Jurnal Info Kesehatan
Vol. 24, No. 1, March 2026, pp. 185-195
P-ISSN 0216-504X, E-ISSN 2620-536X
DOI: *10.31965/infokes.Vol24.Iss1.2319*
Journal homepage: *https://jurnal.poltekkeskupang.ac.id/index.php/infokes*

RESEARCH Open Access

Meta-Analysis Study of Correlation Between Olfactory Dysfunction and Cognitive Impairment in Parkinson's Disease

Juliana Sie[1a*], Junita Maja Pertiwi[1b], Rizal Tumewah[1c], Ansye Momole[1d], Seilly Y Jehosua[1e], Windy Mariane Virenia Wariki[2f]

[1] Department of Neurology, Faculty of Medicine, Sam Ratulangi University, Manado, North Sulawesi, Indonesia
[2] Department of Community Medicine, Faculty of Medicine, Sam Ratulangi University, Manado, North Sulawesi, Indonesia

[a] Email address: juliana.sie77@gmail.com
[b] Email address: pertiwijunita01@gmail.com
[c] Email address: rizaltung@yahoo.com
[d] Email address: ansyenancy@yahoo.com
[e] Email address: seillyneuro@gmail.com
[f] Email address: wwariki@unsrat.ac.id

Received: 31 December 2025 Revised: 2 February 2026 Accepted: 7 February 2026

Abstract

Disturbance in olfactory perception is commonly identified as a non motor manifestation in Parkinson's disease and is often interpreted as an early biological signal reflecting ongoing degeneration of neural structures. This study was specifically formulated to conduct an in depth evaluation of the association between reduced smell performance and impaired cognitive functioning in Parkinson's disease by applying systematic numerical aggregation techniques that adhere to internationally accepted research protocols. A broad and methodologically organized literature exploration was conducted using PubMed Wiley and ScienceDirect to identify empirical studies examining the association linking smell processing ability with mental functioning measures in individuals diagnosed with Parkinson's disease. The screening process was carried out in accordance with clearly defined inclusion requirements. Assessment of smell function relied on the olfactory recognition assessment developed by the University of Pennsylvania Test UPSIT while evaluation of cognitive condition employed the MMSE alongside the MoCA cognitive screening tools. Pooled odds ratio values along with 95% confidence interval ranges were calculated using a random effects modeling framework. Overall 3 eligible studies comprising 773 individuals conducted in populations from America, Korea, and Britain met the established inclusion standards. Quantitative synthesis revealed a statistically meaningful relationship between impaired olfactory ability and reduced cognitive performance in Parkinson's disease, with individuals experiencing hyposmia or anosmia showing a markedly increased probability of cognitive impairment compared with participants exhibiting intact smell perception OR 2.57 95% CI 1.15 to 5.74. The results of this analysis suggest a strong and statistically significant relationship between diminished olfactory capacity and cognitive impairment in Parkinson's disease, highlighting its potential role as an early detectable clinical indicator of progressive cognitive deterioration. Despite the presence of variability among included studies and a relatively small pool of eligible research, the meta analytic evidence supports the usefulness of olfactory assessment as a non invasive and economically efficient approach for identifying cognitive risk in Parkinson's disease. Additional large scale investigations employing uniform evaluation protocols are necessary to confirm these outcomes and enhance their relevance in clinical practice.

Keywords: Parkinson, Olfactory Dysfunction, Cognitive Impairment.

Corresponding Author:

Juliana Sie
Department of Neurology, Faculty of Medicine, Sam Ratulangi University, Manado, North Sulawesi, Indonesia
Email: juliana.sie77@gmail.com

1. INTRODUCTION

Parkinson's disease represents a gradually worsening progressive neurological disorder characterized by diverse motor manifestations and additional non motor symptoms that collectively lead to substantial reductions in patient quality of life. Although classical motor signs including tremor rigidity and bradykinesia dominate clinical recognition, non motor features such as cognitive impairment constitute a significant yet frequently overlooked clinical concern. Among people living with Parkinson's disease cognitive decline can first manifest in the form of mild cognitive impairment MCI or gradually progress into Parkinson's disease dementia which results in substantial disruption of daily functioning diminished independence and increased reliance on caregiver support. Identifying early indicators associated with cognitive impairment remains a critical priority in PD research and clinical practice (Avanipully et al., 2022; Bologna, 2021; Zafar, Lui, & Yaddanapudi, 2025)

Parkinson's disease currently impacts a global population exceeding 10 million people and ranks as the second most frequently occurring condition involving progressive neuronal degeneration, positioned directly after Alzheimer's disease, with worldwide incidence showing a steady upward trend that is strongly influenced by the increasing proportion of older adults. Epidemiological studies indicate that cognitive impairment is common among individuals with PD, with a substantial proportion developing MCI or dementia over the disease course. In light of the escalating worldwide impact of PD and the frequent emergence of cognitive disturbances, the development of early stage indicators that are widely available and economically feasible has become essential for recognizing individuals who face an elevated probability of experiencing cognitive deterioration (Ben-Shlomo et al., 2024; Jellinger, 2023).

