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Elevated levels of 4-hydroxynonenal-histidine Michael adduct in the hippocampi of patients with Alzheimer's disease

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ABSTRACT

Alzheimer's disease (AD) is among the most common causes of progressive cognitive impairment in humans and is characterized by neurodegeneration in the brain. Lipid peroxidation is thought to play a role in the pathogenesis of AD. 4-hydroxynonenal (HNE) results from peroxidation of polyunsaturated fatty acids and it in turn gives evidence of lipid peroxidation *in vivo*. HNE reacts with protein histidine residue to form a stable HNE-histidine Michael adduct. To clarify the influence of lipid peroxidation on the pathogenesis of AD, we measured HNE-histidine Michael adduct in hippocampi from four AD patients and four age-matched controls by means of semiquantitative immunohistochemistry using a specific antibody to cyclic hemiacetal type of HNE-histidine Michael adduct. This antibody does not react with the ring-opened form of HNE-histidine Michael adduct and the pyrrole form of HNE-lysine Michael adduct. The HNE adduct was detected in the hippocampi of both AD and control donors, especially in the CA2, CA3 and CA4 sectors. Immunoreactive intensity of HNE adduct in these sectors were significantly higher in AD patients than in the controls. The HNE adduct was found in the perikarya of pyramidal cells in the hippocampus. These results show that the hippocampi of patients with AD undergo

lipid peroxidation and imply that this activity underlies the production of cytotoxic products such as HNE that are responsible for the pathogenesis of AD.

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