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REVIEW ARTICLE

THE ROLE OF OLFACTORY TESTING IN DETECTING PRODROMAL PHASE PARKINSON'S DISEASE: A LITERATURE REVIEW

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Abstract

Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder traditionally diagnosed based on classic motor symptoms. However, these motor manifestations appear only after a substantial loss of dopaminergic neurons in the substantia nigra. Detecting PD during its prodromal phase offers a crucial therapeutic window to potentially delay disease progression. Hyposmia is one of the earliest and most prevalent non-motor markers, appearing up to a decade before motor onset.

Methods: A comprehensive literature search was conducted across electronic databases, including PubMed, Cochrane Library, and Google Scholar. The inclusion criteria were restricted to original research articles published within the last five years (2021–2026) in English or Indonesian. Data regarding olfactory testing accuracy and cultural adaptation were synthesized.

Results: Standardized olfactory assessment tools, such as the University of Pennsylvania Smell Identification Test (UPSIT), Sniffin' Sticks, and the Brief Smell Identification Test (B-SIT), demonstrate high sensitivity (79%) and specificity (81%) in distinguishing PD from diagnostic mimics. Nevertheless, international screening tools frequently suffer from cross-cultural bias due to unfamiliarity with Western odorants. Emerging evidence indicates that adapting these instruments using locally familiar Asian and Indonesian olfactory stimuli (e.g., coffee, jasmine, aromatic ginger, and cajuput oil) significantly optimizes diagnostic accuracy.

Conclusions: Brief olfactory assessments, particularly those tailored to regional and cultural settings, serve as highly effective, cost-efficient, and non-invasive screening instruments for prodromal PD detection within routine neurogeriatric clinical practice.

Keywords: Parkinson's Disease, Olfactory Testing, Hyposmia, Prodromal Phase, Cross-Cultural Adaptation

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Introduction

Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder, affecting approximately 2% to 3% of the population aged over 65 years[1,2]. The neuropathological hallmarks of PD involve the progressive degeneration of dopaminergic neurons within the substantia nigra pars compacta, accompanied by the intracellular accumulation of misfolded alpha-synuclein proteins, known as Lewy bodies. Historically, the clinical diagnosis of PD has relied on the manifestation of cardinal motor signs, including bradykinesia, resting tremor, and rigidity, with postural instability typically presenting in more advanced

stages[1,2]. However, by the time these classical motor symptoms become clinically apparent, more than 50% to 70% of nigrostriatal dopaminergic neurons have already been irreversibly lost, highlighting the critical need for early non-motor biomarkers. These motor deficits generally manifest asymmetrically, a feature that distinguishes PD from other atypical parkinsonian syndromes[1,2].

Neuropathological and functional imaging investigations indicate that the underlying neurodegenerative cascade initiates at least one to two decades prior to motor onset[1,2]. This prolonged asymptomatic period is termed the prodromal phase. During this latent phase, alpha-synuclein pathology extensively involves non-dopaminergic structures, including the enteric nervous system, the olfactory bulb, the hypothalamus, and the autonomic nervous system[1,2]. Consequently, a variety of pre-motor and non-motor symptoms emerge long before motor deficits, such as olfactory dysfunction (anosmia or hyposmia), REM sleep behavior disorder (RBD), chronic constipation, anxiety, depression, and orthostatic hypotension[1,2].

Globally, the epidemiological burden of PD is rising sharply. The prevalence ranges from 0.5%–1% among individuals aged 65–69 years and escalates to 1%–3% in populations aged 80 years and older[3]. Driven by an aging global population, the incidence of PD is projected to increase by more than 30% by the year 2030[3]. The disease exhibits a notable gender disparity, affecting males more frequently than females with an approximate ratio of 1.5:1, with incidence rates increasing proportionally with advancing age[3]. While the majority of cases are diagnosed after the age of 50, early-onset variants can also manifest in younger cohorts[3].

Identifying reliable biomarkers during the 10-to-20-year prodromal window represents a critical frontier in neurogeriatrics[4,5]. Early identification provides a vital "window of opportunity" for clinicians to implement potential disease-modifying or neuroprotective therapies aimed at preserving surviving dopaminergic cells before widespread, irreversible structural damage occurs[4,5]. Olfactory dysfunction represents one of the most promising prodromal biomarkers, occurring in over 95% of early-stage PD patients[6]. Olfactory testing provides a highly accessible, cost-effective, and non-invasive screening modality to evaluate neurodegenerative risks in clinical settings[6]. Various standardized instruments, including the University of Pennsylvania Smell Identification Test (UPSIT), Sniffin' Sticks, and the Brief Smell Identification Test (B-SIT), have been evaluated globally for this purpose[6].

