Exogenous Adult Mouse Post Mortem Neural promote functional recovery in a mouse model of Parkinson disease and differentiate in TH-positive neurons

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Parkinson's disease is the second most common neurodegenerative disease, after Alzheimer's disease, and the most common movement disorder. Drug treatment and deep brain stimulation can ameliorate symptoms, but the progressive degeneration of dopaminergic neurons in the substantia nigra eventually leads to severe motor dysfunction. The transplantation of stem cells has emerged as a promising approach to replace lost neurons in order to restore dopamine levels in the striatum and reactivate functional circuits. Post Mortem Neural Precursor Cells (PM-NPCs) are a subclass of SVZ-derived neural progenitors, capable of surviving hours after donor death. The *in vitro* differentiation yields more neurons (about 30-40%) compared to regular NPCs. Recently from a transgenic mouse strain expressing green fluorescent protein (GFP) under the promoter C of the ubiquitin gene (C57BL/6-Tg(UBC-GFP)30Scha/J) we isolated PM-NPCs-GFP, from mice at 6 hours after death (T6). The potential of PM-NPCs in terms of replacement therapy was investigated in a mouse model of Parkinson disease. The degeneration of dopaminergic neurons was obtained with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) at the dosage of 36 mg/kg intraperiteoneally. Then the lesion was stabilized by a second injection (i.p.) of the drug at the dosage of 20 mg/kg. 1x 10^5 of PM-PCs-GFP were administered to C57/BL mice by stereotaxic injection unilaterally in the striatum 3 days after the second MPTP administration. The effects of transplanted cells were determined by means of performance tests aimed at detecting behavioral improvements. In order to perform histology studies aimed at investigating the fate of transplanted precursors after transplantation, animals were perfused 2 weeks after transplantation. Our results show that animals treated with T6 GFP-PM-NPCs had a remarkable improvement of parameters measured by means of both horizontal and vertical grid tests (wall time, forepaw fault and time required to grab on the grids while turning and climbing down) starting within the third day after transplantation. These improvements were very significant and the average values were close to control. This was maintained throughout 2 weeks of experimental observation. By means of immunofluorescence staining we observed that the majority of transplanted T6 GFP-PM-NPCs were vital and able to migrate ventrally and caudally from the injection site lengths as far as 1000 microns into the striatum, and could reach the ipsilateral and contralateral substantia nigra pars compacta. Morphological analyses revealed that transplanted cells in the striatum can differentiate into dopaminergic (40%), cholinergic (40%), and gabaergic neurons (20%). Moreover, by means of HPLC technique we determined cathecolamines and their metabolites levels into the cortex, striatum, mesencephalon of T6 GFP-PM-NPCs or saline injected mice without finding any significant variation between the two animals groups. Our findings suggest how these stem cells may represent a liable source for cellular therapy in neurodegenerative disorders such as Parkinson Disease.