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

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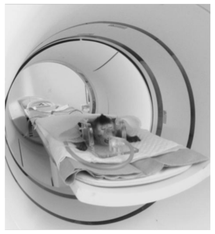
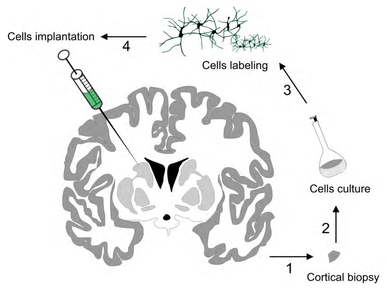
Introduction

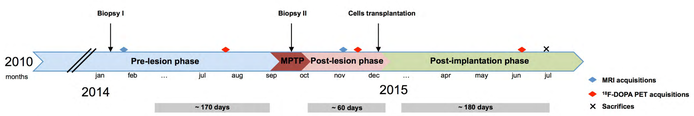
Autologous cells transplantation overcomes several issues raised by the use of human ESC including ethical controversies and immune limitations. The present investigation intended to assess the impact of autologous neural cells ecosystem (ANCE) transplantation in four cynomolgus macaque monkeys exhibiting 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 from the prefrontal zone were performed and the gray matter material obtained put into culture according to the protocol developed by Brunet et al. (2005). Additionally, at all phases of the protocol, the integrity of the nigro-striatal system was followed-up by ^{18}F-dopa PET. scan.

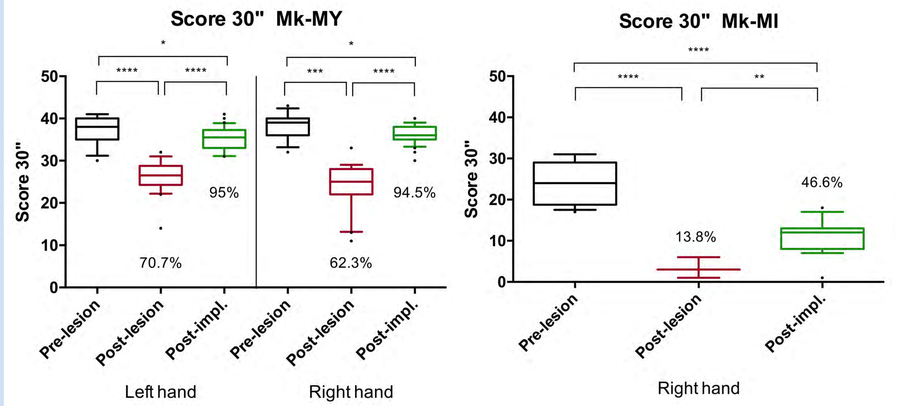


Discussion

Out of the four animals, two were severely affected by the MPTP lesions whereas the other two exhibited mild symptoms. Furthermore, the ^{18}F-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 ^{18}F-dopa striatal uptake. Taken together these new data open new therapeutic perspectives for the ANCE approach regarding neurodegenerative disorders like Parkinson's diseases.

Results

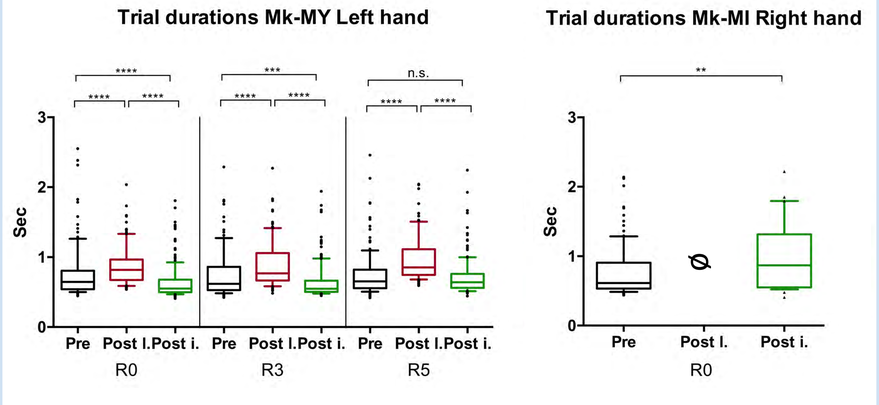
Fine manual dexterity



After MPTP intoxication: impairments of fine manual dexterity in Mk-MY and Mk-MI, whereas Mk-LL and Mk-LY were affected to a lesser extent (data not shown).

After ANCE transplantation: improvement of the fine manual dexterity in Mk-MY and Mk-MI (6 months post-implantation).

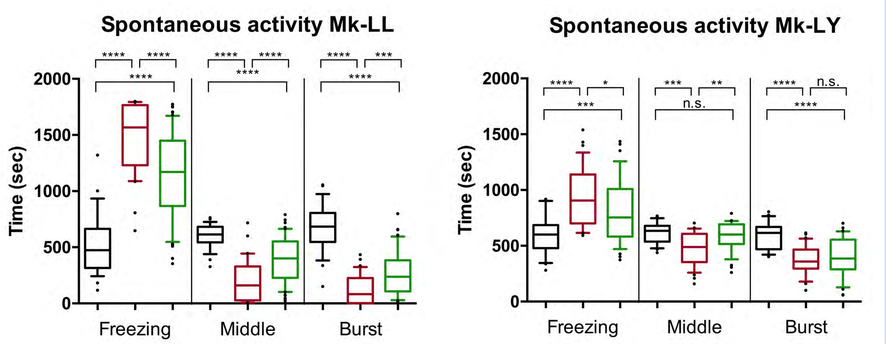
Reach and grasp movement



After MPTP intoxication: in Mk-MY, increase of the trial durations at all resistances for both hands (right hand not shown). Mk-MI was not able to perform the task.

After ANCE transplantation: 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 at resistance R0.

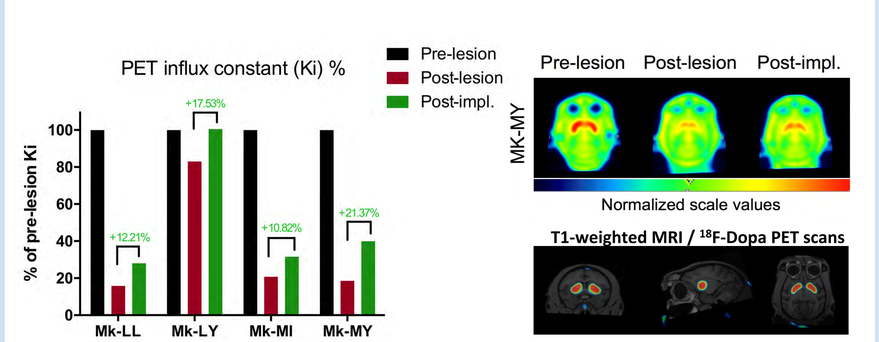
Spontaneous activity



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

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

^{18}F-dopa PET scan



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

After ANCE transplantation: all subjects showed a significant but limited increase of their striatal uptakes, ranging from 10% to 21%.

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