OXIDATIVE STRESS IN THE FRONTAL CORTEX OF DOWN SYNDROME BRAIN

A.L.S. Dowling¹, G. Cenini², F.A. Schmitt¹, D.A. Butterfield¹,², E. Head¹,³

¹Sanders-Brown Center on Aging, ²Department of Chemistry, Center of Membrane Sciences, ³Molecular
and Biomedical Pharmacology, University of Kentucky, Lexington, KY, USA

Introduction: Down syndrome (DS) is the most common genetic cause of mental retardation in children, and the number of adults with DS reaching old age is increasing. However, by the age of 40 years, virtually all people with DS have sufficient neuropathology for a neuropathological diagnosis of Alzheimer’s disease (AD). The triplication of chromosome 21 in DS leads to an overexpression of two important proteins involved in oxidative stress and AD, superoxide dismutase 1 (SOD1) and amyloid precursor protein (APP). Oxidative stress is known to be involved in the pathogenesis of AD.

Aim: We tested the hypothesis that brains of individuals with DS with AD have more oxidative and nitrosative stress than those of individuals with DS alone.

Methods: Protein carbonyls, 3-nitrotyrosine, and HNE-bound protein levels were measured in frozen frontal cortex samples from 68 autopsy cases using slot blots methods.

Results: Protein carbonyls but not 3-nitrotyrosine, and HNE-bound protein levels were significantly increased in the frontal cortex of individuals with DS with AD, as compared to individuals with DS alone.

Conclusions: Our results indicate that oxidative damage increases with age in DS, and is higher in those individuals with both DS and AD pathogenesis. These results suggest that oxidative damage may be involved with AD pathogenesis in DS. Treatment with antioxidants may provide a point of intervention to slow pathological aging in DS.

Supported by NIH/DHHS Grants #HD064993 to EH & FAS and #AG-05119 to DAB.