

Immunohistochemical localization of advanced glycation end products, pentosidine, and carboxymethyllysine in lipofuscin pigments of Alzheimer's disease and aged neurons.

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Abstract

Lipofuscins are intracellular fluorescent pigments accumulating in the central nervous system (CNS) with aging and degenerative processes such as Alzheimer's disease (AD). Although they are thought to be lipid peroxidation products derived from malondialdehyde, their biogenesis remains controversial. We further characterize the chemical nature of lipofuscins in brain tissues from AD patients and normal aged subjects. Advanced glycation end products (AGEs), pentosidine and carboxymethyllysine (CML), were identified by appropriate specific antibodies. They have physicochemical properties similar to those of lipofuscin and also increase with aging. Pentosidine and CML were identified in the neuronal perikarya and the extraneuroperikaryal deposits of both the AD and aged brain. Pentosidine, but not CML, was present in the fiber-like structure within the neuropil and the core of classical senile plaque. In the brain of young subjects without CNS disease, pentosidine and CML staining was faint. Pentosidine and CML co-localized with lipofuscin pigments in the neuronal perikarya of both the AD and aged brain. We demonstrate for the first time that lipofuscin is constituted not only of lipid peroxidation products but also from glycation products which may be the origin of fluorescent pigments. Lipofuscins should thus be considered as fluorescent pigments generated by lipid- and sugar-derived Schiff base-protein polymers.