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Research Article

Could Influenza Virus Be a Potential Risk Factor for Parkinson's Disease?An Updated Systematic Review and Meta-Analysis along with a Review of Various Physiopathological Hypotheses

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Abstract

Background

Influenza represents a significant public health problem. Recent epidemiologic research has indicated a potential elevated risk of Parkinson's disease (PD) among influenza patients. Nevertheless, the relationship remains unclear. This meta-analysis was carried out to assess the association between Influenza infection and PD occurrence and summarize various hypotheses.

Materials and Methods

This systematic review and meta-analysis were conducted following the PRISMA flow diagram (2020). It was an updated meta-analysis which conducted by Wang.A total of seven articles were included. Review Manager 5.3 software and Comprehensive Meta-analysis Version 3 performed data analysis.

Results

In this present meta-analysis, we found that influenza infection had a significant effect on PD occurrence, with a 39% higher risk regardless of the timing of the infection (1.11% vs 0.58%, pooled OR= 1.39 [95% CI: 1.02-1.89], p=0.04, I2=31%) and with 61% higher risk when the infection occurs more than 5 years before the PD onset (pooled OR=1.61 [95% CI:1.18-2.19], p=0.003, I2=0%). Meanwhile, we did not observe any relationship between severity of Influenza infection and the onset of PD.

Conclusion

This meta-analysis revealed an increased risk of PD among patients who had experienced Influenza, notably after 5 years of the infection. This implies various Physiopathological pathways. Further studies are required to elucidate this relationship.

Keywords: Influenza virus;Parkinson's Disease; Physiopathology;-Time period

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Introduction

Parkinson's disease (PD) is a neurodegenerative disorder that leads to progressive deterioration of motor function due to the loss of dopamine-producing brain cells. Early symptoms are resting tremor, rigidity, bradykinesia, gait instability, and difficulty walking [1]. It is estimated that PD affects 6.1 million people worldwide, and the prevalence rises with age [2]. Meanwhile, its etiology remains largely unknown. Researchers speculate that both genetic and environmental factors are involved, notably the potential role of various infections [3-4]. Consequently, there has been a prolonged and ongoing debate regarding whether there is a connection between Influenza virus (IV) and PD, which has endured for an extended period. Interestingly, according to American research, the emergence of PD cases increased in the aftermath of the 1918 Spanish flu pandemic. This suggested that the flu virus could attack neurons producing dopamine.Even if the decrease in these cell numbers does not actually lead to PD, it could be an additional factor in promoting the disease's development [5]. Regarding the fact that Influenza is a public health problem and the association between this virus and the development of PD remains elusive in the literature, we conducted this meta-analysis with the aim of assessing the potential link between Influenza and its features and the development of PD. Our second aim is to summarize different hypotheses leading to PD after influenza disease.

Patients and Methods

Study design

This systematic review and meta-analysis were conducted following the 2020 guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [6].

Literature search

This systematic review and meta-analysis is an update to the previously meta-analysis conducted by Wang et al. [7]. We included the 4 studies that have been included in the meta-analysis of Wang. Furthermore, we conducted a search on the PubMed database from inception to August 2023 to identify additional studies. The Mesh terms were chosen by referring to the website www.hetop.eu, and the terms that

were kept are: Influenza, "*Viral infection*", "*Human influenza*", Parkinson, "*Parkinson disease*" and "*Parkinson's disease*". Search terms were connected through the utilization of the Boolean search operators "AND", "OR". The search syntax employed for retrieving bibliographic data on PubMed was: (Parkinson OR "*Parkinson disease*" OR "*Parkinson's disease*") AND (Influenza OR "*Viral infection*" OR "*Human influenza*"). This search was limited to the human species. Two investigators individually assessed the suitability of records by reviewing titles and abstracts through the systematic review tool Rayyan (https://www.rayyan.ai/). Subsequently, the next stage was to evaluate the complete texts of the identified papers for eligibility.