Impairment of the sense of smell represents one of the most frequent early manifestations unrelated to movement in PD and commonly appears several years prior to the development of motor abnormalities, while from a biological perspective this deficit is believed to indicate early spread of alpha synuclein related pathology within the olfactory structures before higher brain areas involved in cognition become affected. A growing body of research indicates a potential link between deficits in olfactory function and reduced cognitive performance in PD, encompassing conditions such as MCI and dementia related to Parkinson's disease, yet results reported in the literature are often contradictory because of differences in methodological approaches, evaluation instruments, and measured outcomes, thereby restricting firm conclusions about the magnitude and practical relevance of this relationship (Dahbour et al., 2022; Mertens et al., 2019; Torres-Pasillas et al., 2023).

Systematic review and meta-analysis offer a rigorous methodological approach to synthesizing existing evidence, overcoming limitations of individual studies, and providing more precise estimates of association. By consolidating findings from several independent studies and applying standardized analytical techniques meta analytic approaches can clarify the association between reduced smell capacity and mental decline in PD while also supporting evaluation of smell disturbance as a reliable marker of cognitive susceptibility (Aarsland et al., 2021; Bagherieh et al., 2023).

Accordingly this study was undertaken to perform a structured a structured synthesis and statistical integration of previous studies to evaluate the association reduced olfactory function and cognitive impairment among individuals individuals clinically confirmed to have Parkinson's disease. This study aims to determine the strength of the observed association and to examine the usefulness of smell disturbance as an initial non invasive marker of cognitive decline in PD.

2. RESEARCH METHOD

This research was organized as a methodical evidence synthesis combined with statistical pooling following PRISMA guidelines Meta Analyses PRISMA 2020

framework. A detailed methodological plan was established prior to data collection to ensure transparency reproducibility and adherence to recognized principles of meta analytic investigation. An extensive and methodically organized search of the scientific literature was undertaken to locate studies that explored the association of smell loss with mental deterioration in participants diagnosed with Parkinson's disease, utilizing electronic sources including PubMed MEDLINE, ScienceDirect, Wiley Online Library, and Google Scholar. In the case of articles published in the Indonesian language, Google Scholar served as the main retrieval platform, while the overall search approach was formulated in alignment with the research objectives and predetermined inclusion requirements. A comprehensive search strategy was constructed by systematically integrating keywords and conceptually related subject terms through the application of Boolean operators AND and OR, with primary emphasis placed on "Parkinson's disease," "olfactory dysfunction," "olfactory loss," "hyposmia," "anosmia," "cognitive impairment," "cognitive decline," "cognitive dysfunction," and "dementia," while restricting eligible publications to those written in English or Indonesian. The literature identification strategy was conducted without applying any restrictions related to the year of publication, and in addition to searching multiple electronic databases, the reference sections of every included article were manually scrutinized in detail in order to identify further studies that met the relevance criteria.

The process of determining study inclusion followed the structured PICOS framework, where the Population consisted of individuals clinically identified as having Parkinson's disorder, the Exposure referred to olfactory dysfunction including hyposmia or anosmia, the Comparison involved Parkinson's disease patients with preserved olfactory ability, the Outcome focused on cognitive impairment assessed using established cognitive instruments including MMSE and MoCA, and the Study Design comprised observational methodologies including cross sectional and cohort studies. Articles were excluded from eligibility when they consisted of review articles, editorial publications, conference abstracts, case reports, or animal based investigations, as well as when the presented data were inadequate to support quantitative synthesis.

Within the context of this meta analysis, olfactory dysfunction was operationally defined as the occurrence of hyposmia or anosmia among individuals diagnosed with Parkinson's disease, as established through assessment using the Penn-developed standardized odor recognition examination. Each included study applied study-specific UPSIT cut-off values to classify participants as having impaired or normal olfactory function. Participants categorized by the original study authors as having olfactory impairment (hyposmia or anosmia) were classified as the exposed group, while those with UPSIT scores above the reported cut-off thresholds were classified as having normal olfactory function. When olfactory function was reported as a continuous UPSIT score, values were dichotomized using the cut-off points defined in the original studies to allow consistent classification and pooling of effect estimates across studies (Rashed et al., 2020; Turkmen et al., 2021).

Cognitive status was assessed using established and validated screening tools, namely the MoCA together with the MMSE cognitive screenings which functioned as standardized evaluation instruments. Cut-off values determined by individual studies for MoCA and MMSE were considered acceptable, including thresholds adjusted according to educational level when reported by the respective investigators. Participants meeting the cognitive impairment criteria according to each study's predefined thresholds were classified as cognitively impaired, while those above the thresholds were classified as cognitively unimpaired. To enable quantitative synthesis across studies using different assessment tools and diagnostic criteria, exposure and outcome variables were harmonized by dichotomization.

