Ultrastructural Analysis of b-Amyloid, Islet Amyloid and Prion Protein Induced Cell Death in Cultured Neurons [MAS]

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Previous investigations have demonstrated aggregated, but not soluble, synthetic b-amyloid (Ab) may induce cell death in cultured neurons via programmed cell death, or apoptosis. Aggregated Ab is characterized by a secondary b-pleated sheet structure which may contribute to its toxicity. In order to further explore the role of b-pleated sheet 2° structure in neuronal toxicity, we undertook a comparative ultrastructural morphological analysis of three peptide aggregates that share the b-pleated sheet configuration, Ab (23-35), prion protein and islet amyloid. Scanning electron microscopic analysis of Ab (25-35) treated cultures revealed limited somal blebbing as early as 4 hrs following treatment and continued to increase in occurrence throughout the 24 hr experimental period. Blebbing occurred globally on an affected cell and did not appear restricted to sites of visible amyloid contact. Ultimately, continued blebbing resulted in somal fragmentation into multiple apoptotic bodies. Transmission electron microscopic analysis of all three peptide treatment groups revealed distinct chromatin condensation and nuclear fragmentation, prominent cytoplasmic vacuole formation, dispersal of polyribosome rosettes and the disappearance of the golgi complex, smooth endoplasmic reticulum and microtubules with increased cytoplasmic electron density. Reduced numbers of mitochondria and cisternae of rough endoplasmic reticulum remained intact throughout the process of cell death. These structural alterations are consistent with earlier morphological descriptions of apoptosis suggesting that all three peptides share a common mechanism of programmed cell death in which the b-pleated sheet configuration may play an important role.