Primate adult brain cell autotransplantation for brain repair.

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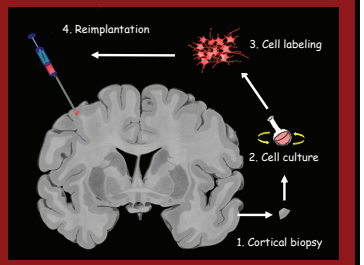
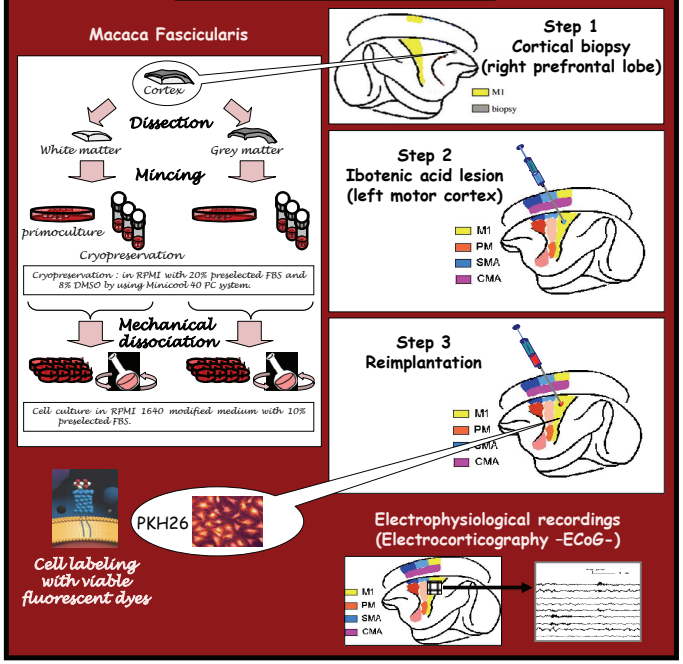
INTRODUCTION

Restoring function of the central nervous system is a challenging task since, unlike most of the organs, the mature brain and spinal cord have a limited ability for self-repair. Despite the great enthusiasm generated by the promising results of fetal transplantation in the context of Parkinson's disease and Huntington's disease, ethical controversies and lack of fetal donors remain a major problem. Therefore, autotransplantation of adult brain cells represents an attractive restoration alternative to bypass the caveats of fetal grafting.

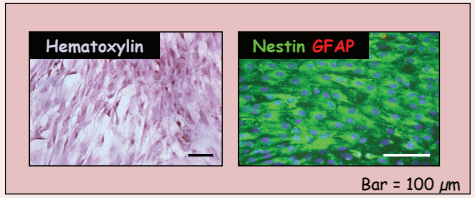


Scheme for autologous cell transplantation

MATERIAL AND METHODS

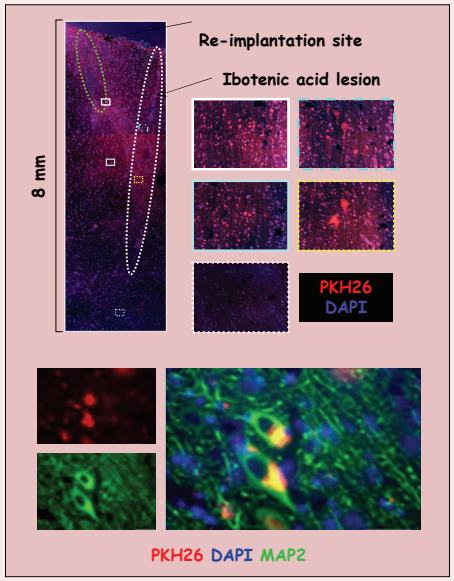


Primate adult grey matter cortical cells *in vitro (Macaca Fascicularis)*



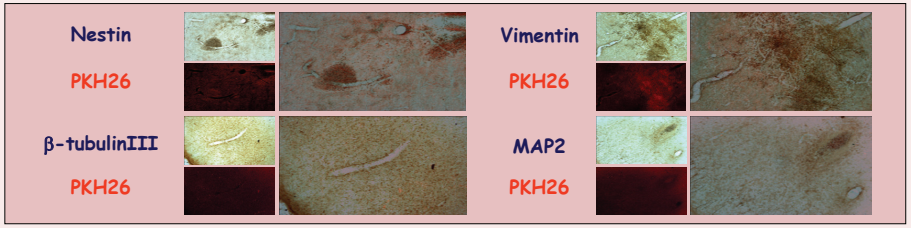
90 days after reimplantation near the lesioned site

PKH26-labeled cells, reimplanted 43 days after the lesion,survived *in vivo* for three months and migrated towards the lesioned area and deeper along the needle tract. Some cells presented orientated processes and expressed MAP2, a neuronal marker.



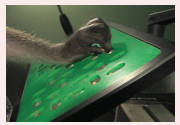
5 months after reimplantation into the lesioned site

The surviving PKH26-labeled cells, reimplanted 15 days after the lesion, stayed in clusters close to vessels, entangled in the reactive gliosis. These cells have hardly differentiated, expressing mainly nestin, and seem to be in apoptosis process.



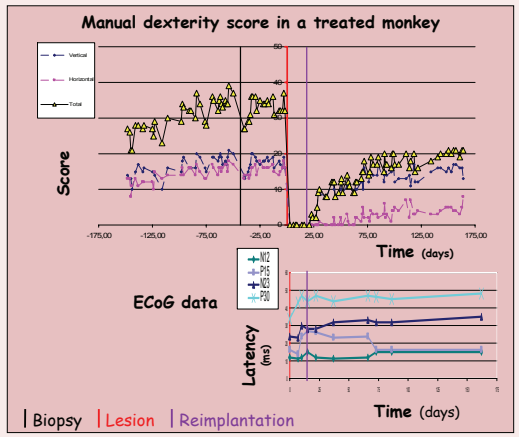
Behavior and electrophysiology

After reimplantation, the monkey showed a progressive recovery which reached 43% of prelesion score. This result is similar to data obtained in control monkeys from previous studies of M1 lesion (Wyss et al., P217.21).



Brinkman board

Variation of the somesthesic evoked potentials by stimulation of the median nerve and functional recovery follow a comparable time course.
There was a significant increase of the latency of the complex (N12)-P15 from post-lesion day 10 to day 66. In parallel, the progressive recovery of manual dexterity took place from post-lesion day 20 to day 70.



CONCLUSIONS

These preliminary data show that:
· Primate adult cortical cells can be easily obtained, cryopreserved and kept in culture, and then be reimplanted in the donor and survive *in vivo*.
· For 3 monkeys, 90 days after reimplantation, cells have migrated and changed their fate.
· For 1 monkey, 5 months after reimplantation, some cells have survived, but haven't well migrated nor differentiated. The recovery of this monkey's manual dexterity was not better than the one of a control monkey.
· ECoG represents a potential tool for a tentative prognostic value of recovery and its time course, possibly predicting the beginning of the plateau.

PERSPECTIVES

More experiments are needed to show the long term impact of reimplanted cells and their roles in brain repair. In case of promising results, it would open new perspectives in the field of brain repair and regeneration.

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