Eligibility criteria

The criteria for inclusion were as follows: (i) case-control papers, cross-sectional papers, or analytical cohort studies, aiming to establish the PD risk in individuals infected with Influenza; (ii) inclusion of the number of PD cases and control groups, the number of Influenza infection in PD cases and control groups, and the availability of odds ratios (OR) with 95% confidence intervals (95% CI).

Quality of studies

To assess the reports' quality, the validated Newcastle-Ottawa quality assessment scale (NOS) was applied [8]. Three investigators independently screened the quality of papers by evaluating three key aspects: (i) participant selection, (ii) comparability of groups, and (iii) determination of the exposure of interest for a case-control study and the outcome of interest for a cohort study.

Data extraction

A standardized form for data collection was employed to retrieve the following information from every study: paper title, first author, publication year, number of PD cases, number of control groups, number of Influenza infection in PD cases, number of Influenza infection in control groups, severity of Influenza infection when available in PD cases and control groups, the number of Influenza infection in PD cases within 5 years prior to the PD diagnosis (<5 years) and the number of control groups in this time (<5 years), the number of PD cases that had experienced Influenza infection more than 5 years before the onset of the PD (≥5 years)and the number of infection in control groups in this time (≥5 years), OR and 95% CI.

Statistical analysis

The analysis of the data was conducted using Review Manager 5.3 software developed by the Cochrane Collaboration. We define statistical significance as $p<0.05$. OR was combined using the generic inverse variance method of DerSimonian and Laird, wherein each study's weight was inversely proportional to its variance [9]. Considering the potential significant heterogeneity stemming from variations in study origins and populations, we opted for a random-effects model over a fixed-effects model. The Cochran Q-test ($p<0.1$ was defined as significant) and I^2 statistic was employed to assess the heterogeneity among the different studies. The I^2 statistic quantifies the percentage of total variation among studies that is attributed to heterogeneity instead of randomness. An I^2 value of 0-25% indicates negligible heterogeneity, 25%-50% suggests low heterogeneity, 50%-75% indicates moderate heterogeneity, and more than 75% indicates significant heterogeneity. If significant heterogeneity was observed, a sensitivity analysis by eliminating studies one by one was conducted to identify the potential reasons behind this heterogeneity. Additionally, a funnel plot, Begg's and Egger's tests ($p<0.1$ was defined as significant) were utilized to evaluate the potential presence of publication bias. Funnel plot was performed utilizing Review Manager 5.3 software. Begg's and Egger's test were calculated utilizing Comprehensive Meta-analysis Version 3.

Results

Study characteristics and literature quality

We included four articles from Wang meta-analysis [10-13]. Additionally, our exploration approach produced 366 records from PubMed. After screening titles and abstracts, we yielded 28 reports, and we retrieved 26 reports after verifying full-text availability. Among these, 23 were excluded because they did not match the criteria for inclusion. Overall, we included seven articles, which were all case-control studies. The outcomes of our exploration and selection procedures for relevant literature are depicted in Figure 1.

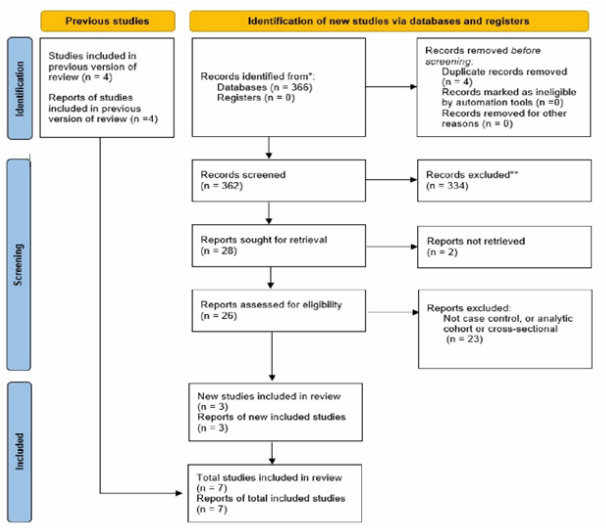

Figure 1: PRISMA flowchart illustrating the process of information selection across the different phases of a systematic review and meta-analysis.

