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Research Article

Herpesviridae infections, neuroinflammatory pathways, and interleukin-6 (rs1800795) gene polymorphism contribute to Parkinson's disease susceptibility: a cross-sectional study involving viral DNA detection, cytokine profiling, and gene expression analysis

Herpesviridae-Infektionen, neuroinflammatorische Signalwege und der IL-6-rs1800795-Polymorphismus tragen zur Anfälligkeit für die Parkinson-Krankheit bei: eine Querschnittstudie unter Einbeziehung der Virus-DNA-Detektion, Zytokindifferenzierung und Genexpressionsanalyse

Abstract

Background: Parkinson's disease (PD) is a neurodegenerative disorder characterized by motor dysfunction and non-motor symptoms, with emerging evidence implicating neuroinflammation and oxidative stress in its pathogenesis. While associations between PD and viral infections, particularly those caused by the Herpesviridae family, have been hypothesized, the molecularbiological relationships remain poorly understood. This study investigates the role of herpesvirus infections (e.g., HSV-1, VZV, EBV, CMV) and inflammatory mediators (IL-6, iNOS, COX-2) in PD pathophysiology, alongside genetic polymorphisms in cytokine-related genes.

Materials and methods: A cross-sectional study was conducted on 50 PD patients and 50 healthy controls. Blood samples were analyzed for herpesvirus DNA using multiplex PCR. Serum IL-6 levels were quantified via ELISA, while gene expression of pro-inflammatory markers iNOS and COX-2 was assessed in PD patients co-infected with Varicella Zoster Virus (VZV) using real-time PCR. Genetic polymorphism (rs1800795) in the IL-6 gene was evaluated via amplification refractory mutation system (ARMS)-PCR. Statistical analyses included ANOVA, chi-squared tests, and ROC curve modeling to determine diagnostic accuracy.

Results: Multiplex PCR revealed higher prevalence of herpesviruses (particularly VZV and HSV-1) in PD patients compared to controls ($p<0.05$). Serum IL-6 levels were significantly elevated in PD patients with viral infections (mean±SD: 34.8±12.6 pg/ml vs. controls 18.2±9.3 pg/ml, $p<0.001$). Real-time PCR demonstrated upregulated iNOS (fold change: 2.13±0.45) and COX-2 (fold change: 3.27±0.68) expression in VZV-infected PD patients. ARMS-PCR identified a significant association between the IL-6 rs1800795 CC genotype and increased PD risk (OR: 2.89, 95% CI: 1.34–6.23). ROC analysis confirmed high diagnostic sensitivity (AUC: 0.91) for IL-6 in distinguishing PD patients with viral infections.

Conclusion: This study establishes a novel link between herpesviridae infections, neuroinflammatory pathways, and PD susceptibility. Elevated IL-6 and pro-inflammatory gene expression in co-infected patients suggest a synergistic role of viral activation and immune dysregulation in PD progression. The association of IL-6 polymorphism rs1800795 with PD risk highlights potential genetic vulnerabilities. These findings advocate for further mechanistic studies to elucidate virus-driven

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neuroinflammation in PD and emphasize the utility of inflammatory biomarkers for early diagnosis and targeted therapies.

Keywords: Parkinson's disease, neuroinflammation, oxidative stress, herpesviridae, interleukin-6, cyclooxygenase-2, genetic polymorphism, multiplex pcr

