

Grafting of subcommissural organ cells improves neurological deficits in the hydrocephalic brain

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Introduction

It is now understood that hydrocephalus is not only a disorder of CSF dynamics, but also a brain disorder, and that derivative surgery does not resolve most aspects of the disease. Indeed, 80-90% of the neurological impairment of neonates with fetal onset hydrocephalus is not reversed by derivative surgery. We have begun to explore new strategies for diminishing such deficits, including the grafting of subcommissural organ (SCO) in the cerebrospinal fluid (CSF). Why SCO? Because SCO cells release neurotrophic compounds such as SCO-spondin, transthyretin (TTR), and the fibroblast growth factor (FGF-2). Goal of this research was to elucidate if grafting of SCO cells diminish neurological deficits in the hydrocephalic brain.

Methods

Hydrocephalic HTx rats (n=10) were grafted at postnatal day 7 (PN7). Ventriculomegaly was studied by computed tomography (TC) and histology. Neurological and cognitive condition was evaluated by standardized tests, such as the Object Recognition and Spontaneous Alternation in T Maze, at PN30. Non hydrocephalic HTx rats and sham- HTx rats were used as control.

Results and conclusions

Grafting of SCO-cells significantly improved neurological and cognitive condition in the hydrocephalic animals. It was not associated to a reduction of ventriculomegaly. Histological studies of grafted brains showed SCO cells integrated in the wall of the lateral ventricles. They were strongly reactive with antibodies against SCO-spondin and TTR, supporting that effects reported on neurological and cognitive conditions are mediated by SCO secretory compounds. These findings open an avenue for the development of a neurotrophic therapy for hydrocephalus.

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