Every study that was incorporated underwent evaluation using the NOS for case-control studies. All studies obtained a NOS score exceeding 7 except the study of Marttila, which had a score of 6 [14]. This result signifies a favorable quality level among the included studies. His characteristics of the included studies and NOS scores are presented in Table 1.

Prevalence of Influenza infection in Parkinson cases vs control

We gathered data from 15385 patients diagnosed with confirmed PD and 68 974 control individuals. The occurrence of IVwas found to be 3.45% among PD cases, compared to 1.92% in the control groups. The confirmation methods for PD and Influenza infection were summarized in Table 1.

The duration from infection to disease diagnosis was documented in 2 case-control studies. We found that 0.45% of PD cases had contracted Influenza within 5 years prior to the disease diagnosis (<5 years), in contrast to 0.14% in the control groups. Furthermore, 0.65% of PD cases had experienced Influenza infection more than 5 years

Study	Origin	Study design	PD	Control	Diagnostic of Influenza	Diagnostic of PD	Influenza in PD	Influenza in control	NOS
Marttila	Finland	Case-control	431	444	Questionnaire*	Clinical criteria	117	135	6
Sasco	United States	Case-control	137	548	Registry records	Clinical criteria	32	118	8
Hertzman	Canada	Case-control	57	111	Questionnaire**	Clinical criteria	6	3	7
Toovey	Switzerland	Case-control	3976	15 891	Registry records	Clinical criteria	223	847	8
Harris	Canada	Case-control	403	405	Questionnaire***	Clinical criteria	43	26	8
Vlajinac	Serbia	Case-control	110	220	Questionnaire*	UPDRS	70	42	8
Cocoros	Denmark	Case-control	10 271	51 355	Registry records	Diagnosis code based on ICD	40	159	7
Total	-	-	15 385	68 974	-	-	531	1 330	-

NOS: Newcastle-Ottawa quality assessment scale; PD: Parkinson's Disease; UPDRS: Unified Parkinson's Disease Rating Scale;*, based on patient's history;*, based on questionnaire indicating Influenza infection during the flu;***, based on six specific questions pointing towards influenza infection; ICD: International Classification of Diseases.

Table 1: Characteristics of included studies.

before the onset of the disease (≥5 years), compared to 0.25% in the control groups.

The severity of Influenza infection was reported in 2 publications. We observed that 1.61% of PD cases encountered severe Influenza infection, while the corresponding figure in the control groups was 4.11%.

Analysis of the association between Influenza infection and Parkinson disease and publication bias

Our meta-analysis revealed that PD was significantly higher among patients with Influenza infection than control groups (pooled OR= 1.64 [95%IC: 1.05-2.57], p=0.03, Q-test p-value <0.00001, I2=90%) (Figure 2, Panel A). Performing a sensitivity analysis by eliminating studies one by one based on their bias risk, revealed that three studies were responsible for the observed heterogeneity. The exclusion of these studies resulted in a significant reduction in heterogeneity (Q-test p-value=0.23, I2=31%). The pooled OR was recalculated and showed a significant association between IV and the occurrence of PD with low and insignificant heterogeneity (1.11% vs 0.58%, pooled OR=1.39 [95% CI: 1.02-1.89], p=0.04, Q-test p-value=0.23, I2=31%) (Figure 2, Panel B).

The association between Influenza infection within 5 years prior to the disease diagnosis and the risk of PD was not significant (pooled OR=1.33 [95%IC: 0.77-2.32], Q-test p-value=0.19, I2=41%)(Figure 2, Panel C). Meanwhile, Influenza infection more than 5 years before the onset of the PD was significantly associated with the risk of PD with insignificant and negligible heterogeneity (pooled OR=1.61 [95% CI:1.18-2.19], p=0.003, Q-test p-value=0.68, I2=0%) (Figure 2, Panel D). The severity of the IV was not significantly associated with the PD with significant heterogeneity (pooled OR=0.54 [95% CI=0.05-5.32], p=0.6, Q-test p-value< 0.00001, I2=98%) (Figure 2, Panel E).