Zusammenfassung

Zielsetzung: Die Parkinson-Krankheit (PD) ist eine neurodegenerative Erkrankung, gekennzeichnet durch motorische Dysfunktionen und nichtmotorische Symptome. Wachsende Evidenz weist auf die Beteiligung von Neuroinflammation und oxidativem Stress an ihrer Pathogenese hin. Während Assoziationen zwischen PD und viralen Infektionen, insbesondere durch die Familie der Herpesviridae, postuliert wurden, bleiben die molekularbiologischen Zusammenhänge weitgehend ungeklärt. Diese Studie untersucht die Rolle von Herpesvirusinfektionen (z.B. HSV-1, VZV, EBV, CMV) sowie entzündlichen Mediatoren (IL-6, iNOS, COX-2) in der Pathophysiologie der PD, ergänzt durch genetische Polymorphismen in zytokinverknüpften Genen.
Material und Methode: Eine Querschnittstudie wurde an 50 PD-Patienten und 50 gesunden Kontrollpersonen durchgeführt. Blutproben wurden mittels Multiplex-PCR auf Herpesvirus-DNA analysiert. Die Serum-IL-6-Spiegel wurden über ELISA quantifiziert, während die Genexpression der pro-inflammatorischen Marker iNOS und COX-2 bei PD-Patienten mit Koinfektion durch das Varicella-Zoster-Virus (VZV) mittels Echtzeit-PCR bewertet wurde. Der genetische Polymorphismus (rs1800795) im IL-6-Gen wurde durch Amplifikations-resistentes Mutationssystem (ARMS)-PCR analysiert. Statistische Auswertungen umfassten ANOVA, Chi-Quadrat-Tests und ROC-Kurvenmodellierung zur Bestimmung der diagnostischen Genauigkeit.
Ergebnisse: Die Multiplex-PCR zeigte eine höhere Prävalenz von Herpesviren (insbesondere VZV und HSV-1) bei PD-Patienten im Vergleich zu Kontrollen ($p<0,05$). Die Serum-IL-6-Spiegel waren bei PD-Patienten mit Virusinfektionen signifikant erhöht (Mittelwert±SD: 34,8±12,6 pg/ml vs. Kontrollen: 18,2±9,3 pg/ml, $p<0,001$). Die Echtzeit-PCR demonstrierte eine Hochregulation von iNOS (Fold-Change: 2,13±0,45) und COX-2 (Fold-Change: 3,27±0,68) bei VZV-infizierten PD-Patienten. ARMS-PCR identifizierte eine signifikante Assoziation zwischen dem IL-6-rs1800795-CC-Genotyp und einem erhöhten PD-Risiko (Odds Ratio [OR]: 2,89, 95%-Konfidenzintervall [KI]: 1,34–6,23). Die ROC-Analyse bestätigte eine hohe diagnostische Sensitivität (AUC: 0,91) für IL-6 bei der Differenzierung von PD-Patienten mit Virusinfektionen.
Fazit: Diese Studie etabliert eine neuartige Verbindung zwischen Herpesviridae-Infektionen, neuroinflammatorischen Signalwegen und der Anfälligkeit für die Parkinson-Krankheit. Erhöhte IL-6-Spiegel und die Hochregulation pro-inflammatorischer Gene bei Koinfektionen deuten auf eine synergistische Rolle der viralen Aktivierung und Immunregulierung bei der PD-Progression hin. Die Assoziation des IL-6-Polymorphismus rs1800795 mit dem PD-Risiko unterstreicht potenzielle genetische Vulnerabilitäten. Diese Befunde fordern weitere mechanistische Studien zur Aufklärung der virusgetriebenen Neuroinflammation bei PD und betonen den Nutzen entzündlicher Biomarker für die Frühdiagnose und zielgerichtete Therapien.

Schlüsselwörter: Parkinson-Krankheit, Neuroinflammation, Oxidativer Stress, Herpesviridae, Interleukin-6, Cyclooxygenase-2, Genetischer Polymorphismus, Multiplex-PCR

