TrkB and neurogenesis are involved in enhancement of learning and memory by oral administration of food-derived hydrophilic amino acid ergothioneine in mice

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Oral administration of a food-derived hydrophilic amino acid ergothioneine (ERGO) enhances memory function in mice at clinically achievable plasma concentration. In the present study, we first tried to clarify effect of deficiency of ERGO in the memory function. Mice fed ERGO-free diet (ERGO-free mice) showed less cognitive function compared with mice fed with normal diet according to novel object recognition and spatial recognition tests. The decline in memory function in ERGO-free mice was recovered by oral administration of ERGO with a concomitant increase in ERGO concentration in hippocampus which plays an important role in memory. To evaluate mechanisms underlying the cognitive recovery by ERGO, we focused on hippocampal neurogenesis induced by tropomyosin receptor kinases B (TrkB), one of the neurotrophin receptors. The ERGO deficiency decreased area of new-born neuron marker Dcx-positive cells in hippocampus with a concomitant decrease in protein expression of phosphorylated-TrkB, whereas oral ERGO administration recovered these decreases. Moreover, a TrkB inhibitor ANA-12 significantly suppressed ERGO-induced enhancement of memory function and neurogenesis in the ERGO-free mice. These results suggest that memory deficits by ERGO deficiency would be at least partially caused by suppression of TrkB-mediated neurogenesis.