

Long-Term Supplementation With Fruits and Vegetables Prevents Western-Style High-Fat Diet-Induced Cognitive Impairment in Mice

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Objectives: Aging, obesity and a high-fat diet is associated with increased risk of cognitive impairment. Epidemiological studies suggest that increased fruits and vegetables (FV) intake is associated with a reduced risk of cognitive dysfunction. However, causal relationship between FV intake and cognition has not been established. The objective of this study was to investigate the causal effect of long-term FV supplementation in context of a low fat or Western-style high-fat diet in mice.

Methods: Using a 2×2 factorial prospective design, male C57BL/6J (5-wk) were randomly assigned to one of four groups (20/group): low fat control (LF-C, 10% kcal fat), high fat control (HF-C, 45% kcal fat), and each with 15% of a unique mixture of FV (patent pending) (w/w) (LF-FV and HF-FV). Novel object recognition test (NOR), a cognitive test for measuring exploration, memory, and object recognition, was performed to evaluate mouse cognitive function at

18 months. As rodents have an innate preference for exploring novelty, a mouse that remembers the familiar object will spend more time exploring the novel object, which indicates intact cognitive function. Next, recognition index (RI) was calculated based on the time the mouse spent exploring the new object over total object exploration time. The performance was analyzed with ANOVA, followed by Tukey's multiple comparisons test when appropriate.

Results: Compared to the LF-C group, mice fed the HF diet for 18 months had significantly lower RI in the NOR test (RI = 0.2100 for LF-C and RI = -0.04559 for HF-C, respectively, $p < 0.0001$), indicating cognitive impairment in the HF-C group. FV supplementation significantly mitigated the HF diet-induced cognitive impairment (RI = 0.2066 for HF-FV vs. RI = -0.04559 for HF-C, $p < 0.0001$). No significant difference in RI was observed between the LF-C mice (RI = 0.2100) and the LF-FV mice (RI = 0.2323).

Conclusions: This study provides evidence for a causal role of high intake of FV in preventing Western-style high-fat diet-induced cognition impairment in mice. The mechanisms by which FV improves cognitive function is currently under investigation.

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