Research shows connection between dementia and AGE-rich diets

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Western diets are often rich in advanced glycation end-products (AGEs). Also known as glycotoxins, AGEs are found in processed foods. Weijing Cai of The Icahn School of Medicine at Mount Sinai and his colleagues have found that AGE-rich diets could suppress the activity of the protective enzyme NAD+-dependent sirtuin 1 (SIRT1). Suppression of this enzyme can lead to dementia, type 2 diabetes and metabolic syndrome (MS). The research appears in the *Proceedings of the National Academy of Sciences*.

Glycotoxins form when sugars react with fats, proteins and nucleic acids. Heating food increases its glycotoxin content. Scientists already know of links between high dietary glycotoxin levels and type 2 diabetes, metabolic syndrome (MS) and aging. There is a correlation between high levels of the type of AGEs known as neurotoxic methyl-glyoxal derivatives (MGs) and cognitive decline in older people. Studies in mice and humans have shown that AGE-restricted diets can delay the onset of metabolic and vascular disease and improve insulin resistance.

Previous studies have revealed connections between MS, type 2 diabetes and brain dysfunction. The researchers wanted to see if these links had to do with AGE intake. They compared three groups of mice. They fed one group a normal diet, a second group a reduced calorie low-AGE diet and a third group a reduced calorie low-AGE diet supplemented with MG. Both the mice on the normal and reduced calorie MG-supplemented diets developed insulin resistance and gained more weight than the mice on the AGE-restricted diet.

The mice fed the AGE-restricted diet performed better on motor coordination and balance tests than mice on diets supplemented with MG. Mice on MG-supplemented diets performed poorly on tests of exploratory behavior. They found it harder to distinguish between new and familiar objects than mice with restricted AGE intake.

Examination of the brains of the mice revealed that mice on the normal or MG-supplemented diets experienced suppressed SIRT1 activity and had similar levels of AGE deposits, despite the fact that they consumed different amounts of calories. Mice with restricted AGE intake had higher levels of SIRT1 activity and significantly lower AGE levels in the brain.

Previous research has shown an association between caloric restriction and an increase in cognitive function. There is an established link between SIRT1 expression and the effect of caloric intake on cognition. The fact that mice on a low calorie, AGE-supplemented diet experienced suppressed SIRT1 expression and decreases in cognitive performance indicates that reduced calorie intake alone does not halt dementia; AGE-consumption is also a factor.

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