

Low Vitamin K Intake Negatively Affects C57BL6 Mouse Survival and Cognition

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Objectives: Low dietary intake of vitamin K (VK), which is common among older adults, has been associated with age-related dementia and cognitive impairment. Aging and neurodegenerative diseases negatively affect hippocampal neurogenesis, and result in cognitive deficits, such as in learning and memory. The current study investigated the effects of low vitamin K intake on the potential factors affecting the cognitive functions in a C57BL6 mouse model.

Methods: Middle-aged (7–9 mo) C57BL6 mice (Charles River, n = 60) were randomly assigned by sex and diet (n = 15/group): low vitamin K males (LVKM, 80 μ g phyloquinone (PK)/kg diet), control diet males (CM, 1 mg PK/kg diet), low vitamin K females (LVKF), and control diet females (CFM) for 6 months. All animals were fed ad lib, and their body weight were recorded 1–2 times/week. At the completion of the 6-mo feeding period, behavioral tests, including the

rotarod, novel object task, and Morris water maze, were performed. Tissue samples were collected at the time of sacrifice (3 weeks after the behavioral tests) and PK content in liver samples were measured by HPLC.

Results: LVKM had significantly lower survival rate compared to CM (53.3% vs. 93.3% in control, $P < 0.05$). LVKM/F also had reduced body weight increases compared to the CM/F over the 6 mo feeding period ($P < 0.05$). The liver PK content in LVKM/F animals was significantly lower than that of CM/F (male: 6.2 ± 1.1 vs 30.2 ± 7.0 pmol/g, $P < 0.001$; female: 10.9 ± 2.4 vs 47.3 ± 10.3 pmol/g, $P < 0.001$). On the novel object task, LVKM/F showed reduced recognition memory compared to CM/F, while no significant differences were seen between LVKM/F and CM/F on the rotarod test. Additionally, LVKM had a non-statistical trend for a greater time to locate the platform in the Morris water maze, suggesting impaired spatial memory.

Conclusions: Low vitamin K intake significantly impaired survival and weight gain of C57BL6 mice, especially among males. Additionally, low vitamin K negatively impacted the learning- and memory-related cognitive functions. Future studies are required to establish the mechanisms, underlying these observations.

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