Every citation obtained from the database searches was transferred into reference management software, after which duplicate entries were systematically eliminated. The study selection procedure consisted of two distinct phases, beginning with independent screening of titles and abstracts by three reviewers to identify studies of potential relevance, followed by full text evaluation to confirm eligibility in accordance with predetermined inclusion and exclusion standards. Disagreements arising during the study selection stage were addressed through deliberation among the reviewers. The entire selection workflow was summarized employing a PRISMA 2020 schematic outlining article selection stages meta analysis, with adjusted odds ratios extracted when reported and unadjusted odds ratios utilized when adjustments were unavailable, while cohort studies contributed baseline smell performance as an indicator of future mental decline and cross sectional studies supplied prevalence related associations.

Three analysts separately collected study information through a uniform template that systematically recorded details including author name, publication date, research location, methodology, population scale, and subject profiles, methods used for olfactory assessment, cognitive evaluation instruments, and reported effect estimates. All differences of opinion that emerged during the review process were addressed by reaching collective agreement or by seeking guidance from a supervising authority, and in situations where data interpretation remained uncertain or incomplete, the researchers directly communicated with the corresponding authors of the selected publications through electronic mail to obtain clarification.

A standalone critical appraisal of potential methodological distortion was undertaken for each eligible investigation by three independent reviewers using the ROBINS I framework, allowing a structured appraisal of bias vulnerability across seven analytically distinct domains such as confounding factors, recruitment mechanisms, correctness of categorization of intervention levels, protocol deviations, and data absence trends, reliability of outcome assessment, and risks related to selective disclosure of results. A comprehensive bias classification was attributed to every study by considering the most severe risk detected among all evaluated domains, following the methodological guidance provided by ROBINS I, and any differences in reviewer judgment were settled through structured discussion.

Quantitative synthesis of extracted data analysis was executed through RevMan software 5.4.1, facilitating pooled odds ratio estimation with accompanying 95% confidence intervals to formally evaluate the association between reduced olfactory capability and progressive cognitive deterioration in populations diagnosed with Parkinson’s disease. An analytical model incorporating random effects was utilized to accommodate variability among studies, with the degree of heterogeneity quantitatively examined using the I^2 statistic, and the outcomes of the meta analysis were visually summarized through forest plots illustrating both individual estimates and the overall combined effect.

3. RESULTS AND DISCUSSION

The procedure for identifying and selecting relevant studies was implemented following PRISMA 2020 methodological requirements ensure methodological transparency and consistency.

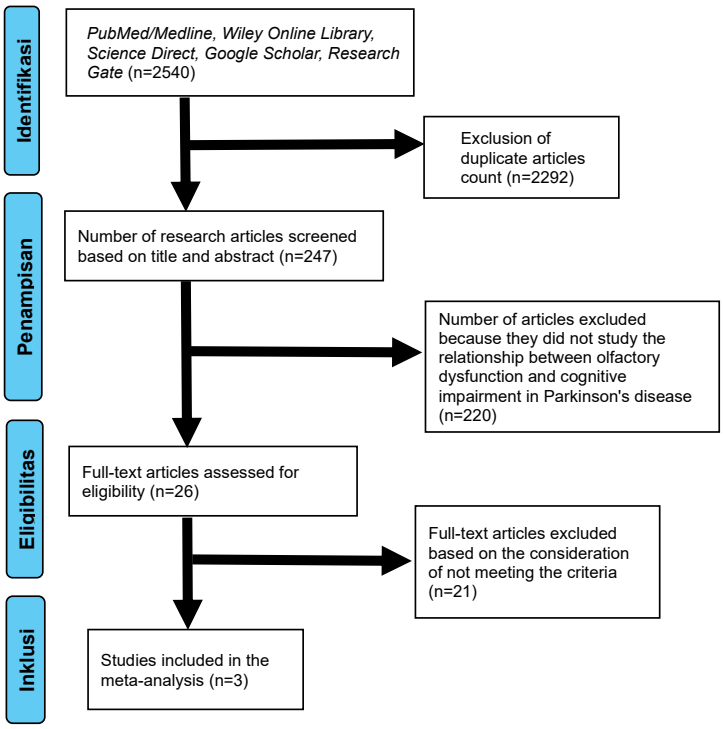

Figure 1. PRISMA flow diagram

Figure 1 illustrated the stages of identifying and selecting studies using the PRISMA 2020 flow diagram, with the primary literature search encompassing all records from the beginning of each database until January 2025, followed by a supplementary search in November 2025 to capture newly published eligible studies, while only articles written in English or Indonesian were included. The PubMed search strategy was as follows: ("Parkinson Disease" OR "Parkinson's disease") AND ("olfactory dysfunction" OR hyposmia OR anosmia) AND ("cognitive impairment" OR "cognitive decline" OR dementia). Equivalent search strategies were adapted for ScienceDirect, Wiley Online Library, and Google Scholar using database-specific syntax. In addition to database searching, the reference lists of all eligible publications were carefully inspected by hand to identify further relevant studies, after which all identified references were uploaded into bibliographic software to eliminate repeated entries automatically followed by manual verification, and the study selection advanced through two clearly defined screening stages. Initially, an independent examination of article titles and abstracts was carried out by three separate evaluators with the objective of detecting studies that might fulfill eligibility requirements, followed by an autonomous appraisal of the complete manuscripts that had been shortlisted in order to confirm eligibility according to criteria established in advance. Divergent opinions that emerged throughout the screening and selection phases were addressed through structured discussions until a shared agreement was achieved among the reviewers, while the entire pathway of study identification and selection is illustrated through a PRISMA 2020 flow chart.