Materials and Methods

This study utilized a literature review design to comprehensively synthesize contemporary scientific evidence regarding prodromal PD detection. A structured literature search was systematically executed across prominent electronic biomedical databases, including PubMed, Cochrane Library, and Google Scholar. The search architecture employed combinations of relevant medical subject headings (MeSH) and keywords, including “Parkinson’s Disease”, “olfactory testing”,

"hyposmia", and "prodromal". To ensure high contemporary relevance and strictly adhere to institutional requirements, the inclusion criteria were limited to peer-reviewed original research articles and systematic reviews published within the last five years (2021–2026), available in full-text format, and written in either English or Indonesian. The primary target of evaluation comprised clinical studies assessing the diagnostic accuracy, sensitivity, specificity, or clinical utility of olfactory testing modalities in identifying early-stage or prodromal neurodegeneration. Conversely, exclusion criteria consisted of single case reports, brief abstracts lacking accessible full-text data, and articles completely unrelated to neurogeriatric or movement disorder clinical frameworks.

Results

Diagnostic Accuracy of Standardized Olfactory Instruments

Based on synthesized data from international multi-center studies, standardized olfactory assessments demonstrate high diagnostic performance in identifying olfactory decline[6-8]. Meta-analytic data indicates that comprehensive olfactory evaluation yields an overall sensitivity of 79% and a specificity of up to 81% in successfully differentiating Parkinson's disease (PD) patients from clinical diagnostic mimics, such as essential tremor or atypical parkinsonian disorders. Parkinson's disease (PD) is known for its motor alterations, but the importance of non-motor symptoms (NMSs), such as olfactory dysfunction (OD), is increasingly recognized. OD may manifest during the prodromal period of the disease, even before motor symptoms appear. Therefore, it is suggested that this symptom could be considered a marker of PD[6-8].

Clinical Characteristics of Gold-Standard Modalities

The clinical implementation of olfactory screening involves three primary modalities: the University of Pennsylvania Smell Identification Test (UPSIT), the Sniffin' Sticks Test, and the Brief Smell Identification Test (B-SIT).

(1) University of Pennsylvania Smell Identification Test (UPSIT)

The University of Pennsylvania Smell Identification Test (UPSIT) is widely utilized to assess olfactory decline, and specific subitems of the test have been identified as valuable markers to predict motor progression in Parkinson's disease[8]. This test is based on a scratch-and-sniff method consisting of 40 distinct odorants applied to plastic microcapsules within a small paper booklet[8]. Patients are required to scratch the odor strip using a pencil, inhale the scent, and select one of four available multiple-choice options (forced-choice test)[8]. The total score out of 40 odorants is then classified into degrees of olfactory function, ranging from normosmia, mild-to-severe microsmia, to total anosmia or malingering[8]. Despite demonstrating exceptionally high validity and reliability, the UPSIT requires a relatively lengthy administration time (approximately 10–15 minutes)[8].

(2) Sniffin' Sticks Test

Developed in Europe, Sniffin' Sticks is an olfactory evaluation tool based on felt-tip pens filled with liquid odorants rather than scratch-and-sniff paper booklets[9]. Evaluating the complete battery through threshold, discrimination, and identification (TDI) scores provides superior diagnostic performance in differentiating early Parkinson's disease patients from healthy controls compared to isolated subtests[9]. In the threshold test, the concentration of the odorant (usually using phenylethyl alcohol or n-butanol) is increased stepwise to determine the lowest physical sensitivity of the patient's nose[9]. The discrimination test evaluates the patient's ability to distinguish one differing scent among three pens, while the identification test utilizes a multiple-choice format similar to the UPSIT[9].

