

OXIDATIVE STRESS AS A RISK FACTOR OF AGE-RELATED MEMORY IMPAIRMENT (AMI) IN C. ELEGANS

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Oxidative stress is associated with progressive declines of biological functions with increasing age. In the nematode, *C. elegans*, the nervous system is well preserved during aging, and thus it was not well explored about the effects of aging and oxidative stress on nervous functions. During aging, age-related decline was observed in an associative learning behavior, called thermotaxis learning. This learning behavior associates paired temperature and food stimulus. We further tested the effects of mutants that have altered levels of intrinsic oxidative stress. We used the Clk mutants (the *isp-1* and *clk-1* mutants) that have deficits in the function of the mitochondrial respiratory chain, leading to reduced levels of oxidative stress, increased longevity, and other phenotypes. The Clk mutants showed an increase in the performance of thermotaxis learning, while they modestly reduced motor activity. Consistently, the pretreatment of a metabolic antioxidant, alpha-Lipoic acid, also increased the performance of learning behavior. In contrast, mutants with increased oxidative stress showed severely impaired learning behavior and modestly reduced motor activity. Thus, it is unlikely that oxidative stress affects learning behavior through altering motor activity. Physiological levels of oxidative stress may be too high for learning behavior even in young adults. We propose that physiological oxidative stress limits the ability for cognitive functions.