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Neural stem cell transplants aid traumatic brain injury recovery

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Traumatic brain injury (TBI) is a major cause of mortality and morbidity, often causing lifelong disability for those who survive. Treatment is limited to supportive care, but stem cell therapy has received recent attention as a way to promote recovery for injuries to the central nervous system (CNS). In this study, researchers transplanted human neural stem cells (hNSCs) into the brains of mice modeled with TBI to investigate whether the hosts' immune systems and the stem cells acting in concert would enhance repair.

The researchers found that the transplanted hNSCs had a beneficial effect when the cells differentiated into a neuroprotective form (M2) of microglia (the main immune cells of the CNS) and subsequently reduced inflammatory responses generated by the injury.

Their study will be published in a future issue of *Cell Transplantation* and is currently freely available on-line as an unedited, early epub.

"Two types of stem cells have been tested in animal models of neurotrauma: mesenchymal stems cells (MSCs) and neural stem cells," explained Dr. Ping Wu of the Department of Neuroscience and Cell Biology at the University of Texas Medical Branch at Galveston. "The attractive feature of hNSCs is their unique nature of being committed to differentiation into neural cell lineages. We hypothesized that hNSC transplantation may provide several layers of benefits as a protective therapeutic strategy for brain injury by positively affecting the post-injury microenvironment and replacing lost neural cells."

The researchers reported that the animals receiving the hNSC transplantation showed "significantly reduced accumulation of amyloid precursor protein (APP)," an indicator of axonal injury. Most importantly, the researchers observed an increase in anti-inflammatory proteins of microglial cells of the protective M2 subtype.

"Our study confirmed the beneficial effect of hNSC transplantation for TBI and suggested that hNSCs have the ability to lessen the damage to neural cells, leading them to differentiate from the damaging M1 subtype into the neuroprotective M2 subtype," explained Wu. "The transition to M2 likely contributes to the neural repair effect of the grafted hNSCs."

The shift from M1 to M2 types is important because M1 cells and their associated cells are known to be toxic, while M2 promotes a regenerative response in the injured CNS.

The researchers also commented that they did not use immunosuppressive drugs following the cell transplantation and that hNSCs are known to be short-lived without immunosuppression, although they still lessened inflammatory responses. In conclusion they suggested that further studies that incorporate immunosuppression post-transplantation are needed to see if immunosuppression affects stem cell-mediated immunomodulation.

"Intracerebral transplantation of hNSCs efficiently leads host microglia/macrophages towards an anti-inflammatory phenotype that presumably contributes to stem cell-mediated neuroprotective effects after severe TBI in mice," concluded the researchers. "In future studies, it will be interesting to determine how cells in brain regions distant from the damage center respond to traumatic injury and cell grafting."

"Traumatic brain injury is a major area of concern for both clinicians

and researchers and can result in devastating, debilitating effects for the patients," said Dr. Paul R. Sanberg, Center of Excellence for Aging and Brain Repair, Department of Neurosurgery and Brain Repair, Morsani College of Medicine, University of South Florida, Tampa, FL and Co-Editor-in-Chief for *Cell Transplantation*. "TBI affects many different groups within our society and, as such, new approaches are sorely needed. This study offers new, mechanistic insight into the efficacy of neural stem cell transplantation and the field of regenerative medicine as a whole. Future studies that help progress this treatment modality to the clinic are warranted."

More information: *Cell Transplantation* , dx.doi.org/10.3727/096368916X691150 , http://www.ingentaconnect.com/content/cog/ct/pre-prints/content-CT-1532_Gao_et_al

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