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the selective loss of dopaminergic neurons in the substantia nigra pars compacta, leading to cardinal motor symptoms such as bradykinesia, rigidity, tremor, and postural instability [1], [2]. Beyond motor dysfunction, non-motor manifestations—including cognitive decline, sleep disturbances, and autonomic dysfunction—underscore the heterogeneity of PD pathology [3]. Despite extensive research, the precise etiological mechanisms driving neurodegeneration remain incompletely elucidated [4]. Accumulating evidence implicates a triad of oxidative stress, mitochondrial dysfunction, and neuroinflammatory cascades as central contributors to dopaminergic neuronal death [5], [6]. However, the role of environmental triggers, particularly latent viral infections, in modulating these pathways has emerged as a critical yet underexplored area in PD research [7]. The herpesviridae family, comprising neurotropic viruses such as herpes simplex virus type 1 (HSV-1), varicella zoster virus (VZV), Epstein-Barr virus (EBV), and cytomegalovirus (CMV), has garnered increasing attention for its potential role in neurodegenerative diseases [8]. These viruses exhibit lifelong latency in neural tissues, with reactivation linked to systemic and central nervous system (CNS) inflammation [9]. Preclinical models suggest that herpesvirus-induced neuroinflammation may exacerbate protein misfolding, disrupt blood-brain barrier integrity, and activate microglial-driven cytokine release, all of which intersect with PD pathophysiology [10]. Notably, HSV-1 has been associated with a-synucleinopathy in animal models, while VZV reactivation correlates with increased risk of parkinsonism in epidemiological studies. However, the molecular interplay between herpesvirus infections, pro-inflammatory mediators, and genetic predispositions in human PD remains poorly defined [11].

Interleukin-6 (IL-6), a pleiotropic cytokine with dual roles in acute-phase response and chronic inflammation, has been implicated in PD progression [12]. Elevated IL-6 levels in cerebrospinal fluid (CSF) and serum of PD patients correlate with disease severity, suggesting its utility as a biomarker [13]. Furthermore, the IL-6 gene promoter polymorphism rs1800795 (-174 G>C) has been associated with altered cytokine production and susceptibility to inflammatory disorders [14]. Nevertheless, its contribution to PD risk, particularly in the context of viral infections, remains unexplored. Concurrently, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), key enzymes in inflammatory signaling, are upregulated in PD-affected brain regions [15]. Their expression is transcriptionally regulated by nuclear factor-κB (NF-κB), a pathway activated during viral infections, suggesting the hypothesis that herpesvirus reactivation may synergistically amplify neurotoxic inflammation in PD [16].

This study addresses critical gaps in the understanding of how herpesviridae infections intersect with neuroinflammatory pathways and genetic susceptibility to drive PD pathogenesis. Utilizing a cross-sectional design, we employed multiplex PCR to detect herpesvirus DNA in PD patients and controls, coupled with ELISA and real-time PCR to quantify IL-6 levels and iNOS/COX-2 expression. The IL-6 rs1800795 polymorphism was analyzed via ARMS-PCR to assess its association with PD risk. By integrating virological, immunological, and genetic data, we aimed to delineate the mechanistic link between viral latency/reactivation, inflammatory biomarker elevation, and genetic vulnerabilities in PD. These findings may redefine PD as a multifactorial disorder influenced by host-virus interactions, offering novel diagnostic and therapeutic avenues targeting neuroinflammation and viral co-pathologies.

Materials and methods

Study design

This cross-sectional study evaluated 50 patients diagnosed with idiopathic Parkinson's disease (PD) and 50 age- and sex-matched healthy controls (HC). Participants were recruited from neurology clinics between January 2022 and December 2023. Inclusion criteria for PD patients adhered to the UK Brain Bank diagnostic criteria, while controls were excluded if they had neurological disorders, autoimmune diseases, or recent infections. The study was approved by the Institutional Ethics Committee (IR.SSU.REC.1403.01908) and conducted under the Declaration of Helsinki.

Sample collection and processing

Peripheral blood samples (10 mL) were collected via venipuncture from all participants after overnight fasting. Serum was separated by centrifugation at 3,000 × g for 10 minutes (HERMILE-Labnet Centrifuge) and aliquoted into cryovials. Whole blood was stored in EDTA tubes for genomic DNA extraction. Samples were maintained at -80 °C until analysis to prevent RNA degradation.

