

Public Abstract

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Title:AMYLOID-BETA PEPTIDE INDUCES TEMPORAL MEMBRANE BIPHASIC CHANGES IN ASTROCYTES THROUGH CYTOSOLIC PHOSPHOLIPASE A2

Oligomeric amyloid-beta peptide (AB) is known to induce cytotoxic effects and damage cell functions in Alzheimers disease. However, mechanisms underlying the effects of AB on cell membranes have yet to be fully elucidated. In this study, AB1-42 (AB42) was shown to cause a temporal biphasic change in membranes of astrocytic DITNC cells using fluorescence microscopy of Laurdan. AB42 made astrocyte cell membranes become more molecularly-disordered after 30 minutes to 1 hour, transitioning to more molecularly-ordered after 3 hours. However, AB42 caused artificial vesicle membranes made of rat whole brain lipid extract to become more disordered only. The trend for more molecularly-ordered membranes in astrocytes was abrogated by either an NADPH oxidase inhibitor, apocynin, or an inhibitor of cytosolic phospholipase A2 (cPLA2), but not by an inhibitor of calcium-independent PLA2 (iPLA2). Apocynin also suppressed the increased production of superoxide anions (O<sub>2</sub><sup>-</sup>) and phosphorylation of cPLA2 induced by AB42. In addition, hydrolyzed products of cPLA2, arachidonic acid (AA), but not lysophosphatidylcholine (LPC) caused astrocyte membranes to become more molecularly-ordered. These results suggest (1) a direct interaction of AB42 with cell membranes making them more molecularly-disordered, and (2) AB42 indirectly makes membranes become more molecularly-ordered by triggering the signaling pathway involving NADPH oxidase and cPLA2.