Perspective Article

HUMAN PAPILLOMAVIRUS AND ITS POTENTIAL IMPACT ON ALZHEIMER'S AND PARKINSON'S DISEASES

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Abstract

Background: Neurodegenerative diseases such as Alzheimer's Disease (AD) and Parkinson's Disease (PD) have been widely studied, with emerging evidence suggesting that viral infections may play a role in their onset and progression. This study utilizes a two-sample Mendelian Randomization (MR) approach to assess potential causal links between Human Papillomavirus (HPV) infection and these neurodegenerative diseases.

Methods: A two-sample MR analysis was conducted using Instrumental Variables (IVs) derived from Genome-Wide Association Studies (GWAS) data. SNPs associated with HPV16 and HPV18 E7 proteins, as well as HPV seropositivity, were analyzed in relation to AD and PD risk. Sensitivity analyses, including Cochran's Q-test and MR-Egger intercept, were performed to evaluate robustness and potential pleiotropy.

Results: The findings indicate that exposure to the HPV18 E7 protein may have a protective effect against PD, whereas HPV seropositivity was identified as a risk factor. However, no significant association was observed between HPV16 E7 protein or HPV seropositivity and AD.

Conclusions: These results highlight the complex role of viral infections in neurodegenerative diseases. Further studies are needed to validate these findings and explore the underlying mechanisms by which HPV may influence PD risk. ***ASEAN Journal of Psychiatry, Vol. 27 (1) January, 2026; 1-2.***

Keywords: Alzheimer's Disease; Parkinson's Disease; Human Papillomavirus; Mendelian Randomization

Introduction

Alzheimer's Disease (AD) and Parkinson's Disease (PD) are among the most prevalent neurodegenerative disorders worldwide, significantly impacting public health and economic resources. Recent studies have suggested that infectious agents, including viruses, might play a role in neurodegeneration. The involvement of the Human Papillomavirus (HPV) in cancers and immune modulation raises questions about its potential impact on neurodegenerative diseases. This study employs a two-sample Mendelian Randomization (MR) approach to investigate potential causal relationships between HPV infection and the risk of AD and PD.

Description

Data sources and selection of instrumental variables

Data on HPV exposure, including HPV16 and HPV18 E7 protein levels and seropositivity, were obtained from the MRC Integrative Epidemiology Unit (IEU) OpenGWAS and GWAS Catalog. The outcome datasets for AD and PD were sourced from the same repository, ensuring population consistency. SNPs significantly associated with HPV exposure ($p<5 \times 10^{-5}$) were selected as Instrumental Variables (IVs) and pruned for linkage disequilibrium ($r^2<0.01$, 5000 kb window).

Mendelian randomization analysis

Seven MR methods were applied, including Inverse Variance Weighted (IVW), MR-Egger regression, weighted median, weighted mode, and MR-PRESSO, to assess potential causal relationships. Sensitivity analyses, including Cochran's Q-test and leave-one-out analyses, were conducted to evaluate heterogeneity and pleiotropy.

Causal effect of HPV infection on Parkinson's disease

The analysis identified a significant association between HPV18 E7 protein exposure and PD, suggesting a protective effect (IVW OR: 0.20, 95% CI: 0.16–0.25, p=1.17E-45). HPV seropositivity was identified as a risk factor for PD (IVW OR: 1.26, 95% CI: 1.02–1.56, p=0.0356).

Causal effect of HPV infection on Alzheimer's disease

No significant causal relationship was detected between HPV16 E7 protein, HPV seropositivity, and AD risk ($p>0.05$ across all MR methods).

Sensitivity analyses

Cochran's Q-test indicated heterogeneity in some models, particularly for HPV18 E7 and PD. The MR-Egger intercept test suggested no significant horizontal pleiotropy. The leave-one-out analysis confirmed the robustness of the observed associations.

Our findings suggest that HPV18 E7 protein may confer a protective effect against PD, while HPV seropositivity may increase PD risk. This aligns with previous studies indicating that viral infections influence neurodegeneration. The protective role of HPV18 E7 could be related to immune system modulation, which warrants further investigation. The lack of association between HPV and AD suggests that different pathogenic mechanisms may underlie these diseases.

Limitations of this study include the use of European population-based GWAS data, which may limit generalizability to other ethnic groups. Additionally, while MR analysis provides evidence of causality, the underlying biological mechanisms remain to be elucidated.

Conclusion

This study provides novel insights into the relationship between HPV infection and neurodegenerative diseases, suggesting a protective role for HPV18 E7 against PD and an increased risk of PD with HPV seropositivity. Further mechanistic and epidemiological studies are needed to confirm these findings and explore potential therapeutic implications.

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