Effect of autologous adult neural progenitor cells transplantation on functional recovery of manual dexterity after lesion of motor cortex in macaque monkeys.

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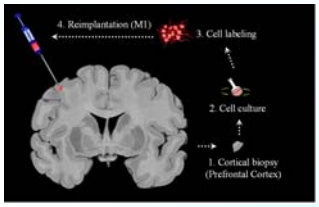
1. INTRODUCTION AND OBJECTIVES

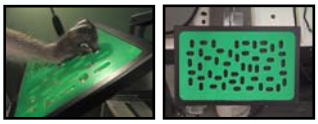
Restoring function of the central nervous system is a challenging task since the mature brain and spinal cord have a limited ability for self-repair.
Despite the great enthusiasm generated by the promising results of fetal transplantation in the context of Parkinson's disease and Huntington's disease, 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.



Autotransplantation

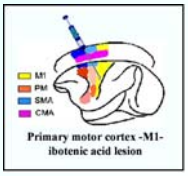
2. METHODS

Six monkeys were trained to perform a manual prehension task requiring precision grip (Modified Brinkman Board).



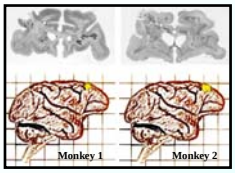
Modified Brinkman Board

When they reached a motor performance plateau, a unilateral lesion was performed by infusing ibotenic acid in the hand representation of the primary motor cortex (M1).



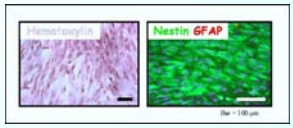
Then, a prefrontal cortical (dlPFC) biopsy was performed in the two treated monkeys. An approximate volume of 8 mm^3 cortical tissue was extracted using a surgical blade.

Biopsy of prefrontal cortical tissue



Cells from grey and white matter were dissected separately and put in culture. Cells from grey matter, expressing mainly nestin, were labelled with viable fluorescent dyes (PKH-26/PKH-67) and reimplanted in the M1 lesioned area.

Cell labelling with viable fluorescent dyes



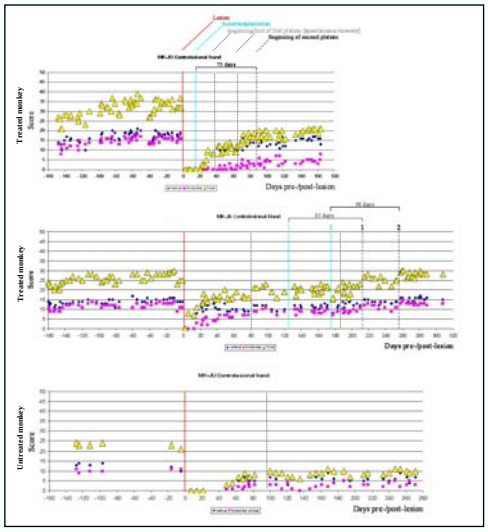
Primate adult grey matter cortical cells *in vitro* *(Macaca Fascicularis)*

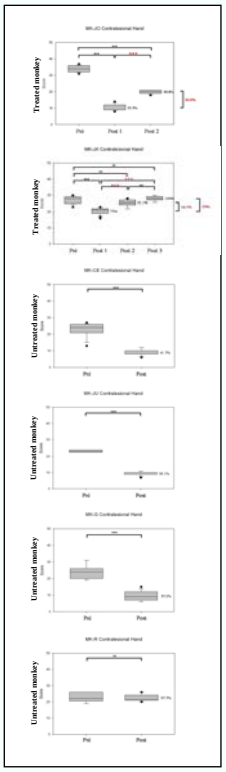
3. RESULTS

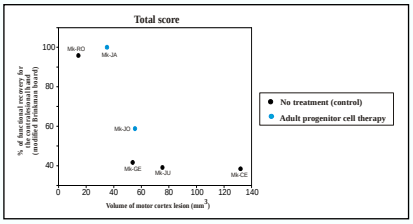
Following the lesion, as expected, there was a dramatic loss of manual dexterity of the opposite hand.

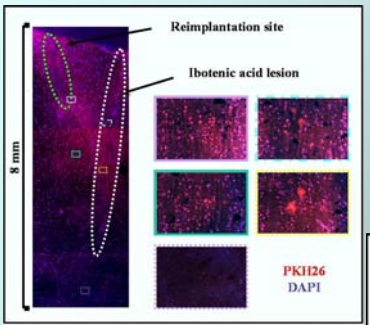
Four control monkeys recovered progressively part of their manual dexterity, reaching a stable plateau.

The other two monkeys (MK-JO and MK-JA) that were treated with autologous adult neural progenitor cells recovered progressively and reached a plateau, but contrarily to the control monkeys, this plateau was not definitive. A second plateau took place, 75 days and 85/90 days after the cells' transplantation respectively, representing an enhancement of 20-25% of the pre-lesional performance.



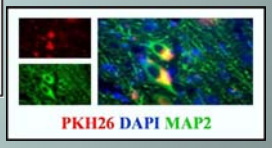




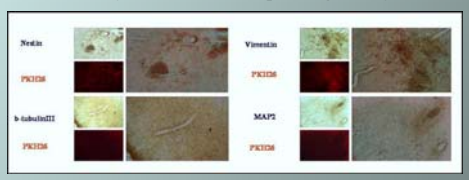


Reimplantation near the lesioned site 43 days after lesion

PKH26-labelled cells reimplanted 43 days (pilot study; Brunet et al., 2005) 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.



The surviving PKH26-labeled cells reimplanted 15 days after the lesion (MK-JO) were in clusters close to vessels, entangled in the reactive gliosis. These cells have hardly differentiated, expressing mainly nestin.



Reimplantation into the lesioned site 15 days after lesion

4. DISCUSSION

These preliminary data showed a second enhancement of motor performance in the order of 25% in the monkeys treated with autologous adult progenitor cells.
We can suppose that this behavioural rebond effect was due possibly to the transplantation of the autologous progenitor cells, which may have for example secreted factors for a favorable subsequent post-lesional recovery.

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