The funnel plot of Influenza infection and the risk of PD was visually asymmetrical, suggesting publication bias (Figure 3, Panel A), meanwhile, removing studies showed a symmetrical funnel plot, suggesting no publication bias (Figure 3, Panel B). The funnel plot of time between infection and PD diagnosis and between the severity of Influenza infection and PD were symmetrical (Figure 3, Panel C-E). Additionally, for IV and the risk of PD, while Begg's test showed a p-value of 0.03 indicating possible publication bias, Egger's test showed a p-value of 0.16 suggesting no publication bias. After removing, they showed a p-value of 0.16 and 0.3 respectively, indicating no publication bias. The Egger's test and Begg's test were not done for time between infection and diagnosis of the PD and the severity of Influenza infection, given the presence of only two studies in each item.

Discussion

To the best of our knowledge, this is the second Systematic review and meta-analysis to assess the risk between IV and PD. The first was conducted in 2020. In comparison to their research, we have updated their meta-analysis by incorporating new studies. While their investigation yielded four studies, we were able to include seven articles in our study. Thus, our meta-analysis includesstudies as well. Additionally, we investigated the association between the timing of the Influenza infection and PD occurrence and between the severity of the infection and PD. In the literature, there was a debate between different studies with varying results, with some endorsing the hypothesis

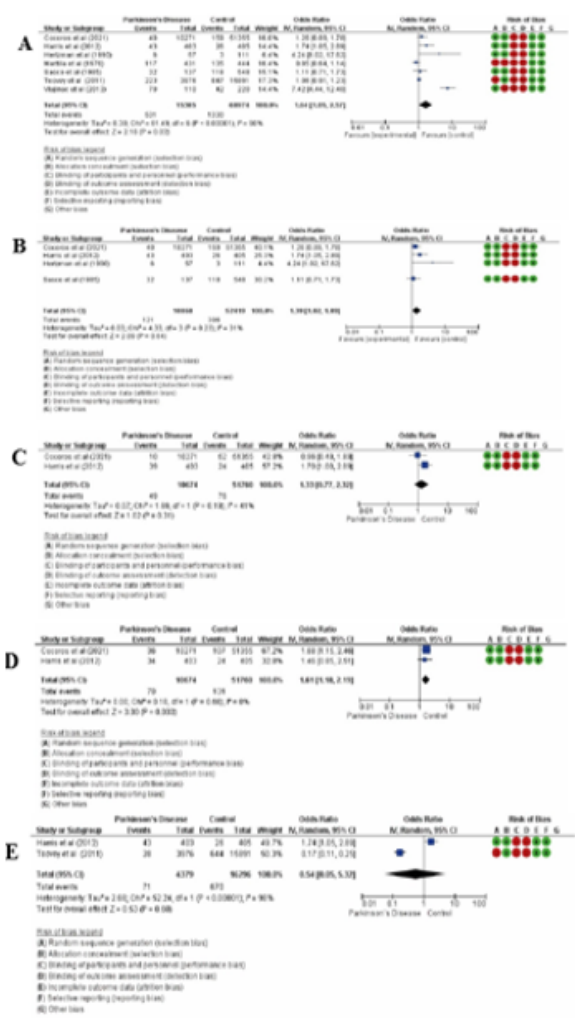

Figure 2: Panel A: Forest plot showed significant association between Influenza infection and the risk of Parkinson's Disease but with high heterogeneity. **Panel B:** Forest plot showed significant association between Influenza infection and of Parkinson's Disease after excluding Vlajinac, Marrtila and Toovay with low heterogeneity. **Panel C:** Forest plot showed an insignificant association between Influenza infection (<5years) and the risk of Parkinson's Disease. **Panel D:** Forest plot showed a significant association between Influenza infection (≥5years) and the risk of Parkinson's Disease. **Panel E:** There was no significant association between severity of Influenza infection and the risk of Parkinson's Disease.