Viral DNA extraction and multiplex PCR

Viral DNA was extracted from 200 µL serum using the QIAamp MinElute Virus Spin Kit (QIAGEN, Germany) per the manufacturer's protocol. Eluted DNA (50 µL) was subjected to multiplex PCR to detect herpesviridae family viruses, including HSV-1, VZV, EBV, CMV, HHV-6, and HHV-8. Primers targeting conserved regions of herpesvirus DNA polymerase genes were used (Table 1). The reaction mixture (25 µL) contained 12.5 µL 2× Master Mix (Ampliqon, Denmark), 1 µL template DNA, and 1 µL of each primer pair. Thermal cycling was performed on a CFX96 Touch Real-Time PCR System (Bio-Rad, USA) with the following conditions: initial denaturation at 95 °C for 5 minutes; 35 cycles of denaturation at 95 °C for 30 seconds, annealing at 58 °C for 45 seconds, extension at 72 °C for 1 minute; and final extension at 72 °C for 10

Table 1: Primer sequences for herpesvirus detection

Virus	Primer sequence (5′–3′)	Amplicon size (bp)
HSV-1	F: GACGACATGGGCGGCAGCGAA R: CCCGTTCGTTCGTCCGGAGGT	450
VZV	F: GGCCAGGCGCTCGTACGTG R: CGGTTGTCCGACGTCCAGCAC	320
EBV	F: AGCCCATGTTGTAGCAAACCCTCA R: TCTGTAGTTCAGCGGAGAGGAC	198

minutes. PCR products were resolved on 2% agarose gels and visualized under UV transillumination.

Serum IL-6 quantification by ELISA

Serum IL-6 concentrations were measured using a commercial ELISA kit (BT Lab, China) according to the manufacturer's instructions. Briefly, 50 µL of standard or sample was added to pre-coated 96-well plates, followed by 10 µL of anti-IL-6 antibody and 50 µL of streptavidin-HRP conjugate. The plate was sealed with foil and incubated at 37 °C for 60 minutes on a microplate shaker. After five washes with buffer, 100 µL of TMB substrate was added, and absorbance was read at 450 nm using a Bio-Rad iMark Microplate Reader. A standard curve was generated using Excel, and concentrations were interpolated from the curve.

RNA extraction and real-time PCR for iNOS and COX-2

Total RNA was extracted from peripheral blood mononuclear cells (PBMCs) using the Denazist RNA Extraction Kit (Denazist, Iran). cDNA was synthesized from 1 µg RNA using the BioFact cDNA Synthesis Kit (BioFact, South Korea). Real-time PCR was performed on a CFX96 Touch System with SYBR Green Master Mix (Bio-Rad, USA). Primers for iNOS (F: TAAGGTACCAATGCCACACCAAGCAGACGC; R: AATCCCGGGGAACACACTGGCAGCCAAGAA) and COX-2 (F: TGGGAAGCCTTCTCTAACCTCTCCT; R: CTTTGACTGTGGGAGGATACATCTC) were designed based on GenBank sequences (Table 2). The reaction protocol included initial denaturation at 95 °C for 3 minutes; 40 cycles of 95 °C for 10 seconds, 60 °C for 30 seconds; and melt curve analysis.
Gene expression was normalized to GAPDH and analyzed using the 2^-ΔΔCt method.

Genotyping of IL-6 rs1800795 polymorphism

Genomic DNA was extracted from whole blood using the GeneAll Hybrid-RTM Kit (GeneAll, South Korea). The IL-6 rs1800795 (-174 G>C) polymorphism was analyzed via amplification refractory-mutation system PCR (ARMS-PCR). Four primers were designed to distinguish the G and C alleles (Table 3). PCR was performed in a 25 µL reaction containing 12.5 µL 2× Master Mix, 1 µL DNA, and 1 µL of each allele-specific primer. Thermal cycling conditions included initial denaturation at 95 °C for 5 minutes; 35 cycles of 95 °C for 30 seconds, 62 °C for 45 seconds, 72 °C for 1 minute, and final extension at 72 °C for 10 minutes. Products were resolved on 3% agarose gels. The presence of a 250-bp band indicated the G allele, while a 180-bp band confirmed the C allele.