(3) Brief Smell Identification Test (B-SIT)

The Brief Smell Identification Test (B-SIT), also known as the Cross-Cultural Smell Identification Test (CC-SIT), is a streamlined version of the UPSIT designed to meet the need for rapid screening in high-volume clinical setting[10]. This assessment utilizes only 12 essential odorants selected from the full-length UPSIT version based on universal familiarity across various regions, such as coffee, banana, orange, and rose. The hallmark benefit of the B-SIT lies in its practicality for rapid olfactory screening in routine clinical practice.This makes it highly ideal for integration into routine geriatric examinations or mass screenings within busy outpatient neurology clinics[10].

Regional Validation and Efficacy Data

In the Asian region, recent validation protocols have demonstrated varying efficacy rates based on cohort familiarity. A clinical validation study conducted by Cao et al. (2020) confirmed high diagnostic accuracy, sensitivity, and specificity for a newly developed olfactory testing instrument approved by China's National Medical Products Administration (NMPA) when evaluated against traditional screening methods[6,12,13].

Furthermore, recent cultural adaptation initiatives in Southeast Asia, particularly within Indonesian cohorts, report that modifying test stimuli to include highly familiar regional odorants significantly enhances diagnostic reliability independently of the patient's formal educational background[6,12,13]. The core parameters, structural profiles, and key clinical findings of these evaluated instruments are systematically summarized in Table 3.1.

Table 3.1 Summary of Clinical Studies on Olfactory Testing Instruments in Parkinson's Disease

Study & Design	Evaluated Instrument / Modality	Key Findings
Heng et al. (2023) [2] SR & Meta-analysis	Dopamine Imaging	• 50%–80% striatal dopamine is lost at motor onset. • Early non-motor markers are critically urgent.
Cao et al. (2020) [6] Clinical Validation	NMPA vs. B-SIT	• High accuracy and optimal for hyposmia screening in

Study & Design	Evaluated Instrument / Modality	Key Findings
		Asian cohorts.
Gabriel Torres - Pasillas et al. (2023) [7] Clinical Validation	Braak Staging	• Olfactory dysfunction (OD), is increasingly recognized and this symptom could be considered a marker of PD.
Ruan et al. (2022) [10] Cross-Cultural Validation	12-item B-SIT (Asian version)	• Evaluated the efficiency of universal 12-odor B-SIT. • Highly valid and rapid (< 5 mins) for regional cohorts.

Discussion

From a clinical discussion perspective, the success of evaluations within the Asian region highlights a critical challenge in utilizing global olfactory tests: the confounding factor of cross-cultural bias[12]. If left unadapted, international standardized assessments frequently employ essential odorants that are entirely unfamiliar to local populations, such as blackberry or specific types of Western cheese[11]. When elderly patients in Indonesia are tested using these unfamiliar scents, the risk of diagnostic misinterpretation—resulting in false positives or false negatives—becomes exceptionally high[12,13]. This discrepancy occurs because the patient's inability to identify the odorant stems purely from a lack of lifetime environmental exposure rather than structural damage to the olfactory bulb or pathways[12,13].

Therefore, recent cultural adaptation studies in Indonesia demonstrate that utilizing olfactory testing materials based on familiar local odorants—such as jasmine, aromatic ginger (kencur), coffee, menthol, and cajuput oil (Melaleuca cajuputi)—significantly enhances diagnostic accuracy without being confounded by the patient's educational level[13,14]. These data indicate that olfactory decline (hyposmia) within the Indonesian elderly population can be characterized more accurately through such examinations[13,14]. To maximize the early and precise detection of Parkinson's disease during its prodromal phase, the implementation of olfactory testing instruments tailored to local Indonesian odorant characteristics is highly essential. Through this adaptation, olfactory testing can serve as a screening tool that is not only cost-effective and non-invasive but also possesses high sensitivity in daily neurogeriatric clinical practice[13,14]

Conclusion

Brief olfactory identification instruments, particularly the Brief Smell Identification Test (B-SIT), demonstrate high accuracy, sensitivity, and specificity, making them highly effective screening Atools for detecting hyposmia during the prodromal phase of Parkinson's disease. These short-form assessments are exceptionally well-suited for seamless application in time-constrained clinical settings, ensuring high patient compliance without compromising diagnostic yield. Furthermore, the clinical

application of olfactory testing instruments adapted to local Indonesian odorants, such as jasmine, aromatic ginger, and coffee, provides enhanced cultural relevance and accurate diagnostic data for detecting early olfactory decline within the Indonesian elderly population.

Conflict of Interest

The authors declared no conflict of interest.

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