COMMENT

Antiaging Supplement Holds Promise to Halt Age-Related Cognitive Deterioration

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The factors that affect aging processes are complex and poorly understood. However, the closely related molecules, growth hormone (GH) and insulin-like growth factor-1 (IGF-1), and corresponding downstream signaling factors play a major role in the regulation of aging and life span (1). Reduced signaling of this pathway profoundly slows aging and extends life span in yeast, worms, flies, and mice, a significant indication of an evolutionarily conserved mechanism.

It is well documented that GH levels begin to decline soon after the peripubertal period of rapid growth (reviewed in Ref. 2). This progressive decline in GH secretion has been termed the "somatopause" in humans. Decreased plasma IGF-1 concentrations parallel the decline in plasma GH levels. The lower levels of GH and IGF-1 in the elderly are thought to be responsible for many aspects of physical change in aging, including decreased muscle mass, strength, bone mineral density, energy, and increased fat mass. The enthusiasm for the potential benefits of GH replacement in aged individuals is severely dampened by the known adverse side effects (arthralgia, carpal tunnel syndrome, edema, hyperglycemia, and cancer; Ref. 3). Yet both GH and IGF-1 have been shown to be neuroprotective (4,5).

Endocrine mutant mice have provided tremendous insight into the role of hormones in aging. Transgenic mice overexpressing GH were created over 20 years ago and have been extensively studied since that time (reviewed in Ref. 6). Pathological changes in multiple organ systems and the shortened life spans observed in these mice are consistent with elevated oxidative damage. Surprisingly however, cognitive function in young GH transgenic mice is enhanced compared to age-matched normal mice (7). In a report selected as the Best Paper Award in the Experimental Biology category for 2003, Lemon and co-workers describe significant studies showing that a dietary supplement eliminates the age-related decline in cognitive function observed in GH transgenic mice (8).

This study was designed to determine (i) how the cognitive abilities of the GH transgenic mice change with age and (ii) if a specially formulated dietary supplement could alter the progression of the cognitive changes observed. Previously, Rollo and colleagues (7) showed that 50% of young GH transgenic mice learned a specific task before a single normal control. In addition, 30% of normal mice didn't even learn the task, while all the transgenic mice learned it within 24 trials. In the current study, female GH transgenic mice and age-matched normal mice were subjected to an eight-choice cued maze monitored with an overhead video camera and scored based on the number of trials required to learn the task and the total number of errors committed during learning. Mature mass data were also collected on these mice and larger groups of male transgenic and normal mice. The supplement used in this study consisted of 31 ingredients (detailed in the paper) with reported antiaging efficacy that could be ingested orally and safely (in humans). The dosages for mice were reformulated, prepared in a liquid form, and dried on bagel bits to facilitate consumption.

These important studies indicate that young untreated GH transgenic mice (<270 days of age) made fewer errors and required fewer trials to learn than age-matched normal mice. However, as early as 150 days of age, the learning

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ability of the untreated transgenic mice began to deteriorate. The deterioration increased to ~330 days, when most were unable to learn the task. Overall, scores of the young untreated GH transgenic mice were lower than age-matched normals and either group of older untreated mice. Importantly, the transgenic mice receiving the supplement had qualitatively and quantitatively different age-related patterns of learning compared to the untreated mice. A dramatic loss of cognitive function with increasing age was observed in the untreated GH transgenic mice, while a progressive improvement in learning ability with age was found in the treated transgenic group. The supplement had virtually no effect on growth of either the GH transgenic or the normal mice of either sex.

GH and IGF-1 are widely expressed in brain and may be operating at multiple levels that impact brain function. Insulin-like growth factors regulate brain development, and both GH and IGF affect neurotransmitter systems, particularly in regions involving cognition and memory. Importantly, the GH/IGF signal transduction pathways overlap with those involved in oxidative metabolism. The fact that these hormones influence antioxidative and apoptotic processes may be the underlying mechanism most affected by the antiaging supplement. Supplement administration offers a simple, noninvasive approach to reduce both inflammation and the harmful by-products of metabolism that cause significant cellular damage. Thus, this model may be promising in the quest to relieve age-related cognitive deterioration.

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