AMD-like lesions delayed in mice fed lower glycemic index diet

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Feeding older mice a lower glycemic index (GI) diet consisting of slowly-digested carbohydrates delays the onset of age-related, sight-threatening retinal lesions, according to a new study from the Laboratory for Nutrition and Vision Research at the Jean Mayer USDA Human Nutrition Research Center on Aging (USDA HNRCA) at Tufts University.

The researchers studied middle-aged and older mice that consumed either a higher or lower GI diet. Mice fed the lower GI diet developed fewer and less-severe age-related lesions in the retina than the mice fed the higher GI diet. The lesions included basal laminar deposits, which typically develop after age 60 in the human retina and are the earliest warning sign of Age-Related Macular Degeneration (AMD).

"To our knowledge, we have established the first mature, mammalian model indicating a delay in the development of AMD-like lesions as the result of a lower GI diet," says Allen Taylor, PhD, director of the Laboratory for Nutrition and Vision Research at the USDA HNRCA. "The only difference between the two groups of mice we studied is the GI of their meals, which suggests that diet alone is enough to accelerate or delay the formation of lesions. These results, coupled with similar observations made by our laboratory in earlier human epidemiologic studies imply that lower GI diets hold potential as an early intervention for preventing onset and progress of AMD."

The dietary glycemic index (DGI) measures the rate at which glucose is

delivered to the bloodstream after consuming carbohydrates. Higher GI foods including white bread and white potatoes trigger a rapid delivery of glucose that pushes the body to work overtime to absorb, whereas lower GI foods, like whole grain bread and fruits and vegetables, initiate a slower release of glucose that is more easily processed by cells.

Compared to the mice on the lower GI diet, mice on the higher GI diet demonstrated elevated accumulations of debris known as advanced glycation end products (AGEs) in the whole retina, particularly in the cells of the RPE. The RPE plays a crucial role in maintaining vision and its dysfunction results in the gradual central vision loss that is the hallmark of AMD. AGE accumulation has also been linked to tissue damage in other age-related diseases such as Type 2 diabetes and cardiovascular disease.

"We presume the elevated accumulation of AGEs we saw in the retina of the higher GI group is associated with toxicity. The AGEs result from the modification of proteins by excess glucose and this compounds the normal protein damage that happens as we age," says Karen Weikel, first author and a PhD candidate at the Friedman School of Nutrition Science and Policy at Tufts. "While previous research has linked higher GI diets to AGE accumulation in the blood, ours appears to be the first to show diet-related AGE presence in tissue, such as the retina, which becomes the site of the eye disease."

The research, published online in October in the journal *Aging Cell* traces the drop-off in AGE accumulation in the lower GI diet to the ubiquitin-protease system pathway and the lysosome/autophagy pathway. "In cell models we saw that both the ubiquitin pathways and lysosome pathways processed proteins more efficiently and kept cells healthier when glucose levels were lower," says Taylor, who is also a professor at the Friedman School and Tufts University School of Medicine (TUSM). "Both pathways are well-known for their ability to remove damage from

cells, but this had not been previously systematically explored for removal of AGEs."

The Centers for Disease Control reports AMD is the chief cause of irreparable vision loss in Americans over age 65 and that 1.8 million people in the U.S. are living with the disease, a number that is expected to approach 3 million by 2020.

"Although our laboratory has shown in epidemiological studies and now in a live laboratory model that lower GI diets may prevent or delay the progression of AMD, future studies are needed. Trials involving more animals and human clinical trials could more carefully describe the protein-editing machinery that appeared to determine the development and severity of the lesions we saw," Taylor says. "With such information, we may begin to develop cost-effective dietary interventions as well as a new generation of drugs that mimic the presumed effects of the lower GI diet to prolong vision."

More information: Uchiki T, Weikel KA, Jiao W, Shang F, Caceres A, Pawlak D, Handa JT, Brownlee M, Nagaraj R, and Taylor A. "Glycation-Altered Proteolysis as a pathobiologic mechanism that links dietary glycemic index, aging and age-related disease (in non-diabetics). Aging Cell. Published online October 3, 2011. DOI: 10.1111/j.1474-9726.2011.00752.x

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