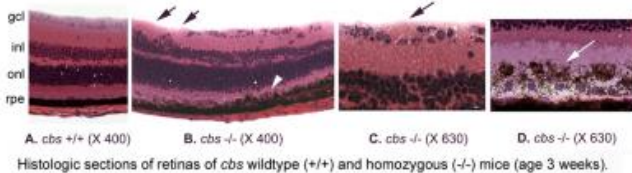


Impact of elevated homocysteine levels on vision under study

15 October 2007



Histologic sections of retinas of *cbs* wildtype (+/+) and homozygous (-/-) mice (age 3 weeks).

Retina: Panel A shows the retina of a healthy mouse with normal homocysteine levels. Panels B, C and D are from mice with a genetic defect that results in a 40-fold increase in homocysteine levels. These retinas show fragmentation in less than three weeks of life. Credit: Medical College of Georgia

Homocysteine, an amino acid believed to contribute to heart attack, stroke and dementia, likely also is a player in retinal damage and vision loss, researchers say.

Homocysteine levels rise when folic acid levels drop, a common problem for Americans whose diets are often poor in folate-rich fruits, tomatoes, vegetables and grains, according to Dr. Sylvia Smith, cell biologist at the Medical College of Georgia.

Scientists want to know the impact of resulting elevated homocysteine levels on the extensive blood vessel and neuronal network of the retina; their preliminary evidence suggests that it isn't good.

"You don't have to be a cell biologist to see that there is a problem in this retina. It's terribly disrupted," Dr. Smith says, looking at images of a fragmented 10-layer retina exposed to high levels of homocysteine. A healthy retina – tissue at the back of the eye that receives light and transforms it to a neural impulse that goes to the brain – is "beautifully" organized, horizontally and vertically, she says.

"What is the consequence of slightly elevated homocysteine on the retina, on its architecture, its functioning, its ability to withstand stress?" Dr. Smith hopes to find the answers with a \$1.8 million grant from the National Institutes of Health.

She and Dr. Vadivel Ganapathy, chair of the MCG Department of Biochemistry and Molecular Biology, have been studying how folate gets to the retina and how diseases such as diabetes interfere. They found it hard to ignore homocysteine as they studied folate, a vitamin essential to life.

Folate and vitamin B12 – which Americans typically get plenty of – convert homocysteine to methionine, an amino acid essential to protein synthesis.

Without the conversion, rising homocysteine levels interfere with the folding and structure of collagen, a component of bone, tissue and the basement membrane of blood vessel walls. When pregnant women don't get enough folate, the result can be devastating neural tube defects, such as spina bifida, in their babies. People with a genetic defect that results in a homocysteine level 40 times the norm are tall, thin, have osteoporosis and a markedly increased risk of clotting, Dr. Ganapathy says. Tiny clots cause small, frequent strokes, cumulative tissue damage and, eventually, mental retardation. "If you are having thrombotic attacks in the retina like what happens in the brain, it will affect visual function, too" he says. Excess homocysteine is even bad for the folate transporter protein, the researchers have shown.

They are studying a mouse model with a slightly elevated homocysteine level that simulates a low-folate diet in humans; a version of the mouse that also has diabetes, which goes hand-in-hand with cardiovascular disease and retinopathy; and a second model of the rare genetic defect that results in extraordinarily high homocysteine levels.

They will follow the mice over their lifetime, putting

them on diets that elevate and lower folate levels, measuring resultant homocysteine levels and the impact on the retina. Next year, they will test the animals' vision in conjunction with the Cleveland Clinic.

They hypothesize that sustained elevation will compromise retinal function and degrade the once well-stratified tissue. They have shown in pilot studies that adding diabetes to the mix makes bad matters worse.

“At any point in your life, too much homocysteine can be problematic, whether you are talking about pregnant women, cardiovascular disease or dementia,” says Dr. Smith. “If homocysteine is not converted into methionine or cysteine (by vitamin B6) to aid protein synthesis, it can do something bad.”

Dr. Ganapathy notes that people need only about 1 microgram per day of vitamin B12, which comes from microorganisms common in animals' gastrointestinal tract. Strict vegetarians are typically the only Americans who have problems with B12 deficiency, he says. People need about 400 micrograms of folate daily. Pregnant women as well as those trying to become pregnant need at least double that.

Source: Medical College of Georgia

APA citation: Impact of elevated homocysteine levels on vision under study (2007, October 15) retrieved 13 June 2021 from <https://medicalxpress.com/news/2007-10-impact-elevated-homocysteine-vision.html>

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