HERPES SIMPLEX VIRUS TYPE I (HSV-1) INDUCES THE ACCUMULATION OF INTRACELLULAR β-AMYLOID IN AUTOPHAGIC COMPARTMENTS IN HUMAN NEUROBLASTOMA CELLS

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Introduction: HSV-1 is a neurotropic virus that has been implicated in the pathogenesis of several neurological disorders, including Alzheimer's disease (AD). In addition, it has been reported that HSV-1 is also able to modulate autophagy. Autophagy, a process involved in the degradation of proteins via the lysosomal compartment, might be involved in the aberrant deposits of aggregated proteins seen in brains affected by neurodegenerative diseases.

Aims: A model based on the human neuroblastoma cell line SK-N-MC stably expressing human APP was used to analyze the effect of HSV-1 infection on β-amyloid peptide (Aβ) levels and the autophagic process.

Methods: Aβ and LC3 distribution was analyzed by confocal microscopy. Aβ quantification was performed by ELISA assays. Observation of autophagic structures was performed by electronic microscopy.

Results: This work reports that HSV-1 provokes the intracellular accumulation of Aβ and induces an intense inhibition of Aβ secretion. Further, HSV-1 induces a strong increase in LC3 lipidation, the main marker of autophagy, and triggers the accumulation of intracellular autophagic compartments. HSV-1 induced-autophagy is incomplete because the fusion of autophagosomes with lysosomes is aborted. In addition, Aβ is localized in the autophagic compartments indicating that accumulation of Aβ and autophagosomes are strongly related in HSV-1-infected cells.

Conclusions: The accumulation of Aβ in autophagosomes induced by HSV-1 could be caused by the inhibition of Aβ secretion and the failure of Aβ degradation in the autophagic compartments. These data suggest that HSV-1 infection modulates autophagy and APP processing, contributing to the accumulation of Aβ characteristic of AD.