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Changes in lipid membrane may trigger amyloid toxicity in Alzheimer's disease.

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Alzheimer's disease (AD) is a neurodegenerative disease characterized by dementia and memory loss for which no cure or prevention is available. Amyloid toxicity is a result of the non-specific interaction of toxic amyloid oligomers with the plasma membrane which induce damage and death of neuronal cells. Understanding these interactions is of high importance.

We studied interaction of amyloid beta (1-42) peptide with lipid membrane using atomic force microscopy (AFM), Kelvin probe force microscopy (KPFM), black lipid membrane (BLM) and surface Plasmon resonance (SPR). We demonstrated that composition, structure and properties of lipid membrane play an active role in amyloid binding and toxicity: changes in membrane composition mimicking AD increase amyloid binding and toxicity. Effect of lipid composition, the presence of cholesterol and melatonin are discussed. We demonstrated that membrane cholesterol creates nanoscale electrostatic domains which induce preferential binding of amyloid peptide, while membrane melatonin changes the properties of the membrane and protects the membrane from amyloid binding and damage. These findings contribute to better understanding of the molecular mechanisms of Alzheimer's disease and aid to the developments of novel strategies for cure and prevention of AD.

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