During the phase of complete manuscript evaluation, several studies were removed due to factors such as non relevant outcome measures, unsuitable methodological design, lack of olfactory or cognitive measurement information, or inadequate data for quantitative aggregation, while 2,540 records in total were initially retrieved from electronic database searches. Following the elimination of 2,292 duplicated entries, a total of 247 articles proceeded to the title and abstract review stage, from which 220 were excluded because they failed to

investigate the association of smell loss with mental decline in Parkinson's patients leaving 26 full articles that were assessed for eligibility, after which 21 were removed for not satisfying predefined inclusion criteria or lacking sufficient quantitative data. In the final stage of the selection procedure, only three studies successfully fulfilled every eligibility requirement and were therefore incorporated into the concluding meta analysis.

The concluding sample consisted of three qualified studies encompassing a total of 773 participants and conducted within the United States, South Korea, and the United Kingdom, where two studies employed a cohort oriented design and one followed a cross sectional model, and olfactory ability across all investigations was consistently assessed using the UPSIT odor recognition tool, while mental capacity was evaluated through established and validated instruments, where two studies implemented the MoCA tool, with a separate investigation utilizing the MMSE MMSE, alongside follow up durations that ranged from 1 to 6 years (Doty & Hawkes, 2022; Morley et al., 2018).

Table 1. Study Characteristic.

Researchers, Country, Year of Publication,	Sample Size	Research Duration	Research Method	Olfactory Examination Method	Cognitive Assessment Tools	Effect Size Used in Meta-analysis
Fullard et al., 2016) (Philadelphia, USA)	423	6 Years	Cohort	UPSIT Test	MoCA	OR = 1.52 (95% CI: 0.91–2.55), adjusted
Yoo et al., 2020 (Seoul, Korea)	228	3 Years	Cohort	UPSIT Test	MoCA	OR = 2.48 (95% CI: 1.32–4.66), adjusted
Thomas et al., 2022 (United Kingdom)	122	1 Years	Cross Sectional	UPSIT Test	MMSE	OR = 6.27 (95% CI: 2.61–15.09), unadjusted

The potential risk of bias present in the included studies was evaluated through application of the ROBINS I Risk Of Bias In Non randomized Studies of Interventions instrument, with the findings summarized in Figure2 and Figure 3, as this tool systematically examines seven domains including bias factors including sample recruitment, exposure grouping, protocol adherence, data gaps, result evaluation, and reporting transparency.

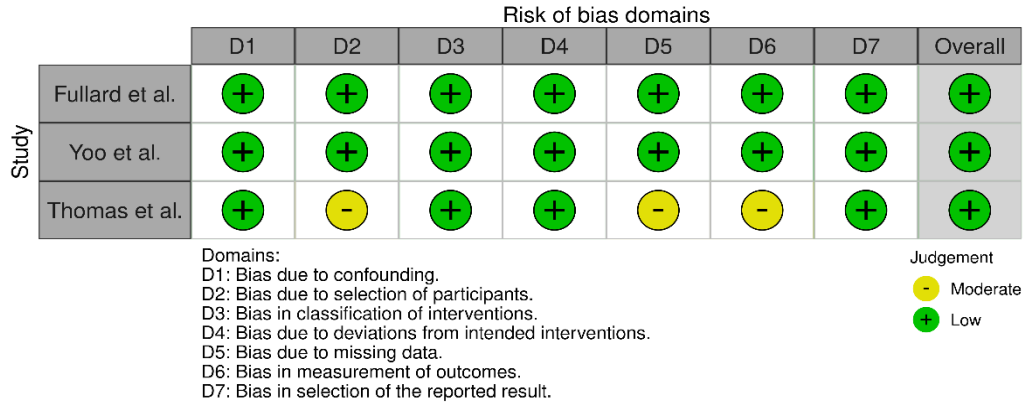

Figure 2. Summary of the risk of bias assessment in the studies reviewed

Figure 2 provides an overview of the overall bias risk observed across all included studies, where the evaluation demonstrates that most bias domains were judged to fall within low to moderate risk levels, indicating generally acceptable methodological quality, with no study identified as having a critical bias risk, thereby justifying inclusion in quantitative synthesis.