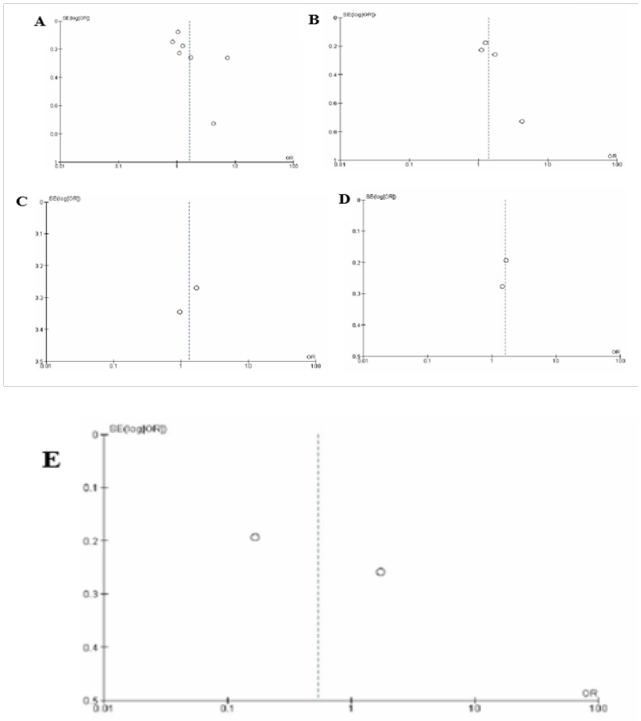

Figure 3: Panel A: Funnel plot was asymmetrical for the study on the association between Influenza infection and the risk of Parkinson's Disease. **Panel B:** Funnel plot showed no evidence of publication bias after removing Vlajinac, Marrtila and Toovay for the association between Influenza infection and Parkinson's Disease. **Panel C:** Funnel plot showed no publication bias for the association between infection (<5 years) and diagnosis of the PD. **Panel D:** Funnel plot showed no publication bias for the association between infection (≥5 years) and diagnosis of the PD. **Panel E:** Funnel plot showed no publication bias for the relationship between the severity of Influenza infection and Parkinson's Disease.

while others did not. While Wang et al identified an insignificant association between IV and PD after excluding study(pooled OR=1.227 [95% CI: 0.786-1.917], p=0.175, I2=61.5%), we found a significant association between IV and PD occurrence after excluding studies(pooled OR= 1.39 [95% CI: 1.02-1.89], p=0.04, I2=31%). Furthermore, we observed a significant higher risk of PD when the infection occurs more than 5 years before the onset of PD (pooled OR=1.61 [95% CI: 1.18-2.19], p=0.003, I2=0%). We excluded regarding their risk bias graphic with a significant reduction in heterogeneity. In fact, this could be explained by the utilization of a questionnaire that relied on patients' subjective responses to the question "*Have you ever been infected by Influenza*?" in studies. Additionally, selected the population not randomly but from another study, increasing the heterogeneity. Toovey chose their population study from a large, encompassing database, which could introduce variations in participant characteristics (age, gender, etc.).

To date, the precise mechanisms underlying the link between IV and the risk of developing PD remain unclear. Various hypotheses were proposed in different studies. Essentially, this could possibly be a direct effect of IV leading to para-infection PD (immediate PD within 15 days following the episode of infection) or indirect factors (delayed PD within a few months) leading to post-infection PD [15-16]. IV can be broadly categorized as either neurotropic IV(NIV) or non-neurotropic IV (NNIV). NIV has the capacity to penetrate the central nervous system (CNS) through various routes such as infecting microvascular endothelial cells or traveling along the olfactory, vagus, or trigeminal nerves [17-18]. Yet, NNIV can enter the CNS through Systematic infection after replicating in the respiratory tract. Once the NIV or NNIV reaches the CNS, the IV specifically targets the ventral substantia nigra to induce neuroinflammation, microglial activation, protein aggregation, and degradation of neurons [19]. In fact, in an animal model, NIV induces a buildup of phosphorylated α-synuclein (α-synuclein misfolding) in the neuron of the substantia

