Cognitive Deficits of Early Aging Are Prevented by Vitamin D3: Underlying Mechanisms from the Hippocampal Transcriptome

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Despite the prevalence of vitamin D (VitD) deficiency, relatively little is known about how VitD affects the brain and cognitive function. Because calcium regulation in the brain is altered with aging and VitD is a major calcium regulatory hormone, we hypothesized that an increase in VitD levels may protect against age-related changes in behavioral and genomic function that are associated with cognitive decline. Since the decline in cognitive ability begins during midlife we reasoned this age may represent a critical window of opportunity for manipulating VitD levels.

In order to test the hypothesis that age-related brain decline is mediated by circulating VitD levels, dietary manipulation of VitD was initiated at midlife and continued for 4-5 months. Male rats (12 month old) were divided into three groups and fed diets containing varying amounts of VitD: low, normal (conventional), or high. Following chronic treatment, a memory-based water maze task was used to assess whether VitD status affects age related brain decline. Additional microarray studies were performed to identify potential gene pathways targeted by VitD in the brain.

We found that maintaining higher levels of VitD during middle-age appeared to be an important factor in preserving and extending healthy brain function and cognitive ability. Compared to animals on low or normal VitD diets, rats fed the high VitD diet were more successful in the memory-based task and showed selective expression of genes involved in synaptic function and plasticity.