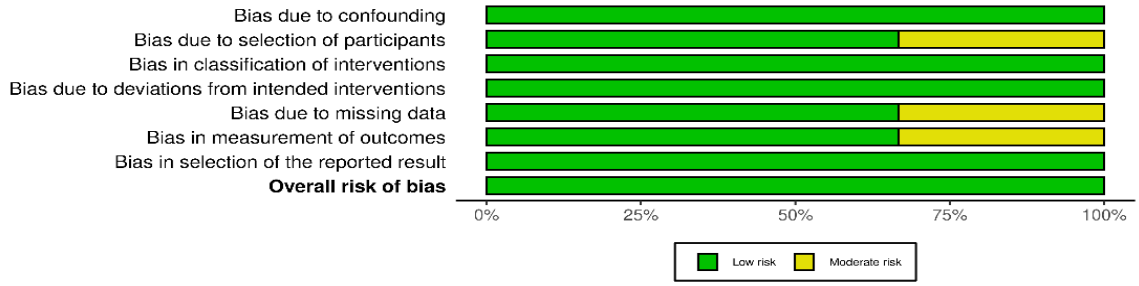

Figure 3. Graph of the risk of bias assessment in the studies reviewed

Figure 3 provides a detailed visual representation of bias risk across methodological domains for every included investigation through a traffic light style diagram. The majority of domains focusing on exposure determination and outcome evaluation received low bias ratings, which indicates the consistent application of well established olfactory and cognitive instruments including UPSIT, MMSE, and MoCA. The systematic use of these validated tools substantially minimizes the potential for measurement related distortion across the analyzed studies.

Nonetheless, several methodological domains exhibited a moderate level of bias, with the most prominent concerns arising from confounding factors and participant selection processes. Such sources of bias are commonly embedded within observational research frameworks because variations in age, length of illness, Parkinson's disease severity, and accompanying medical conditions are often difficult to regulate comprehensively. Furthermore, a single investigation showed an elevated bias risk associated with how participants were recruited and the length of follow up, factors that could affect the reliability of cognitive outcome measurements over time. Even with these methodological weaknesses, the comprehensive bias evaluation indicates that the body of evidence remains adequate for statistical aggregation. The convergence of results among studies exhibiting different bias profiles strengthens confidence in the combined effect estimate. A structured evaluation of publication bias was not undertaken, as the restricted quantity of eligible studies reduces the interpretive accuracy of funnel plot analysis (Jia et al., 2021).

The meta analytical procedure applied a random effects framework in order to accommodate heterogeneity across studies. The aggregated results revealed a statistically meaningful relationship linking impaired olfactory function to cognitive decline in Parkinson's disease. Individuals experiencing hyposmia or anosmia showed a substantially increased probability of cognitive impairment when contrasted with participants who retained normal olfactory abilities (OR = 2.57, 95% CI: 1.15–5.74). Statistical heterogeneity was moderate to high (I^2 = 73%), indicating variability among the included studies. Forest plot analysis illustrates individual study estimates and the pooled effect size.

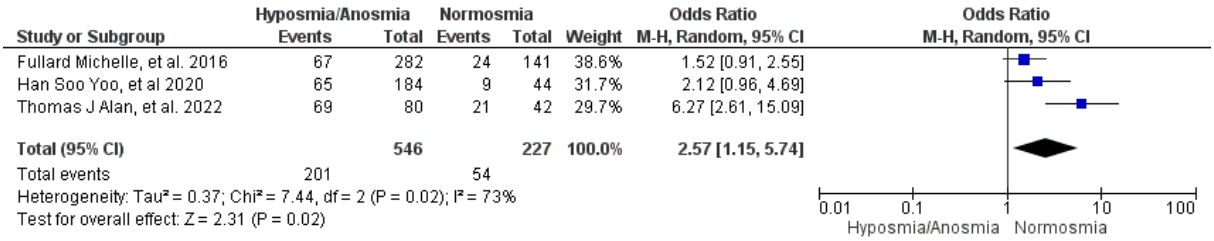

Figure 4. Forest plot of the relationship between olfactory dysfunction and cognitive impairment in Parkinson's disease

Figure 4 presents a forest plot illustrating the association between olfactory dysfunction and cognitive impairment in individuals with Parkinson's disease using a random-effects meta-analysis. The figure summarizes the direction and consistency of effect estimates across the included studies and demonstrates a uniform trend in which patients with impaired olfactory function exhibit a higher likelihood of cognitive impairment compared with those with preserved olfactory ability. Although variation in effect size was observed across studies, this inconsistencies probably arise from methodological diversity and sample traits, follow-up duration, and cognitive assessment methods rather than contradictory findings.

Consequently, the adoption of a random-effects analytical approach was justified in order to appropriately accommodate the detected variability. In general, the forest plot illustrates a consistent pattern across the included investigations, with each study indicating an elevated likelihood of cognitive impairment among Parkinson's disease patients presenting with olfactory dysfunction, thereby reinforcing the presence of a meaningful association between impaired olfactory function and cognitive decline (Fullard et al., 2016; Thomas et al., 2022; Yoo et al., 2020).

