Novel Analysis of Oxidative Stress and Inflammation on Amyloid-beta, Tau, and Motility in Transgenic C. elegans models: Targeting Potential Therapeutics for Alzheimer's Disease

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As the 6th leading cause of death in the United States, Alzheimer's disease (AD) is a progressive neurodegenerative disease that affects over 5.4 million Americans. Recent studies have hypothesized oxidative stress and inflammation as possible AD mechanisms, relating to toxic amyloid-beta (AB) plaque formation. The purpose of this study was to evaluate and compare the roles of antioxidants and anti-inflammatory agents on various AD aspects (AB aggregation, tau hyperphosphorylation, and neurodegenerative symptoms) to target potential therapeutics. Three transgenic strains of C. elegans were used: CL2006 (GFP-tagged AB), CL2120 (AB-related paralysis), and VH254 (tau hyperphosphorylation). The compounds examined were antioxidants a-lipoic acid and EGCG, and anti-inflammatory ibuprofen. Each strain was tested with and without each compound. Data was collected on days 1, 4, and 7 following age synchronization and inoculation. Fluorescence microscopy with Thioflavin S staining was used to study AB aggregation and tau fibril formation from hyperphosphorylation, while paralysis was used as a neurodegenerative motility indicator. All data was analyzed with a one-way ANOVA Scheffe post-hoc test or Bonferroni post-hoc test ($p<.05$). Day 7 data revealed a significant decrease in AB aggregation for all three treatments when compared to the control with a-lipoic acid as most effective ($p=.0046$). Ibuprofen was most proficient in significantly decreasing tau hyperphosphorylation ($p=.00426$) and paralysis ($p<.0001$). This study suggests that inflammation may have a larger role than oxidative stress in neurodegenerative AD symptoms. However, since each type of therapeutic had different significant effects, combinations of the two types may be synergistically beneficial in future therapies.

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