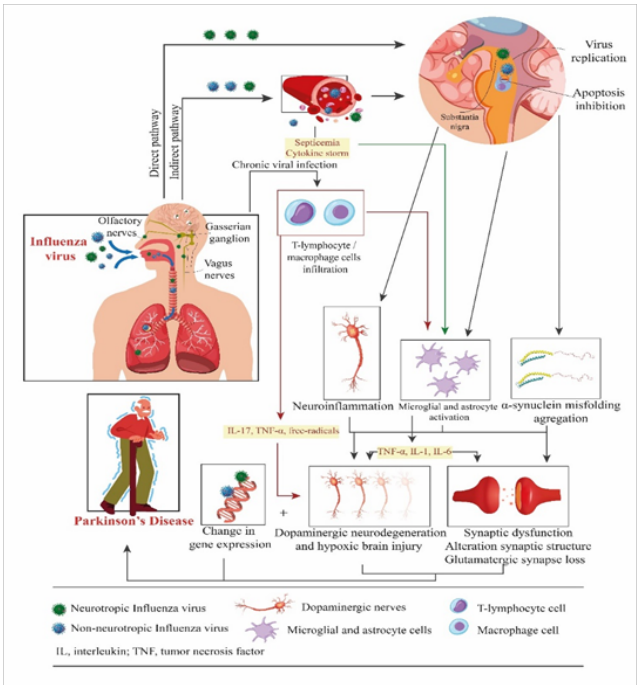

Figure 4: Physiopathological mechanism of Influenza virus-induced Parkinson's Disease. The figure illustrates how the Influenza virus can trigger Parkinson's Disease through both direct (nerve system) and indirect (blood system) pathways. In essence, the virus can target the substantia nigra, where it replicates and inhibits apoptosis. Subsequently, it induces neuroinflammation and activates microglial and astrocyte cells, with misfolding of α-synuclein accumulation. Microglial cells release TNF-α, IL-1, IL-6. These processes collectively result in the degeneration of dopaminergic neurons and impaired synaptic function and structure. The virus can also interfere with genetic expression. Through these pathways, the Influenza virus has the potential to induce Parkinson's Disease. The long-term effect of the Influenza virus is induced by chronic Influenza infection through T-lymphocyte and macrophage cells.

nigra pars compacta in mice. This accumulation might lead to synaptic dysfunction [20]. It had also demonstrated that in cases of PD infected by Influenza, there was a reduction in glutamatergic synapses and a shift in the distribution of synaptic proteins [21]. Additionally, in mice model, Influenza A and IV antigens were found in the CNS, which triggered autophagy, leading to an increase in IV replication [22]. Interestingly, following infection either with NIV or with NNIV, there was an increase in the quantity of astrocytes and microglia cells [23]. Furthermore, other indirect mechanisms were proven in various papers. In fact, immune distribution and cytokine storms can lead to several neurodegenerative disorders, including PD. The release of cytokines in the peripheral system after an Influenza infection can indirectly trigger microglia, increasing their number, activating them, and producing central inflammation and gliosis [24]. Microglial activation releases proinflammatory cytokines (TNF-α, IL-1, IL-6) and reactive oxygen species with neurotoxic effects [25-26]. These peripheral proinflammatory cytokines also affect neuronal morphology, synaptic structure, and function [27]. Additionally, other studies suggest that immune reactions induced by IV could potentially lead to damage in the CNS and dopaminergic neurodegeneration. Meanwhile, in a mouse model, investigators showed that chronic viral infection in CNS leads to T-lymphocyte and macrophage cell infiltration leading to microglial activation with neurons damage. T-lymphocytes release IL-17, TNF-α and free radicals, leading to dopaminergic neuronal death. Overall, while the loss of dopaminergic neurons was shown to be temporary, neuroinflammation, microglial activation, α-synuclein phosphorylation and the distribution of innate immune plasticity endure as long-lasting effects. Some studies suggest that cytokine storm and IV can change gene expression. This might lead to a vulnerable subject developing PD after several years, and PD can occur once a triggering factor arises. This Physiopathological mechanism might explain our finding that revealed the high risk of occurrence of PD after 5 years of IV. Meanwhile, the long-term relationship betweenIV and PD remained unclear. In our study, we found no significant relationship between the severity of IV and PD occurrence. This might be explained by the high heterogeneity and bias risk in included studies. In fact, the pooled OR was estimated by combining two studies, so the high heterogeneity cannot be elucidated by sensitivity analysis. Interestingly, to attenuate the PD cases, studies suggest annual vaccination against Influenza A.[28].

