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GENETICS

Herpes Simplex Virus type 1 DNA associated with brain region specific Tau levels measured by PET imaging

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Abstract

Background: Evidence suggests Herpes simplex virus type 1 (HSV-1) infection is associated with Alzheimer's Disease (AD). Latent herpes infections may contribute to the development of amyloid and tau pathology, however, the specific relationship between HSV-1 presence in cells and the deposition of amyloid or tau remains poorly understood.

Method: HSV-1 DNA was quantified in whole-genome sequencing (WGS) data generated by the Alzheimer's Disease Sequencing Project (ADSP) that were obtained from participants (**67 cases** and **505 cognitively normal controls)** of **ADNI** and the Wisconsin Registry for Alzheimer's Prevention**, of which the majority were of European ancestry.** Amyloid-β and tau PET imaging data were obtained from the ADSP phenotype harmonization consortium. The association between HSV-1 DNA quantity and log-transformed standardized uptake value ratios (SUVRs) of amyloid-β and tau that were measured in several brain regions was evaluated using linear regression models including covariates for AD status, age, and gender.

Result: 300 participants had detectable HSV-1 DNA. No significant associations were identified between HSV-1 DNA and amyloid PET imaging metrics. However, we identified an association of HSV-1 with decreased tau in numerous brain regions, but saw no association with increased tau levels once all covariates were accounted for. HSV-1 was associated with decreased tau levels in the right hippocampus (β = -0.063, $p = 7.93 \times 10^{-11}$) and left hippocampus (β = -0.054, $p = 1.12 \times 10^{-7}$). Additionally, we observed negative associations between HSV-1 DNA and tau in cerebral white matter (β = -0.0406, $p = 3.94 \times 10^{-9}$), amygdala (β = -0.0547, $p = 2.70 \times 10^{-8}$), CSF (β = -0.0302, $p = 7.61 \times 10^{-8}$), and caudate (β = -0.0631, $p = 6.81 \times 10^{-15}$).

Conclusion: Our findings suggest that the effect of HSV-1 infection is complex and potentially protective against tau buildup in many brain regions. Conversely, tau may have a protective effect against HSV-1. These findings highlight the need for further research to elucidate the mechanisms underlying the relationship between HSV-1 and tau and their potential implications for neurodegenerative processes.