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Influence of Neurodegenerative Peptide and Non-steroidal Anti-inflammatory Drugs on the Dynamics of Brain Lipid Membrane Mimetic Systems

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Amyloid β42 (Aβ42), a neurodegenerative peptide, undergoes various morphological changes in the pathway of forming plaques, a principal cause of Alzheimer's disease, and can alter the membrane integrity. Furthermore, non-steroidal anti-inflammatory drugs (NSAIDs) are the most widely prescribed for their anti-inflammatory, antipyretic, analgesic and antiplatelet characteristics. The influence of Aβ42 and NSAIDs on the dynamics of single lipid membrane mimetic systems is widely studied. However, a single lipid membrane mimetics system is not an ideal representative of a multicomponent and complex cell membrane. Here, we have investigated the influence of Aβ42–monomer (m), aspirin (Asp), diclofenac (Diclo) and ibuprofen (Ibu), at different concentrations, on the dynamics and structure of BLs-ULVs using quasielastic neutron scattering (QENS), neutron spin echo (NSE) and small angle neutron scattering (SANS). We have prepared unilamellar vesicles (ULVs) using brain lipids (BLs), extracted from the porcine brain tissues, representing a physiologically relevant membrane system. Normalized QENS spectra showed that Aβ42–m induces higher QE broadening, suggesting substantially faster dynamics than pure BLs. For NSAIDs, higher QE broadening is observed for Asp at 10 and 30mol%, Diclo at 10mol% and Ibu at 10 and 20 mol%. This suggests that each NSAIDs at a different concentration has a unique effect on the BLs dynamics. The QENS spectra corresponding to BLs with and without Aβ42–m, Asp, Diclo and Ibu are described by two Lorentzian such that there are motion on two different time scales slow lateral and fast internal motion of BLs. Variation of half width half maxim (HWHM) shows that Aβ42–m mainly enhances internal motion (Γint) and does not affect the lateral motion (Γlat). In the case of NSAIDs, Γlat and Γint are increases in the presence of Asp at 10 and 30mol%, and Ibu at 10 and 20mol%. Whereas, Diclo does not affect the Γlat but enhances Γint at 10mol%. NSE spectra, described by the Zilmann and Granek model, showed that Aβ42–m does not affect the bending rigidity modulus (κKBT). Whereas, Asp enhances the κKBT at all concentrations and Diclo and Ibu reduce and increase the κKBT at 30 and 20mol%, respectively. The SANS result showed that Aβ42–m and NSAIDs do not affect the BLs-ULV structures. This study provides insights into the influence of Aβ42–m and NSAIDs on the dynamics of physiologically relevant BLs-ULVs membrane systems.

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