In summary, although there are some hypotheses that elucidate the relationship between IV and PD, establishing clear and definitive mechanisms remains challenging. Thus, we summarized various hypotheses in the literature in Figure 4. Moreover, future research is imperative to gain a deeper understanding of any possible relationship between IV and PD. Robust epidemiological studies, experimental research, and clinical investigators are essential to conclusively proving any causal association.

Our study had some limitations. First, information about Influenza infection was collected differently in the included studies. The questionnaire was based on subjective responses in two studies, yet it was more consistent and specific in two other studies. Three studies referred to the registry to collect this information. This heterogeneity of information collection represents the first limit in our meta-analysis. Secondly, the number of available studies in the literature is limited. Additionally, the time between IV and PD diagnosis and the severity of IV were available only in 2/7 studies.

Conclusion

Our meta-analysis demonstrated that contracting the Influenza virus raises the risk of developing PD by 39% regardless of when the infection occurs, and this risk increases to 61% when the infection took place more than 5 years before the PD diagnosis. Further studies are required to elucidate this relationship.

Declarations

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Conflicts of interest/Competing interests: All authors declare that they have no conflict of interest.

Ethics approval: Not applicable.

Consent to participate, consent for publication, Code availability: Not applicable.

Availability of Data and material: data can become accessible when it is requested.

Authors' contributions

Dr. Ketata Imen: Study design, methodology, literature search, data extraction, statistical analysis and interpretation, quality assessment, draft writing, final approval of manuscript.

Dr. Emna Ellouz: Methodology, literature search, screening for eligibility, quality assessment, draft review and editing, supervision and validation, final approval of manuscript.

Dr. Rahil Mizouri: Literature search, data extraction, screening for eligibility, quality assessment, draft writing, final approval of manuscript.

All authors agreed with the content and that all gave explicit consent to submit the manuscript.