This association is biologically plausible and can be explained by shared neuropathological mechanisms underlying disease progression. Smell-related neural regions are some of the first sites impacted by α-synuclein accumulation in Parkinson's disorder, often during the prodromal stage. These regions maintain close anatomical and functional connections with limbic and cortical networks responsible for memory, attention, and executive function. According to the Braak staging hypothesis, neurodegenerative pathology may spread from olfactory regions to higher-order cortical areas, thereby linking early olfactory impairment with subsequent cognitive deterioration. Moreover, olfactory dysfunction likely reflects a broader neurodegenerative burden involving dopaminergic and cholinergic neurotransmitter systems that are essential for both olfactory processing and cognitive performance. Consequently, patients with Parkinson's disease who exhibit marked olfactory deficits may represent a subgroup with more extensive neural involvement and an increased vulnerability to cognitive decline (Abraham et al., 2025; Rietdijk et al., 2017; Seyedmirzaei et al., 2024).

Beyond its neuropathological relevance, olfactory dysfunction may also reflect early disruption of large-scale brain networks that are critical for higher cognitive functioning. Functional and structural neuroimaging studies have demonstrated that olfactory Parkinson's-related dysfunction corresponds with disrupted neural communication between the olfactory cortex, limbic system, and frontal regions, particularly the orbitofrontal cortex and hippocampus. These regions play a central role in executive function, memory formation, and attentional control. Degeneration within these interconnected networks may therefore provide a mechanistic explanation for the observed association between reduced olfactory performance and declining cognitive abilities. This network-based perspective supports the notion that olfactory dysfunction is not an isolated sensory deficit but rather a manifestation of widespread neurodegenerative processes affecting cognition-related circuits. Furthermore, cholinergic dysfunction may contribute substantially to the connection between smell loss and mental deterioration in Parkinson's disorder (Oikonomou et al., 2026; Ponsen et al., 2004).

While dopaminergic degeneration predominates in early motor symptoms, cognitive impairment has been closely linked to cholinergic deficits arising from degeneration of the basal forebrain and related projections. The olfactory system is heavily modulated by cholinergic inputs, and impairment in this neurotransmitter system may simultaneously affect olfactory processing and cognitive performance. Consequently, olfactory dysfunction may serve as a surrogate marker for underlying cholinergic system involvement, which is known to predict more rapid cognitive deterioration and progression to Parkinson's disease dementia (Degirmenci et al., 2023; Ponsen et al., 2004).

The results of this systematic review combined with meta analytic synthesis provide strong evidence of a significant relationship between impaired olfactory function and cognitive deterioration among individuals affected by Parkinson's disease. Aggregated estimates reveal that patients diagnosed with hyposmia or anosmia face a risk of cognitive impairment exceeding twofold relative to those retaining normal olfactory capacity. These results are consistent with current neuropathological models of Parkinson's disease, including the Braak staging hypothesis, which proposes that α-synuclein pathology initially affects the olfactory structures before spreading to cortical regions involved in cognitive processing (Ropper et al., 2014). The identified association lends support to the theoretical framework proposing that olfactory impairment may serve as an indicator of early neurodegenerative processes occurring prior to or alongside cognitive deterioration. When viewed through a clinical lens, evaluation of olfactory capacity represents a procedure that is non invasive, cost efficient, and easily applied in routine practice, thereby offering healthcare professionals a practical tool for identifying patients who may face an increased likelihood of developing cognitive impairment at an early stage. Integration of olfactory testing into standard clinical examinations may improve early risk classification, especially in the initial phases of Parkinson's disease when motor manifestations are often minimal or absent (Turana et al., 2014; Zhou et al., 2023).

Nevertheless, certain several constraints should be recognized, such as relatively small number of eligible studies and the presence of considerable heterogeneity, which is probably attributable to variations in research design, length of disease progression, participant characteristics, and cognitive evaluation techniques. Furthermore, given that the included investigations were largely based on observational study designs, limitations persist in determining clear causal relationships, a constraint that may ultimately affect the extent to which the findings can be generalized across diverse patient populations. Upcoming investigations are encouraged to prioritize extensive longitudinal research frameworks that apply uniform olfactory and cognitive evaluation instruments in order to more clearly determine how impairments in smell function may predict progressive cognitive deterioration in Parkinson's disease. Such studies would strengthen the evidence base and support the integration of olfactory testing into routine clinical practice (He et al., 2020; Louis et al., 2022; Wal et al., 2022).

4. CONCLUSION

This meta-analysis provides evidence of a statistically meaningful relationship linking olfactory dysfunction with cognitive impairment in Parkinson's disease, revealing that individuals experiencing hyposmia or anosmia exhibit an elevated risk of cognitive impairment relative to patients who maintain normal olfactory abilities, thereby underscoring the potential role of olfactory deficits as a non motor indicator of cognitive deterioration. Despite noticeable variability across the examined studies and the relatively small volume of eligible research, the combined results indicate that smell based assessments may serve as a practical and minimally intrusive approach for detecting individuals who face an elevated likelihood of cognitive impairment. Further methodologically robust investigations employing standardized evaluation protocols are necessary to confirm the present findings and to clarify in greater detail the role of olfactory disturbances within cognitive screening strategies and evidence based clinical decision making for Parkinson's disease.