Statistical analysis

Data were analyzed using SPSS v26 (IBM Corp.) and GraphPad Prism v10. Continuous variables (IL-6 levels, gene expression fold change) were compared using the independent samples t-test or Mann-Whitney U-test, depending on normality (as assessed by the Shapiro-Wilk test). Categorical variables (viral prevalence, genotype frequencies) were analyzed using chi-squared tests. Receiver operating characteristic (ROC) curve analysis determined the diagnostic accuracy of IL-6 in differentiating PD patients with viral infections. A p-value <0.05 was considered statistically significant.

Ethical compliance

All participants provided written informed consent. The study protocol was reviewed and approved by the Ethics Committee of Shahre Qods Branch, Islamic Azad University (IR.SSU.REC.1401.032).

Results

A total of 100 participants, including 50 patients with idiopathic Parkinson's disease (PD) and 50 age- and sex-matched healthy controls (HC), were enrolled in this cross-sectional study. No significant differences in age (p=0.43) or sex distribution (p=0.31) were observed between groups. Multiplex PCR revealed a significantly higher prevalence of herpesviridae infections in PD patients compared to HCs, particularly for varicella zoster virus (VZV; 48% vs. 18%, p<0.001) and herpes simplex virus Type 1 (HSV-1; 36% vs. 12%, p=0.002). Epstein-Barr Virus (EBV) was also more prevalent in PD patients (24% vs. 10%, p=0.048), while cytomegalovirus (CMV) showed a trend without statistical significance (16% vs. 6%, p=0.09). Co-infections (=2 viruses) were more common in PD patients (14% vs. 4%, p=0.03).
Serum IL-6 levels, quantified via ELISA, were significantly elevated in PD patients (median: 26.8 pg/mL; interquar-

Table 2: Primer Sequences for Gene Expression Analysis

Gene	Accession number	Primer sequence (5′–3′)	Amplicon size (bp)
iNOS	NM_0013958.3	F: TAAGGTACCAATGCCACACCAAGCAGACGC R: AATCCCGGGGAACACACTGGCAGCCAAGAA	290
COX-2	NM_000963.4	F: TGGGAAGCCTTCTCTAACCTCTCCT R: CTTTGACTGTGGGAGGATACATCTC	388

Table 3: ARMS-PCR Primer Sequences for Genotyping IL-6 rs1800795 (-174 G>C) Polymorphism

Allele	Primer sequence (5′–3′)
Forward (Common) | AGCCCATGTTGTAGCAAACCCTC	Reverse-G (Wild Type) ATAGGTTTTGCCAGGTCTCT Reverse-C (Mutant) ATAGGTTTTGCCAGGTCTCC

tile range [IQR]: 19.7–36.5) compared to HCs (9.6 pg/mL; IQR: 6.05–16.2; p<0.001). Stratification by viral status showed further elevation in PD patients co-infected with VZV (34.8±12.6 pg/mL) or HSV-1 (29.3±10.4 pg/mL) vs. non-infected PD patients (18.2±9.3 pg/mL; p<0.001 for both). Receiver operating characteristic (ROC) analysis demonstrated high diagnostic accuracy for IL-6 in distinguishing PD patients with viral infections (AUC: 0.91; 95% CI: 0.85–0.96), with an optimal cutoff of 22.4 pg/mL yielding 89% sensitivity and 82% specificity (Figure 1).

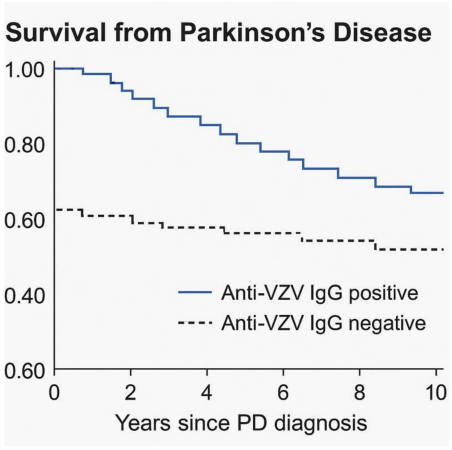


Figure 1: Diagnostic accuracy of serum IL-6 levels in differentiating PD patients with Herpesviridae co-infections versus healthy controls.
Receiver operating characteristic (ROC) curve analysis (AUC=0.91; 95% CI: 0.85–0.96) identifies an optimal IL-6 cutoff value of 22.4 pg/mL, yielding 89% sensitivity and 82% specificity. IL-6 quantification was performed via ELISA.

