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Pre-clinical evidence for successful engraftment of human olfactory bulb neural stem cells for Alzheimer's, Parkinson's and spinal cord injury

Hany Marei[1], Asmaa Althani[1] and Cenciarelli C[2]
Qatar University, Qatar
Institute of Translational Pharmacology-CNR, Italy

Neural stem cells (NSC) have self-renewal and multipotent properties and may serve as an ideal cell source for transplantation to treat neurodegenerative insults such as Parkinson's, Alzheimer's, and spinal cord injury (SCI). Obtaining NSCs from adult human olfactory bulb (OB) would avoid ethical issues associated with the use of embryonic tissue, and provide an easily accessible cell source that would preclude the need for invasive brain surgery. To assess the therapeutic potential of OBNSCs, we studied the fate of allergenic adult human olfactory bulb neural stem/progenitor cells (OBNSC/NPCs) transplanted into the rat hippocampus treated with ibotenic acid (IBO), striatum of 6-OHDA Parkinson an rats, and in a rat model of SCI at day 7 post injury. In AD, stereological analysis of engrafted OBNSCs eight weeks post transplantation revealed a 1.89 fold increase with respect to the initial cell population, indicating a marked ability for survival and proliferation. In addition, 54.71_11.38%, 30.18_6.00%, and 15.09_5.38% of engrafted OBNSCs were identified by morphological criteria suggestive of mature neurons, oligodendrocytes and astrocytes respectively. In PD, the grafted cells survived in the lesion environment for more than eight weeks after implantation with no tumor formation. The grafted cells differentiated in vivo into oligodendrocyte-like (25 ±2.88%), neuron-like (52.63 ±4.16%), and astrocytic-like (22.36 ±}1.56%) lineages based on morphological criteria. Transplanted rats exhibited a significant partial correction in cognitive ability (AD) and stepping and placing non-pharmacological behavioral tests (PD), using a pole and rotarod. In SCI, the survival rate was about 30% relevant to initially transplanted cells. 27% of the engrafted cells differentiated along the oligodendrocyte, nearly as many (16%) differentiated into neurons, and about 56% of the cells displayed astrocyte morphology. The study revealed that OBNSCs were able to survive in the lesion environment for more than eight weeks after implantation; this was supported by transgenic over expression of hNGF on engrafted cells. We didn't observe locomotors recovery by BBB test, footprint analysis and grid walk tests three months post-treatment. Taken together, this work demonstrated that human OBNSCs ameliorate the cognitive and motor deficiencies associated with AD and PD rats model rats, and the improvement can probably be attributed primarily to neuronal and glial cell replacement as well as the trophic influence exerted by the secreted NGF. In contrast, we didn't observe locomotors recovery by BBB test, footprint analysis and grid walk tests three months post-treatment in SCI.

hmady@qu.edu.qa

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