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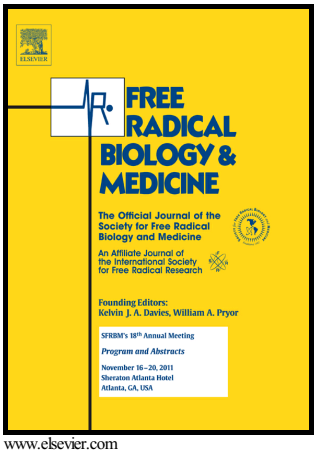

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Markers of oxidative damage to lipids, nucleic acids and proteins and antioxidant enzymes activities in Alzheimer's disease brain: a meta-analysis in human pathological specimens

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Abstract
Oxidative stress and decreased cellular responsiveness to oxidative stress are thought to influence brain aging and Alzheimer's disease, but the specific patterns of oxidative damage and the underlying mechanism leading to this damage are not definitively known. The objective of this study was to define the pattern of changes in oxidative-stress related markers by brain region in human Alzheimer's disease and mild cognitive impairment brain tissue. Observational case-control studies were identified from systematic queries of PubMed, ISI Web of Science and Scopus databases and studies were evaluated with appropriate quality measures. The data was used to construct a region-by-region meta-analysis of malondialdehyde, 4-hydroxynonenal, protein carbonylation, 8-hydroxyguanine levels and superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase activities. We also evaluated ascorbic acid, tocopherol, uric acid and glutathione levels. The analysis was complicated in several cases by publication bias and/or outlier data. We found that malondialdehyde levels were slightly increased in the temporal and occipital lobes and hippocampus, but this analysis was significantly impacted by publication bias. 4-hydroxynonenal levels were unchanged in every brain region. There was no change in 8-hydroxyguanine level in any brain region and protein carbonylation levels were unchanged except for a slight increase in the occipital lobe. Superoxide dismutase, glutathione peroxidase and reductase and catalase activities were not decreased in any brain region. There was limited data reporting non-enzymatic antioxidant levels in Alzheimer's disease brain, although glutathione and tocopherol levels appear to be unchanged. Minimal quantitative data is available from brain tissue from patients with mild cognitive impairment. While there is modest evidence supporting minor regional changes in markers of oxidative damage, this analysis fails to identify a consistent pattern of pro-oxidative changes and accumulation of oxidative damage in bulk tissue analysis in the setting of Alzheimer's disease, as has been widely reported.

Keywords: Mild cognitive impairment, malondialdehyde, hydroxynonenal, carbonylation, hydroxyguanine, superoxide dismutase, glutathione, catalase, tocopherol, ascorbic acid.