REFERENCES

Aarsland, D., Batzu, L., Halliday, G. M., Geurtsen, G. J., Ballard, C., Ray Chaudhuri, K., & Weintraub, D. (2021). Parkinson disease-associated cognitive impairment. *Nature Reviews Disease Primers*, 7(1), 47. https://doi.org/10.1038/s41572-021-00280-3

Abraham, J. N., Rawat, D., Srikanth, P., Sunny, L. P., & Abraham, N. M. (2025). Alpha-synuclein pathology and Parkinson's disease-related olfactory dysfunctions: an update

on preclinical models and therapeutic approaches. *Mammalian Genome*, 36(2), 444–464. https://doi.org/10.1007/s00335-025-10128-w

Avanipully, J. N., Thekkekkara, D., M, S., Parihar, V. K., & Manjula, S. N. (2022). The Role of Olfactory System in the Etiogenesis of Parkinson's Diseases: An Overview. *Journal of Pharmacology and Pharmacotherapeutics*, 13(1), 31–39. https://doi.org/10.1177/0976500X221085802

Bagherieh, S., Arefian, N. M., Ghajarzadeh, M., Tafreshinejad, A., Zali, A., Mirmosayyeb, O., & Safari, S. (2023). Olfactory dysfunction in patients with Parkinson's disease: A systematic review and meta-analysis. *Current Journal of Neurology,* 22(4), 249. https://doi.org/10.18502/cjn.v22i4.14530

Ben-Shlomo, Y., Darweesh, S., Llibre-Guerra, J., Marras, C., San Luciano, M., & Tanner, C. (2024). The epidemiology of Parkinson's disease. *The Lancet*, 403(10423), 283–292. https://doi.org/10.1016/S0140-6736(23)01419-8

Bologna, M. (2021). Pathophysiology of motor symptoms in Parkinson's disease: Role of primary motor cortex. *Journal of the Neurological Sciences*, 429, 117909. https://doi.org/10.1016/j.jns.2021.117909

Dahbour, S. S., Al Murr, M. J., Oweis, L. H., Al Antary, N. T., Mohsen, M., & Al Fegi, S. (2022). Non-motor manifestation of Parkinson's disease: a cross-sectional study in a teaching hospital in Jordan. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, 58(1), 148. https://doi.org/10.1186/s41983-022-00559-6

Degirmenci, Y., Angelopoulou, E., Georgakopoulou, V. E., & Bougea, A. (2023). Cognitive Impairment in Parkinson's Disease: An Updated Overview Focusing on Emerging Pharmaceutical Treatment Approaches. *Medicina*, 59(10), 1756. https://doi.org/10.3390/medicina59101756

Doty, R. L., & Hawkes, C.H. (2022). *Olfactory Dysfunction in Parkinson's Disease and Related Disorders. In N. Gálvez-Jiménez, A. D. Korczyn, & R. Lugo-Sanchez (Eds.), Non-motor Parkinson's Disease (pp. 99–114).* Cambridge: Cambridge University Press. https://doi.org/DOI: 10.1017/9781009039291.011

Fullard, M. E., Tran, B., Xie, S. X., Toledo, J. B., Scordia, C., Linder, C., … Morley, J. F. (2016). Olfactory impairment predicts cognitive decline in early Parkinson's disease. *Parkinsonism & Related Disorders*, 25, 45–51. https://doi.org/10.1016/j.parkreldis.2016.02.013

He, R., Zhao, Y., He, Y., Zhou, Y., Yang, J., Zhou, X., Guo, J. (2020). *Olfactory dysfunction predicts disease progression in Parkinson's disease: A longitudinal study*. Frontiers in Neuroscience, 14, 569777. https://doi.org/10.3389/fnins.2020.569777

Jellinger, K. A. (2023). Pathobiology of Cognitive Impairment in Parkinson Disease: Challenges and Outlooks. *International Journal of Molecular Sciences*, 25(1), 498. https://doi.org/10.3390/ijms25010498

Jia, X., Wang, Z., Huang, F., Su, C., Du, W., Jiang, H., … Zhang, B. (2021). A comparison of the Mini-Mental State Examination (MMSE) with the Montreal Cognitive Assessment (MoCA) for mild cognitive impairment screening in Chinese middle-aged and older population: a cross-sectional study. *BMC Psychiatry*, 21(1), 485. https://doi.org/10.1186/s12888-021-03495-6

Louis, E. D., Mayer, S. A., & Noble, J. M. (2022). *Merritt's Neurology, 14e*. Lippincott Williams & Wilkins, a Wolters Kluwer business.

