Review J Alzheimers Dis. 2020;77(1):15-31. doi: 10.3233/JAD-200607.

Independent and Correlated Role of Apolipoprotein E ε4 Genotype and Herpes Simplex Virus Type 1 in Alzheimer's Disease

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PMID: 32804091 DOI: 10.3233/JAD-200607

Abstract

The ε4 allele of the Apolipoprotein E (APOE) gene in individuals infected by Herpes simplex virus type 1 (HSV-1) has been demonstrated to be a risk factor in Alzheimer's disease (AD). APOE-ε4 reduces the levels of neuronal cholesterol, interferes with the transportation of cholesterol, impairs repair of synapses, decreases the clearance of neurotoxic peptide amyloid-β (Aβ), and promotes the deposition of amyloid plaque, and eventually may cause development of AD. HSV-1 enters host cells and can infect the olfactory system, trigeminal ganglia, entorhinal cortex, and hippocampus, and may cause AD-like pathological changes. The lifecycle of HSV-1 goes through a long latent phase. HSV-1 induces neurotropic cytokine expression with pro-inflammatory action and inhibits antiviral cytokine production in AD. It should be noted that interferons display antiviral activity in HSV-1-infected AD patients. Reactivated HSV-1 is associated with infectious burden in cognitive decline and AD. Finally, HSV-1 DNA has been confirmed as present in human brains and is associated with APOEε4 in AD. HSV-1 and APOEε4 increase the risk of AD and relate to abnormal autophagy, higher concentrations of HSV-1 DNA in AD, and formation of Aβ plaques and neurofibrillary tangles.

Keywords: Alzheimer's disease; apolipoprotein E; cytokine; estrogen therapy; herpes simplex virus type 1; infectious burden; interferon.

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