

Adult neural progenitor cells autotransplantation in a nonhuman primate model of Parkinson's disease: a pre-clinical study





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Introduction

Autologous cells transplantation overcomes several issues raised by the use of human ESC including ethical controversies and immune limitations. The present investigation intended to assess the impact of autologous neural cells ecosystem (ANCE) transplantation in four cynomolgus macaque monkeys exhibiting parkinsonian symptoms.

Methods

The monkeys were extensively trained to perform fine manual dexterity tasks as well as a reach and grasp drawer task before undergoing systemic MPTP lesions. During the MPTP phase, small cortical biopsies were performed and the gray matter material obtained put into culture according to the protocol developed by Brunet and colleagues. Additionally, at all phases of the protocol, the integrity of the nigrostriatal system was followed-up by ¹⁸F-dopa PET scan.



Results

Fine manual dexterity

Reach and grasp movement



After MPTP intoxication: impairments of fine manual dexterity in Mk-MY and

After MPTP intoxication: in Mk-MY, increase of the trial durations at all

Mk-MI, whereas Mk-LL and Mk-LY were affected in a less manner (data not shown).

<u>After ANCE transplantation</u>: improvement of the fine manual dexterity in Mk-MY and Mk-MI (6 months post-implantation). resistances for both hands (right hand not shown). Mk-MI was not able to perform the task.

<u>After ANCE transplantation</u>: recovery of the trial durations at all resistances for both hands (right hand not shown). Mk-MI regained its capacity to perform the task only in RO.



<u>After MPTP intoxication</u>: increase of the time spent in freezing activity in all the four animals (Mk-MY and Mk-MI not shown).

<u>After ANCE transplantation</u>: decrease of the time spent in freezing activity in all the four animals (Mk-MY and Mk-MI not shown).

<u>After MPTP intoxication</u>: dramatic decrease of striatal uptake (loss>80%) in all animals excepts in Mk-LY (17%).

<u>After ANCE transplantation</u>: all subjects were showing a significant but limited increase of their striatal uptakes ranging from 10% to 21%.

Discussion

Out of the four animals, two were severely affected by the MPTP lesions whereas the other two exhibited mild symptoms. Furthermore, the ¹⁸F-dopa striatal uptake was reduced by about 80% in three of them. Six months following ANCE transplantations, all monkeys presented significant improvement of their motor impairments. This functional recovery was accompanied by an increase of ¹⁸F-dopa striatal uptake. Taken together these new data open new therapeutic perspectives for the ANCE approach regarding neurodegenerative disorders like Parkinson's diseases.

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