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Ingredient in hops to treat learning and memory impairments and metabolic changes associated with a high-fat diet

Metabolic syndrome (MetS) is a risk factor for cardiovascular disease and type 2 diabetes. MetS is associated with enhanced risk to develop age-related cognitive impairments and and dementia. Diets high in saturated fat induce inflammation that contributes to the development of MetS. Obesity and consumption of a high-fat diet can impair cognitive function in humans and animal models. In humans, risk factors for developing age-related cognitive decline and dementia include consumption of a high-fat diet, obesity, insulin resistance, type-2 diabetes.

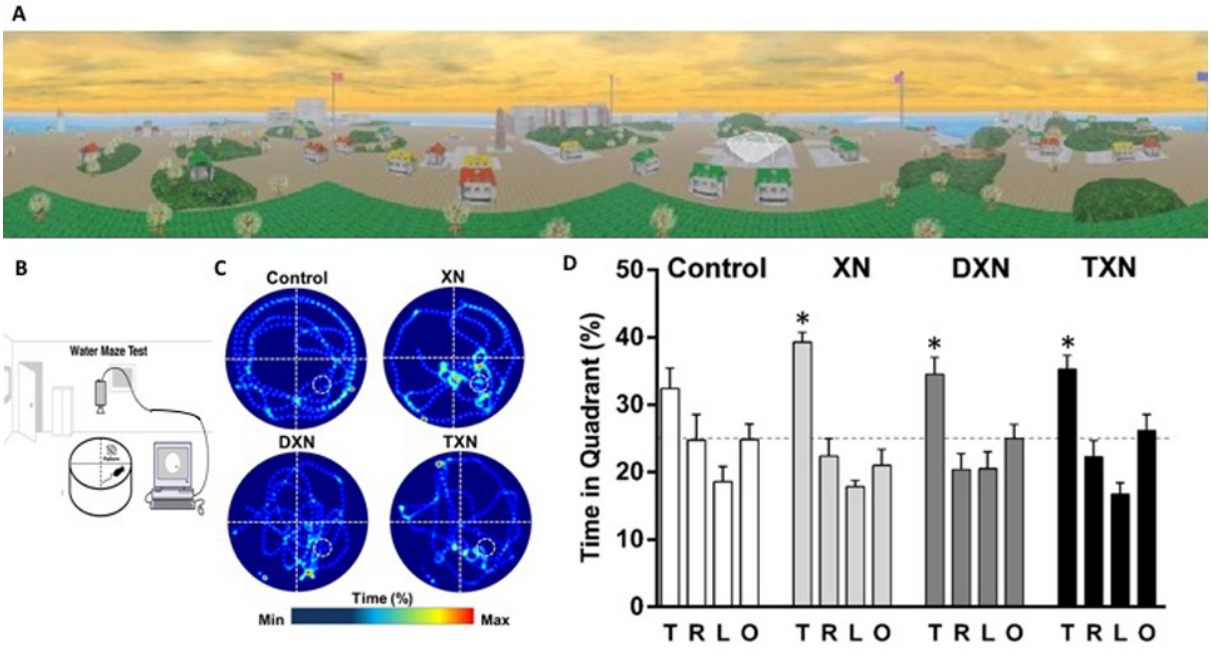

Fig. 1. A. Test to assess spatial navigation in humans using the Memory Island program. B. Test to assess spatial navigation in rodents in the water maze. C. Representative swim paths of mice in the memory trial (platform removed). The white circle indicates the location of the platform during the hidden platform sessions. Mice that show spatial memory will spent more time in the part of the pool (quadrant) that contained the hidden platform (target quadrant or T) than the left (L), right (R), or opposite (O) quadrant. D. Percent time the mice spent in the four quadrants of the pool during the memory trial. Mice that received a high-fat diet in combination with or a XN analogue that cannot be converted into phytoestrogens (DXN or TXN) spend more time in the quadrant that used to contain the hidden platform than the other three quadrants. (*$p < 0.05$).

The principal flavonoid found in hops (*Humulus lupulus*) has anti-obesity effects in the rodent models. However, the use of XN in dietary supplements raises some concerns, as one of its metabolites, is a potent phytoestrogen. Phytoestrogens carry the risk of adverse effects of estrogens. In this study, we used XN along with XN analogues that cannot be converted into phytoestrogens and determined whether they are able to treat

MetS and cognitive impairment associated with obesity. Along with a HFD, we administered XN and two XN analogues that cannot be converted into phytoestrogens orally to young adult wild-type mice for 14 weeks. Cognitive impairments induced by a high-fat diet include impairments in spatial navigation, which in turn requires the ability to generate and recall a spatial map. Spatial navigation is the ability to explore the environment to locate a specific location previously visited using cues in the environment (A). Spatial navigation is impaired as part of age-related cognitive decline and especially in dementia.

Mice treated with XN and XN analogues that cannot be converted into phytoestrogens showed improvements of impaired glucose tolerance and decreased plasma insulin and leptin levels. Mice treated with either of these three compounds showed improved spatial learning as compared to mice only receiving the high-fat diet. The mice treated with either of these three compounds showed spatial memory, which was not seen in mice only receiving the high-fat diet (B-D). Thus, our results demonstrate the potential to prevent or treat the cognitive injury and metabolic alterations associated with a high-fat diet. HFD-induced obesity without risk of estrogenic adverse effects.

Jacob Raber, Jan Frederik Stevens
Oregon Health & Science University, USA
Linus Pauling Institute, Oregon State University, USA

Publication

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