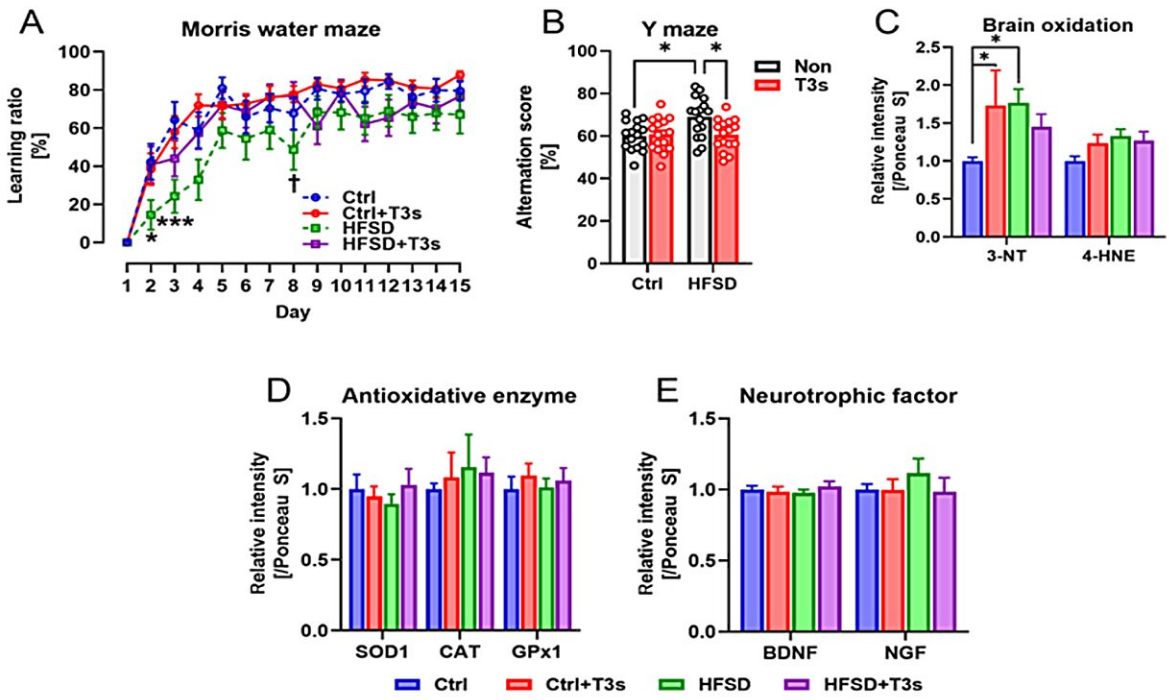
Obesity-induced cognitive decline: Role of brain oxidation and tocotrienols

April 18 2024



Researchers from Shibaura Institute of Technology, Japan investigated the impact of HFSD on mice and found that tocotrienols (T3s), a form of vitamin E, show promise in protecting against cognitive decline associated with obesity, highlighting its therapeutic potential. Credit: Yugo Kato from Shibaura Institute of Technology, Japan.

Obesity has become a pressing worldwide health issue, with rates

steadily rising over recent decades. Beyond its well-documented associations with physical health issues, such as cardiovascular disease and diabetes, obesity has also been linked to cognitive decline, including conditions like Alzheimer's disease and Parkinson's disease. Understanding the complex mechanisms underlying this cognitive impairment is crucial for developing effective interventions.

In a study published in the *International Journal of Molecular Sciences*, Assistant Professor Yugo Kato from Tottori University and Shibaura Institute of Technology, Professor Koji Fukui from Shibaura Institute of Technology and their team offer insights into potential solutions.

The study investigated the neuroprotective effects of tocotrienols (T3s) in mitigating the adverse impact of diet-induced obesity on brain function.

"Our goal is to combat obesity-related diseases using natural compounds and thereby reduce the prevalence of conditions like dementia among individuals affected by obesity," says Prof. Kato.

T3s are a group of naturally occurring chemical compounds belonging to the vitamin E family. Past studies have revealed that T3s have neuroprotective and anti-obesity properties. Additionally, they have also been shown to pass through the blood-brain barrier and enter cells to produce antioxidant effects. However, little is known about how T3s contribute to the decline in brain function brought on by obesity.

To address this gap, the team conducted a comprehensive investigation using a mouse model system. They employed a meticulous experimental design, with C57BL/6 male mice subjected to either a high-fat, high-sucrose diet (HFSD) or a control diet, supplemented with or without T3s.

In the initial phase of the study, the team evaluated the anti-obesity

effects of T3s. To do so, they incorporated a 50mg T3s mixture into 100g of both experimental diets, namely the control and HFSD. Key parameters, including body weight, fat deposition, serum cholesterol, triglyceride, and glucose concentrations, were assessed alongside cognitive function using the Morris water maze and Y-maze tests. Additionally, markers of oxidative stress and proteomic changes in the cortex were analyzed to gain deeper insights into the underlying mechanisms.

The results of the study were highly promising. While HFSD feeding induced obesity in the mice, supplementation with T3s did not mitigate weight gain. However, T3s treatment demonstrated a significant improvement in cognitive function, as evidenced by enhanced learning ability in HFSD-fed mice. Furthermore, the study revealed the role of oxidative stress in obesity-induced cognitive decline, with HFSD-fed mice exhibiting increased brain oxidation levels.

Remarkably, T3s treatment appeared to mitigate this oxidative stress, suggesting a potential mechanism for their neuroprotective effects. Additionally, contrary to expectations, the team found that respiratory metabolism decreased and the temperature around brown adipose tissue increased in mice fed with HFSD. This unexpected finding suggests that HFSD may have a complex impact on metabolic processes and temperature regulation in the body.

"Lastly, we wanted to examine the protein change associated with the consumption of the HFSD. So, we performed a quantitative proteomic analysis of the mouse cortex. Our focus was on the proteins that were expressed differently between the HFSD and control groups," explains Prof. Kato. They discovered that in comparison to the control group, obesity brought on by HFSD feeding changed 12 proteins, and mice treated with T3s showed considerable prevention of these changes.

In conclusion, this study represents a significant step forward in our understanding of the intricate relationship between obesity and cognitive decline. By uncovering the potential benefits of T3s in preserving cognitive function, the research opens up new avenues for therapeutic interventions targeting neurodegenerative diseases associated with obesity.

More information: Yugo Kato et al, Tocotrienols Prevent the Decline of Learning Ability in High-Fat, High-Sucrose Diet-Fed C57BL/6 Mice, *International Journal of Molecular Sciences* (2024). DOI: 10.3390/ijms25063561

Provided by Shibaura Institute of Technology