

Public Abstract

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Title:The role of Phospholipase A2 in Amyloid Beta uptake by microglia

The accumulation of amyloid-beta (Abeta) is a key characteristic of Alzheimer's disease (AD). Microglia are the principle macrophages in the brain and are known to internalize Abeta, however the phagocytic function is impaired as AD progresses. Cytosolic phospholipase A2 (cPLA2) and calcium-independent PLA2 (iPLA2) are two major groups of PLA2s that are involved in modulating membrane properties, intracellular trafficking and the cellular inflammatory response. Here, we study the role of cPLA2 and iPLA2 in the uptake of Abeta1-42 by microglia in vitro. We found that the uptake of Abeta1-42 was rapid (<15 minutes) and remained unchanged up to 60 minutes. Also, inhibition of cPLA2 greatly reduced Abeta1-42 uptake while increasing cPLA2 activation did not affect Abeta1-42 uptake. iPLA2 appears to reduce the rate of Abeta1-42 uptake, but had no influence on the uptake level after 30 minutes. Furthermore, the incomplete depletion of Abeta1-42 occurred within 5 minutes after uptake, with no detectable depletion occurring in the following 60 minutes. cPLA2 and iPLA2 are not involved in intercellular processing of Abeta1-42. Instead, the results suggest the Abeta1-42 undergoes processing in the lysosome to reduce the intercellular presence of Abeta1-42. This study highlights the fact that microglia participate in Abeta1-42 clearance and depletion via cPLA2 endocytosis.