Neural stem cells tracking by MRI in wobbler mouse, a model of motoneuron disease

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Introduction

Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disorder selectively affecting upper and lower motoneurons and leading to muscle atrophy, paralysis and death. Stem cells therapy may be a reliable approach for different neurological disorders. However, the mechanism of interaction with host tissues is still not clear. In the present study, the distribution of neural stem cells (NSCs) transplanted in the brain of early symptomatic wobbler mice were monitored in vivo by MRI. The wobbler mouse displays a recessively inherited neurological disease with degeneration of motoneurons and is considered to be a model of human motoneuron diseases.

Material and Methods

NSCs collected from the sub ventricular zone (SVZ) of 4 week-old mice were double labeled by incubation with the fluorescent dye Hoechst 33258 and with superparamagnetic iron oxide particles (Feridex, Berlex Imaging, Wayne, NJ, USA) for MR imaging. No difference in cell growth, differentiation and survival were found by comparing these cells to untreated NSCs. Wobbler and normal mice received a solution of 500,000 NSCs by bilateral administration in lateral ventricles.
MR imaging experiments were performed at 7T (Pharmascan-Bruker) in 6 animals (n=3 wobbler and n=3 controls) 24h, 48h and 2 weeks after the inoculation of labeled NSCs. Two animals (control and wobbler) were examined 24h up to 2 weeks after the injection of Feridex alone as control. T_2 and T_2^* weighted images were acquired with a high resolution ($156\times156\times625\ \mu m^3$).

Results

In normal animals, 24h post NSCs transplantation the areas of injection were clearly identified in the lateral and 4^{th} cerebral ventricles, whereas 48h post-injection, signal loss due to iron particles was significantly reduced.. In wobbler mice, the labeled stem cells were clearly detected in the different cerebral ventricles 48h and also 2 weeks post transplantation. In either normal or wobbler mice injected with Feridex, no signal loss due to the iron oxide particles were detectable 24h post injection.

Conclusion

This study indicates that adult NSCs transplanted in the lateral ventricles diffuse in the ventricular system and survive for at least 2 weeks. On current studies, it has been observed that NSCs transplantation induce a significant reduction in motoneurons loss compared to untreated wobbler mice. Further MRI experiments are ongoing to follow the migration of these labeled neural stem cells at later stage.