Lesioned motor cortex area reorganized differently in monkeys treated with autologous brain cell transplantation compared to non-treated monkeys

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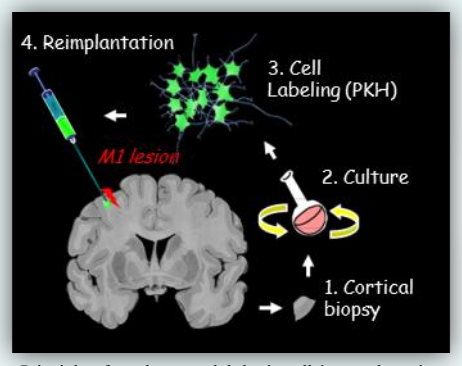
INTRODUCTION

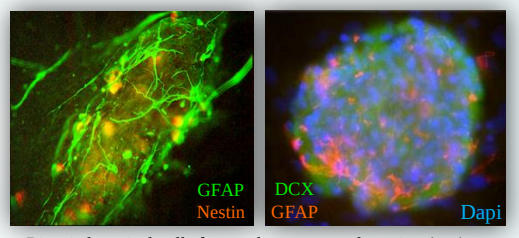
Previously, we reported the beneficial effect of the implantation of autologous adult cortical cells on the functional outcome of macaques subjected to an unilateral lesion of the primary motor cortex affecting their manual dexterity (see Figure G; Kaeser et al., 2011, Neurosurgery 68: 1405-1417).

Here, we investigated the cellular reorganization of the lesioned motor area of treated monkeys (n=2) in comparison to control lesioned monkeys (n=3).



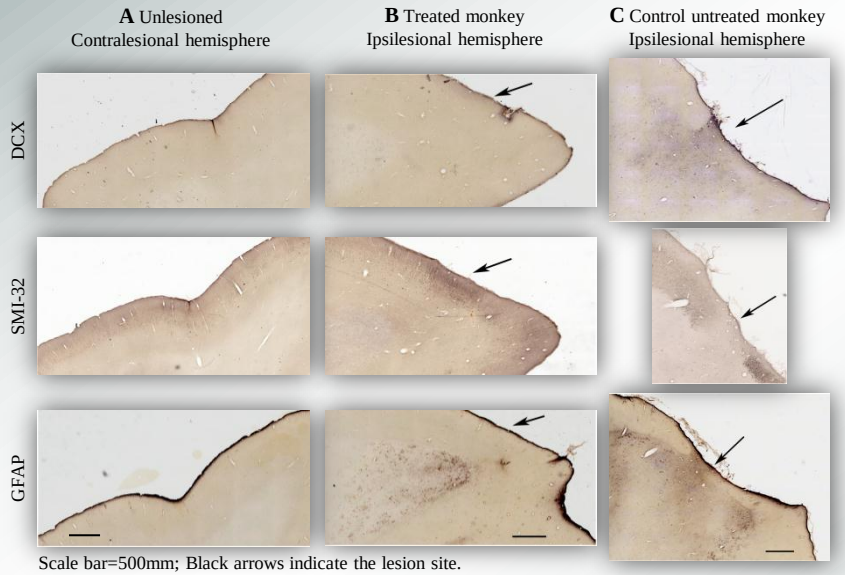
Principle of autologous adult brain cells' transplantation

METHODS

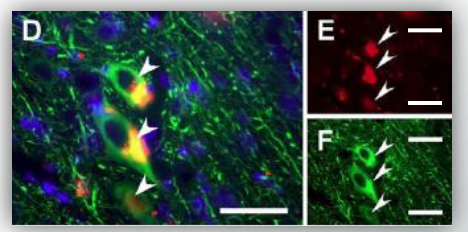


Biopsied cortical cells for autologous transplantation *in vitro* : formation of a neural cell ecosystem (DCX and Nestin positive cells -progenitors- surrounded by GFAP positive cells -astrocytes-)

RESULTS

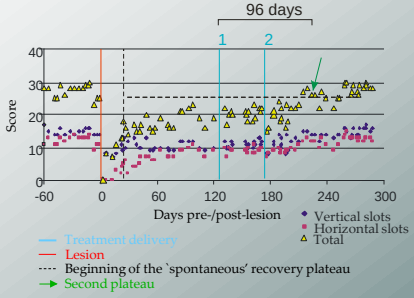


Scale bar=500mm; Black arrows indicate the lesion site.



Immunolabeling of brain section in the lesioned motor cortex after adult brain cell reimplantation.
Merged image (D) of reimplanted PKH26 (red)-labeled cells (E) that express MAP2 -neurons- (green) (F) after migration towards the lesioned area.
White arrows show three PKH26-positive cells that express MAP2. Nuclei are counterstained with Dapi (blue) (scale bar=15µm).

G Recovery of manual dexterity : effect of the treatment (autologous brain cells' transplantation)



Hematoxylin staining was combined with immunostaining for DCX -migrating neuronal precursors-, SMI-32 -pyramidal neurons- and GFAP -astrocytes-.
The results showed that, in the control group (C), a recruitment of endogenous DCX cells occurred that occupied the lesioned area in a diffuse way, conjugated with gliosis, expressed by an increase of GFAP staining at the level of the lesioned area and of the white matter. As expected, there was no expression of SMI-32 in the lesioned area. In contrast, in the treated group (B), nearly no DCX cells were found in the lesioned area, but an increase of SMI-32 cells occurred, originating probably from the transplantation -as some SMI-32 cells were PKH reimplanted cells, with a spread in the lesioned area-, as well as possibly from endogenous progenitor cells recruited after the lesion and then differentiated. Some GFAP staining was found in the white matter, where nerve fibers were probably growing and sprouting.

DISCUSSION

In conclusion, endogenous DCX positive cells were recruited in the control monkeys probably in order to enhance the spontaneous capacity of plasticity of the lesioned area, whereas in the treated monkeys, it is likely that once the endogenous and reimplanted DCX cells were recruited in the lesioned motor area, they differentiated and expressed SMI-32 or MAP2.
This pattern suggests that autologous brain cells' transplantation may induce a favourable environment for structural and functional restoration after lesion.
For the future, various aspects will be investigated in more detail, such as the reorganization of primates' motor cortex at the histological level (e.g. synaptophysin, NF70) and also using electrophysiological recordings (EMG). Furthermore, it is planned to assess the possible beneficial role played by the delivery of an anti-Nogo-A antibody, in combination with the autologous cell transplantation.

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FNSNF Fonds national suisse de la recherche scientifique