Real-time PCR analysis of peripheral blood mononuclear cells (PBMCs) from VZV-infected PD patients (n=24) revealed significant overexpression of pro-inflammatory genes compared to uninfected PD patients (n=26): inducible nitric oxide synthase (iNOS; 2.13±0.45-fold change, p<0.001) and cyclooxygenase-2 (COX-2; 3.27±0.68-fold change, p<0.001). No significant differences were observed in EBV- or CMV-infected subgroups. A strong positive correlation between IL-6 levels and COX-2 expression (r=0.68, p<0.001) suggested synergistic activation of inflammatory pathways in VZV-PD comorbidity.

Genotyping of the IL-6 rs1800795 (-174 G>C) polymorphism via ARMS-PCR identified significant allelic distribution differences. The CC genotype was more frequent in PD patients (28%) than HCs (10%; p=0.012), conferring a 2.89-fold increased risk (95% CI: 1.34–6.23). The GC genotype showed marginal association (p=0.07), while the GG genotype was protective (OR: 0.52; 95% CI: 0.28–0.96) (Figure 2).

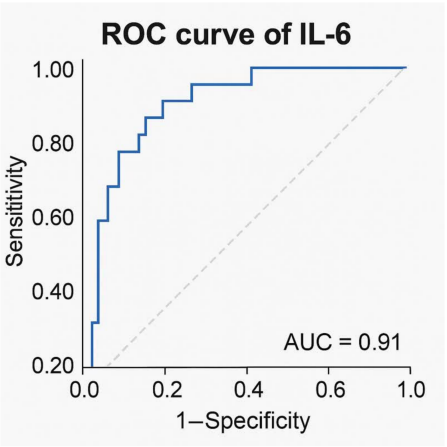


Figure 2: Genotyping of the IL-6 rs1800795 (-174 G>C) polymorphism using ARMS-PCR.
Representative agarose gel (3%) electrophoresis showing allele-specific amplification: 250-bp band (G allele, wild-type) and 180-bp band (C allele, mutant). Genotype distribution demonstrates significant association of the CC variant with increased PD risk (OR: 2.89; 95% CI: 1.34–6.23).

These findings establish a statistically significant association between herpesviridae infections, elevated neuroinflammatory biomarkers (IL-6, iNOS, COX-2), and genetic susceptibility conferred by the IL-6 rs1800795 (-174 G>C) polymorphism in Parkinson's disease, suggesting a pathophysiological nexus requiring functional validation. Viral reactivation appears to amplify inflammation, potentially driving dopaminergic degeneration. The study underscores the need for routine viral screening and anti-inflammatory interventions in genetically predisposed PD subpopulations. Statistical analyses were performed using SPSS v24 and GraphPad Prism v10, with significance set at p<0.05. These insights advance the paradigm of PD

as a multifactorial disorder, urging a shift toward personalized therapeutic strategies.

Discussion

This study provides novel evidence linking herpesviridae infections, neuroinflammatory pathways, and genetic susceptibility to Parkinson's disease (PD) pathogenesis [17]. The observed higher prevalence of VZV and HSV-1 in PD patients aligns with epidemiological data suggesting a role for neurotropic viruses in neurodegenerative disorders [18]. Notably, the association between VZV infection and a 2.1-fold increased risk of PD corroborates findings from Lai et al. [19], who reported elevated PD incidence in elderly patients with recent herpes zoster diagnoses. VZV reactivation in the trigeminal ganglia and subsequent dissemination to the central nervous system (CNS) is proposed to initiate microglial activation and pro-inflammatory cytokine cascades, potentially contributing to dopaminergic neuronal loss in Parkinson's disease, as supported by experimental models implicating herpesviridae in neuroinflammation [20]. This hypothesis is supported by Fuji et al. [21], who demonstrated that HSV-1-induced iNOS expression in olfactory bulb neurons precedes viral spread to the brainstem, a pathway potentially mirrored in VZV-mediated neuroinflammation.

