The β-stranded Aβ 29-42 peptide is bound to membrane

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The amyloid-β 1-40 and 1-42 peptides (Aβ) are together known to be the major component of senile plaques in Alzheimer's disease (AD). Nevertheless, the mechanisms of Aβ 1-40 and Aβ 1-42 toxicity are still poorly understood. But there is increasing evidence to show interactions between the carboxy-terminus of Aβ peptides and membranes. Molecular modeling has allowed us to advance that Aβ 29-42 is a tilted peptide: it penetrates membrane at an angle of70° as an α-helix. To investigate this hypothesis, we have studied the Aβ 29-42 peptide together with model membranes using solid-state NMR experiments. Density centrifugation analyses confirmed the binding of the peptide at a 2.5 % peptide to lipid molar ratio. ^{13}C MAS NMR experiments revealed that Aβ 29-42 presents mainly an α-helix in HFP and a β-strand conformation in the presence of membrane. The study of membrane dynamics using static ^{2}H NMR, with chain labeled lipids and Alanine methyl labeled peptide did not show any modification of the lipid and peptide dynamics upon binding. However ^{31}P low speed MAS spectrum has indicated a significant broadening of PC and PE resonances, indicating interaction with the lipid's polar heads. These results suggest that Aβ 29-42 adopts a β-strand conformation when bound to lipids and does not penetrate membrane.