References

1. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, et al. (2015) MDS clinical diagnostic criteria for Parkinson's disease. MovDisord. 30:1591-601.
2. Rajan S, Kaas B (2022) Parkinson's Disease: Risk Factor Modification and Prevention. Semin Neurol. 42:626-638.
3. Cocoros NM, Svensson E, Szépligeti SK, Vestergaard SV, Szentkúti P, et al. (2021) Long-term Risk of Parkinson Disease Following Influenza and Other Infections. JAMA Neurol. 78:1461-1470.
4. Hertzman C, Wiens M, Bowering D, Snow B, Calne D (1990) Parkinson's disease: a case-control study of occupational and environmental risk factors. Am J Ind Med. 17:349-355.
5. Henry J, Smeyne RJ, Jang H, Miller B, Okun MS (2010) Parkinsonism and neurological manifestations of influenza throughout the 20th and 21st centuries. Parkinsonism RelatDisord. 16:566-571.
6. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, et al. (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 372:n71.
7. Wang H, Liu X, Tan C, Zhou W, Jiang J, et al. (2020) Bacterial, viral, and fungal infection-related risk of Parkinson's disease: Meta-analysis of cohort and case-control studies. Brain Behav. 10:e01549.
8. Stang A (2010) Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 25:603-605.
9. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials. 7: 177-188.
10. Harris MA, Tsui JK, Marion SA, Shen H, Teschke K (2012) Association of Parkinson's disease with infections and occupational exposure to possible vectors. MovDisord. 27:1111-1117.
11. Sasco AJ, Paffenbarger RS Jr (1985) Measles infection and Parkinson's disease. Am J Epidemiol. 122:1017-1031.
12. Vlajinac H, Dzoljic E, Maksimovic J, Marinkovic J, Sipetic S, et al. (2013) Infections as a risk factor for Parkinson's disease: a case-control study. Int J Neurosci. 123:329-332.
13. Toovey S, Jick SS, Meier CR (2011) Parkinson's disease or Parkinson symptoms following seasonal influenza. Influenza Other Respir Viruses. 5:328-333.
14. Marttila RJ, Rinne UK (1976) Arteriosclerosis, heredity, and some previous infections in the etiology of Parkinson's disease. A case-control study. Clin NeurolNeurosurg. 79:46-56.
15. Qian L, Flood PM, Hong JS (2010) Neuroinflammation is a key player in Parkinson's disease and a prime target for therapy. J Neural Transm. 117:971-979.
16. Bozzola E, Spina G, Valeriani M, Papetti L, Ursitti F, et al. (2021) Management of pediatric post-infectious neurological syndromes. Ital J Pediatr. 47: 17.
17. Hara H, Chida J, Uchiyama K, Pasiana AD, Takahashi E, et al. (2021) Neurotropic influenza A virus infection causes prion protein misfolding into infectious prions in neuroblastoma cells. Sci Rep. 11:10109.
18. Barbosa-Silva MC, Santos LE, Rangel B (2018) The Impact of Non-Neurotropic Influenza Strains on the Brain: A Role for Microglial Priming? J Neurosci. 38:7758-7760.
19. Jang H, Boltz D, McClaren J, Pani AK, Smeyne M, et al. (2012) Inflammatory effects of highly pathogenic H5N1 influenza virus infection in the CNS of mice. J Neurosci. 32:1545-1559.
20. Olsen LK, Dowd E, McKernan DP (2018) A role for viral infections in Parkinson's etiology? Neuronal Signal. 2:NS20170166.
21. Yamada T, Yamanaka I, Takahashi M, Nakajima S (1996) Invasion of brain by neurovirulent influenza A virus after intranasal inoculation. Parkinsonism RelatDisord. 2:187-193.
22. Schöndorf DC, Aureli M, McAllister FE, Hindley CJ, Mayer F, et al. (2014) iPSC-derived neurons from GBA1-associated Parkinson's disease patients show autophagic defects and impaired calcium homeostasis. Nat Commun. 5:4028.
23. Hosseini S, Wilk E, Michaelsen-Preusse K, Gerhauser I, Baumgärtner W, et al. (2018) Long-Term Neuroinflammation Induced by Influenza A Virus Infection and the Impact on Hippocampal Neuron Morphology and Function. J Neurosci. 38:3060-3080.
24. Jurgens HA, Amancherla K, Johnson RW (2012) Influenza infection induces neuroinflammation, alters hippocampal neuron morphology, and impairs cognition in adult mice. J Neurosci. 32: 3958-3968.
25. Glenn JD, Smith MD, Xue P, Chan-Li Y, Collins S, et al. (2017) CNS-targeted autoimmunity leads to increased influenza mortality in mice. J Exp Med. 214:297-307.
26. Riazi K, Galic MA, Kentner AC, Reid AY, Sharkey KA, et al. (2015) Microglia-dependent alteration of glutamatergic synaptic transmission and plasticity in the hippocampus during peripheral inflammation. J Neurosci. 35: 4942-4952.
27. Estes ML, McAllister AK (2015) Immune mediators in the brain and peripheral tissues in autism spectrum disorder. Nat Rev Neurosci. 16:469-486.
28. Lehrer S, Rheinstein PH (2022) Vaccination Reduces Risk of Alzheimer's Disease, Parkinson's Disease and Other Neurodegenerative Disorders. Discov Med. 34:97-101.

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