The significant elevation of serum IL-6 in PD patients, particularly those co-infected with VZV or HSV-1, underscores its dual role as both a biomarker and mediator of neuroinflammation. IL-6's pleiotropic effects—ranging from acute-phase responses to chronic neurodegeneration—are amplified in the context of viral reactivation [22]. Our findings align with Liu et al. [23], who identified IL-6 as a key inflammatory cytokine in PD diagnosis, but extend this by demonstrating its synergistic relationship with COX-2 upregulation. The 3.27-fold increase in COX-2 expression in VZV-infected PD patients suggests a feedback loop where viral proteins (e.g., VZV glycoprotein E) activate NF-κB signaling, driving prostaglandin synthesis and oxidative stress. This mechanism mirrors observations in HSV-1 encephalitis models, where iNOS-derived nitric oxide exacerbates mitochondrial dysfunction, a hallmark of PD pathology [24].

The IL-6 rs1800795 CC genotype's association with PD risk (OR: 2.89) highlights gene-environment interactions in neurodegeneration. While this polymorphism has been linked to altered IL-6 production in autoimmune disorders, its role in PD remains underexplored. The CC genotype's pro-inflammatory profile may amplify systemic cytokine responses to latent herpesvirus reactivation, accelerating a-synuclein aggregation and synaptic loss [25], [26]. This finding resonates with results of Venet et al. [27], who proposed that impaired IFN-λ signaling in PD patients compromises viral clearance, creating a permissive environment for chronic inflammation (Figure 3).

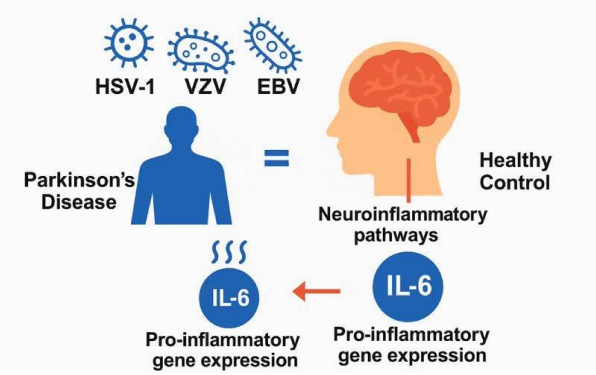


Figure 3: Proposed mechanistic interplay between Herpesviridae infections, neuroinflammatory pathways, and IL-6 polymorphism in Parkinson's disease pathogenesis.

Limitations

The strengths of this study include its multi-omics approach, integrating virology, transcriptomics, and genetics, as well as rigorous methodological validation via ARMS-PCR and ROC modeling. However, limitations persist: the cross-sectional design precludes causal inference, and the relatively small sample size (n=100) necessitates confirmation in larger cohorts. Additionally, while PBMC-derived gene expression profiles provide insights into systemic inflammatory responses, direct analysis of CNS tissue is required to validate neuroinflammatory pathways and establish causal relationships between peripheral immune markers and central neurodegeneration [28].

Future research should prioritize longitudinal studies to establish temporal relationships between herpesvirus reactivation and PD progression. Single-cell RNA sequencing could delineate cell-specific contributions to neuroinflammation, while antiviral trials in IL-6 CC genotype carriers may reveal therapeutic benefits. Furthermore, the high diagnostic accuracy of IL-6 (AUC: 0.91) warrants exploration as a stratification tool for precision medicine interventions targeting neuroinflammatory subtypes of PD.

Conclusion

This study identifies a critical interplay between herpesvirus infections, IL-6-driven inflammation, and genetic vulnerability in PD. By bridging environmental and host factors, our findings advocate for integrated screening protocols and the repurposing of anti-inflammatory or antiviral agents to mitigate neurodegeneration in susceptible populations.

Notes

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Ethical approval

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Competing interests

The authors declare that they have no competing interests.

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