Fetal stem cell transplantation favorably impacts radiation-induced cognitive dysfunction

August 22 2013

Patients receiving cranial irradiation treatment for brain cancer may find the treatment life-saving, but often suffer progressive and debilitating cognitive detriments, including spatial learning and memory deficits. The cognitive deficits are a contributing factor to the often significant adverse impacts on the surviving patients' quality of life after radiation therapy. In an effort to improve post-irradiation cognitive impairment, scientists at the University of California, Irvine, and colleagues at Neuralstem, Inc. (Rockville, MD), have transplanted fetal stem cells into laboratory animals with radiation-induced cognitive impairments and found that this led to a number of cognitive improvements. The study appears as an early e-publication for the journal *Cell Transplantation*.

"Multiple mechanisms contribute to disrupted cognition following irradiation for patients with central nervous system malignancies. These include the depletion of radiosensitive populations of stem and progenitor cells in the hippocampus," said study co-author Dr. Charles L. Limoli of the Department of Radiation Oncology at the University of California, Irvine. "Interventions to combat long-term brain damage resulting from toxic radiation and chemotherapies therapies have yet to be developed. However, stem cell replacement strategies may provide a much needed intervention."

The researchers explored the potential beneficial impact of intra-hippocampal transplantation of fetal-derived human neural stem cells by transplanting the cells into laboratory rats a month after the animals were subjected to cranial irradiation with resulting cognitive deficits. The stem cells were FDA-approved human, fetal-derived neural stem cells provided by Neuralstem, Inc.

"Engrafted stem cells underwent extensive neuronal differentiation, formed new synaptic contacts, released neurotrophic factors, and showed an advanced degree of structural integration into the motor circuitry," reported the research team.

They found that the test animals showed improved hippocampal spatial memory and hippocampal-related "fear conditioning performance" when compared to a control group of irradiated animals that did not receive stem cell transplantation. The engrafted cells also migrated and differentiated into neural and glial subtypes in areas of the hippocampus.

"The engrafted stem cells survived and differentiated throughout an area of the hippocampus and significantly ameliorated cognitive dysfunction as shown at a one-month follow-up on the irradiated animals," said Dr. Limoli. "While it is premature to presume efficacy in the absence of human data, our efforts to thwart cognitive dysfunction by cell replacement therapy with fetal stem cell transplantation may provide an experimental backdrop for a potential treatment for cranially irradiated patients who developed cognitive dysfunctions."

"Cognitive dysfunction is an unfortunate side effect of the therapeutic use of radiation therapy for brain cancer and the identification of ways to ameliorate the dysfunction, such as the application of stem cell transplantation, is a significant area of research" said Dr. Paul R. Sanberg, distinguished professor at the Center of Excellence for Aging and Brain Repair, Morsani College of Medicine, University of South Florida, Tampa, FL.

"This study is an important step towards the development of a clinical therapy, though further research is still required."

More information: Acharya, M. M.; Christie, L-A.; Hazel, T G.; Johe, K. K.; Limoli, C. L. Transplantation of human fetal-derived neural stem cells improves cognitive function following cranial irradiation. Cell Transplant. Appeared or available online: July 17, 2013. www.ingentaconnect.com/content … prints/ct1048acharya

Provided by Cell Transplantation Center of Excellence for Aging and Brain Repair