluating the implementation of intracerebroventricular delivery of hNSCs, as an effective strategy to increase cell dosage, favor a broader spread of transplanted cells and of their secreted healing factors throughout the motor neuraxis by exploiting the liquor circulation. We show that hNSCs (300,000 cells/mice) transplanted into the lateral ventricle of immunodeficient mice are well tolerated and not tumorigenic after 6 months, can extensively migrate and adhere to the ventricle wall occasionally migrating into the parenchyma.
The same dosage was injected into the brain of SOD1^{G93A} mice using a transient immunosuppression protocol. hNSCs survived for at least 2 months and preliminary data suggest that the treatment improved mice motor performances. However, cell survival was not optimal, thus, the reduced sample size prohibits any conclusions on survival.
We are currently evaluating the safety and efficacy of increased dosage of hNSCs (up to 1x10^6 cells) in nude and SOD1^{G93A} mice.