ALZHEIMER'S AMYLOID PEPTIDE AGGREGATION. INFLUENCE OF BIOLOGICAL MEMBRANES

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Amyloid plaques are a hallmark of central nervous systems affected by Alzheimer's disease. These plaques are formed by fibrils in which the main component is the so called b-amyloid peptide. The aggregation capacity of amyloid peptides depends on a conformational change which implies the conversion of α-helical structures into β-structures. This change is accepted to trigger the aggregation process, which follows a sygmoidal kinetics, usually interpreted as describing a nucleation dependent polymerization. The toxicity of the amyloid aggregates is related to the existence of low molecular weight aggregates present during the aggregation process. Extensive evidence for lipid peroxidation being an important factor in neurodegeneration and for the fact that it may influence the formation of fibrils exists in the literature.

Using the dye Thioflavin T, which fluorescence is dependent on the formation of amyloid fibrils, we have characterized the aggregation kinetics of Ab1-40 peptide in the presence of model membranes and as a function of lipid oxidation. Our data suggest that the presence of model membranes (liposomes) made up from a lipid brain extract speeds up the nucleation phase of the polymerization process whereas lipid oxidation slows it down. The effect of oxidized membranes on the peptide aggregation process is related to the appearance of a negative electrostatic surface potential on the lipid vesicles upon oxidation.