Study finds 'Western diet' detrimental to fetal hippocampal tissue transplants

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Researchers interested in determining the direct effects of a high saturated fat and high cholesterol (HFHC) diet on implanted fetal hippocampal tissues have found that in middle-aged laboratory rats the HFHC diet elevated microglial activation and reduced neuronal development. While the resulting damage was due to an inflammatory response in the central nervous system, they found that the effects of the HFHC diet were alleviated by the interleukin (IL)-1 receptor antagonist IL-1Ra, leading them to conclude that IL-Ra has potential use in neurological disorders involving neuroinflammation.

They published their results in a recent issue of Cell Transplantation (20:10), now freely available online.

To carry out the study, the researchers transplanted hippocampal grafts from embryonic 18 day-old rats into the anterior eye chambers of 16-month old host animals that were subsequently fed either a normal rat chow diet or a HFHC diet for eight weeks.

"We hypothesized that damage from the HFHC diet is due, at least in part, to an inflammatory response in the periphery that leads to an inflammatory response in the central nervous system," said study corresponding author Dr. Linnea Freeman of the Medical University of South Carolina's Department of Neuroscience. "We also hypothesized that the drug Kineret, a common treatment for rheumatoid arthritis based on the IL-1Ra, an IL-1 receptor antagonist, might block the inflammatory cascade."

The researchers noted that the intracranial transplantation of fetal neurons, or engineered cell lines, has been proposed as a potential treatment for neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease. However, the quality of graft survival in the aged brain has been questioned.

"It is well known that the aged brain poses special challenges for successfully grafting cells," said Dr. Freeman. "The causes for this are unclear, but factors such as the inflammatory response, reduced growth factor production and reduced cellular support systems have been explored."

The researchers grafted developing hippocampal tissue to middle-aged recipient rats knowing that the grafts may be compromised by increased systemic cytokines and that the HFHC diet would be further detrimental.

After six weeks, the researchers found stunted growth in fetal hippocampal tissues among the animals fed the HFHC diet as opposed to normal development in controls receiving a normal diet. However, when treated topically with IL-1Ra, the HFHC fed animals grew grafts three times the size of HFHC-fed, saline-treated controls.

"All factors taken together, the HFHC diet was shown to exert detrimental effects on hippocampal growth and development," explained Dr. Freeman. "Factors contributing to this effect include, but are not limited to, vascularization and inflammation."

The research team concluded that not only was graft growth altered by the HFHC diet, but that neuronal development and organization was affected as well. However, that treatment with IL-1Ra blocked the detrimental effects of the HFHC diet on hippocampal tissues may indicate a potential use for IL-1Ra in neurological disorders involving neuroinflammation.

"Eight weeks on a Westernized high fat high cholesterol diet causes developmental neuroinflammation in middle-aged rats that can be reversed by an interleukin-1 receptor antagonist" said Dr. John Sladek, professor of neurology and pediatrics at the University of Colorado School of Medicine. "It will be interesting to see if the interleukin-1 receptor antagonist is still effective with a long term Westernized diet and whether this can be translated to humans."

More information: Freeman, L. R.; Small, B. J.; Bickford, P. C.; Umphlet, C.; Granholm, A. C. A High Fat/High Cholesterol Diet Inhibits Growth Of Fetal Hippocampal Transplants Via Increased Inflammation. *Cell Transplant.* 20(10):1499-114; 2011.

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