Alzheimer beta-amyloid peptide 25-35 : electrostatic interactions with phospholipid membranes

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The role of lipids in the aggregation of three Alzheimer model peptides was investigated with circular dichroism spectroscopy and high-sensitivity titration calorimetry under conditions of low ionic strength. In solution, the peptides beta AP(25-35)OH and beta AP(25-35Nle)NH2 exhibit a reversible random-coil<–>beta-sheet (or beta-structured aggregate) transition. Addition of lipid vesicles containing negatively charged lipids shifts the random-coil<–>beta-sheet equilibrium almost completely toward beta-sheet structure, which can be explained by the specific conditions created at the membrane surface: the cationic peptides are attracted to the negatively charged membrane, and the increase in peptide concentration together with the partial alignment of the peptide molecules then facilitates beta-sheet formation. The third peptide, beta AP-(25-35)NH2, also binds to the lipid membrane but was found to adopt an essentially random-coil structure, both with and without lipids. A quantitative characterization of the binding equilibrium was possible with high-sensitivity titration calorimetry. All three peptides exhibited exothermic binding enthalpies which varied between delta H approximately -2 kcal/mol for beta AP(25-35)OH and -8 kcal/mol for beta AP(25-35)NH2. The apparent binding constants, calculated with bulk concentrations, were large and varied between 500 and 5 x 10(4) M-1, depending on the experimental conditions. However, after correction for electrostatic charge effects using the Gouy-Chapman theory, the intrinsic binding constants were found to be constant and much smaller with K approximately 2-10 M-1.(ABSTRACT TRUNCATED AT 250 WORDS)

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