Mertens, A. T., Santo, J. B., Markopoulou, K., & Chase, B. A. (2019). Cognitive processes that indirectly affect olfactory dysfunction in Parkinson's disease. *Clinical Parkinsonism & Related Disorders*, 1, 13–20. https://doi.org/10.1016/j.prdoa.2019.07.003

Morley, J. F., Cohen, A., Silveira-Moriyama, L., Lees, A. J., Williams, D. R., Katzenschlager, R., … Duda, J. E. (2018). Optimizing olfactory testing for the diagnosis of Parkinson's

disease: item analysis of the university of Pennsylvania smell identification test. *Npj Parkinson's Disease*, 4(2),1-7. https://doi.org/10.1038/s41531-017-0039-8

Oikonomou, P., Akhoundi, F. H., Olfati, N., & Litvan, I. (2026). Characteristics and mechanisms of cognitive impairment in Parkinson disease. *Nature Reviews Neurology*, *22*(2), 90–109. https://doi.org/10.1038/s41582-025-01163-x

Ponsen, M. M., Stoffers, D., Booij, J., van Eck-Smit, B. L. F., Wolters, E. Ch., & Berendse, H. W. (2004). Idiopathic hyposmia as a preclinical sign of Parkinson's disease. *Annals of Neurology*, 56(2), 173–181. https://doi.org/10.1002/ana.20160

Rashed, K. H., Bahnasy, W. S., El-Heneedy, Y. A. E., El-Seidy, E. A. S., Tomoum, M. O., Eltomey, M. A., & ELAhwal, S. A. (2020). Patterns of olfactory dysfunctions in patients with Parkinson disease. *The Egyptian Journal of Neurology, Psychiatry and Neurosurgery*, *56*(1), 73. https://doi.org/10.1186/s41983-020-00205-z

Rietdijk, C. D., Perez-Pardo, P., Garssen, J., Van Wezel, R. J., & Kraneveld, A. D. (2017). Exploring Braak's hypothesis of Parkinson's disease. *Frontiers in neurology*, 8, 37. https://doi.org/10.3389/fneur.2017.00037

Ropper, A. H., Samuels, M. A., & Klein, J. (2014). Adams and Victor's principles of neurology. In *Principles of neurology* (Tenth edition.). New York: McGraw-Hill Education Medical.

Seyedmirzaei, H., Rasoulian, P., Parsaei, M., Hamidi, M., Ghanbari, A., Soltani Khaboushan, A., … Sotoudeh, H. (2024). Microstructural correlates of olfactory dysfunction in Parkinson's Disease: a systematic review of diffusion MRI studies. *Brain Imaging and Behavior*, 19(1), 240–252. https://doi.org/10.1007/s11682-024-00934-2

Thomas, A. J., Hamilton, C. A., Barker, S., Durcan, R., Lawley, S., Barnett, N., … Donaghy, P. C. (2022). Olfactory impairment in mild cognitive impairment with Lewy bodies and Alzheimer's disease. *International Psychogeriatrics*, 34(6), 585–592. https://doi.org/10.1017/S1041610221001265

Torres-Pasillas, G., Chi-Castañeda, D., Carrillo-Castilla, P., Marín, G., Hernández-Aguilar, M. E., Aranda-Abreu, G. E., … García, L. I. (2023). Olfactory Dysfunction in Parkinson's Disease, Its Functional and Neuroanatomical Correlates. *NeuroSci*, 4(2), 134–151. https://doi.org/10.3390/neurosci4020013

Turana, Y., Ranakusuma, T. A. S., Purba, J. S., Amir, N., Ahmad, S. A., Machfoed, Moh. H., … Waspadji, S. (2014). Enhancing Diagnostic Accuracy of aMCI in the Elderly: Combination of Olfactory Test, Pupillary Response Test, BDNF Plasma Level, and APOE Genotype. *International Journal of Alzheimer's Disease*, 2014, 1–9. https://doi.org/10.1155/2014/912586

Turkmen, N., Sücüllü Karadağ, Y., & Öztekin, Z. N. (2021). Examination and clinical correlation of olfactory system disorders by an objective method Sniffin' Sticks odor test in Parkinson's disease. *The European Research Journal*, *7*(1), 44–51. https://doi.org/10.18621/eurj.591659

Wal, P., Dwivedi, J., Wal, A., Vig, H., & Singh, Y. (2022). Detailed insight into the pathophysiology and the behavioral complications associated with the Parkinson's disease and its medications. *Future Journal of Pharmaceutical Sciences,* 8(1), 33. https://doi.org/10.1186/s43094-022-00425-5

Yoo, H. S., Chung, S. J., Lee, Y. H., Ye, B. S., Sohn, Y. H., & Lee, P. H. (2020). Association between Olfactory Deficit and Motor and Cognitive Function in Parkinson's Disease. *Journal of Movement Disorders*, 13(2), 133–141. https://doi.org/10.14802/jmd.19082

Zafar, S. Lui, F., & Yaddanapudi, S.S.(2025). *Parkinson Disease.* Treasure Island (FL): StatPearls Publishing. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK470193/

Zhou, Z. D., Yi, L. X., Wang, D. Q., Lim, T. M., & Tan, E. K. (2023). Role of dopamine in the pathophysiology of Parkinson's disease. *Translational Neurodegeneration*, 12(1), 44. https://doi.org/10.1186/s40035-023-00378-6