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Olfactory Dysfunction in Psychiatric and Neurodegenerative Disorders: Clinical Relevance and Potential as a Biomarker

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Abstract

Background. Olfactory dysfunction is increasingly recognized as a feature present in both psychiatric and neurodegenerative disorders. It has been linked to alterations in central neural processing as well as to progressive structural changes within the nervous system.

Aim. The aim of this study was to compare olfactory dysfunction across major depressive disorder, schizophrenia, Alzheimer's disease, and Parkinson's disease, with particular emphasis on its clinical significance and underlying mechanisms.

Materials and methods. A narrative review of current literature was conducted, focusing on studies assessing olfactory function in the selected disorders. Relevant findings were analysed in terms of clinical presentation, neurobiological correlates, and potential diagnostic value.

Results. Olfactory dysfunction was identified across all examined conditions. In psychiatric disorders, deficits appeared to be primarily related to functional alterations and were often

dynamic or partially reversible. In contrast, in neurodegenerative diseases, olfactory impairment was associated with progressive structural and molecular pathology and frequently occurred in the prodromal phase. Across all groups, higher-order olfactory processes, particularly odor identification and discrimination, were most consistently affected.

Conclusions. Olfactory dysfunction represents a multidimensional phenomenon that may reflect either transient functional changes or ongoing neurodegeneration, depending on the disorder. Its non-invasive assessment may provide a useful complementary tool for early detection and monitoring of disease progression. These findings suggest the potential relevance of olfactory assessment in clinical research and early identification of neurological and psychiatric conditions, particularly in the context of preventive strategies and early intervention.

Keywords: olfactory dysfunction; Parkinson's disease; Alzheimer's disease; major depressive disorder; schizophrenia; biomarkers; neurodegeneration; prodromal phase; olfactory identification; early diagnosis

1. Introduction

The sense of smell is a specialized chemosensory system responsible for the detection and interpretation of volatile chemical compounds present in the environment. In humans, olfaction plays a key role in multiple behavioural and physiological processes, including food perception, hazard detection, and social communication. Odor perception is also closely linked to emotional responses and memory formation, reflecting strong interaction between olfactory processing and higher cognitive functions. [1]

From a neurobiological perspective, olfactory perception begins when odorant molecules reach the olfactory epithelium and bind to receptors located on olfactory sensory neurons. This interaction initiates signal transduction mechanisms that convert chemical stimuli into electrical signals, which are then transmitted to the olfactory bulb. Within the olfactory bulb, signals converge in specialized structures known as glomeruli, where initial processing and organization of olfactory information take place. The processed signals are subsequently relayed through the olfactory tract to primary olfactory cortical regions, including the piriform cortex, amygdala, and entorhinal cortex, which are involved in odor identification and

integration with cognitive and emotional processes. Notably, unlike most other sensory systems, olfactory pathways project directly to cortical and limbic structures without obligatory thalamic relay, enabling rapid interactions with neural circuits responsible for memory and affective regulation. [2,3]

Because many neurological and psychiatric disorders involve brain regions that are part of the olfactory network, disturbances in olfactory perception may reflect broader alterations within the central nervous system. For this reason, olfactory dysfunction has increasingly been investigated as a potential indicator of underlying brain pathology. [3,4]

Olfactory dysfunction is a relatively common condition, affecting a substantial proportion of the general population. Epidemiological data suggest that approximately 20% of adults experience some degree of olfactory impairment, while complete loss of smell (anosmia) occurs in around 3–5% of individuals. Its prevalence increases with age and is particularly high among older adults. Olfactory impairment may arise from a wide range of causes, including sinonasal diseases, infections, head trauma, and neurodegenerative processes. [4]

Beyond its prevalence, olfactory dysfunction has important clinical implications. It may significantly affect quality of life and everyday functioning by influencing nutritional behaviour, safety, and social interactions. For example, reduced olfactory ability can limit the detection of environmental hazards or alter the perception of food. Despite these consequences, olfactory disturbances often remain underrecognized, as many individuals are unaware of their deficits without formal testing. [5,6]

In recent years, increasing attention has been directed toward the clinical relevance of olfactory dysfunction, particularly in the context of neurological and psychiatric disorders. At the same time, demographic changes, including population aging and the rising prevalence of neurodegenerative diseases, have emphasized the need for accessible and non-invasive biomarkers. In this context, olfactory impairment has been proposed as a potential indicator of early alterations within brain networks involved in cognition and emotional processing. [6,7]

Understanding these alterations may also have practical implications for early detection and patient management. This review is structured to first discuss olfactory dysfunction in psychiatric disorders, followed by neurodegenerative conditions, and finally to provide a comparative analysis of these findings.

2. Methodology

This study was conducted as a narrative review with a comparative approach, aiming to synthesize current evidence on olfactory dysfunction in selected psychiatric and

neurodegenerative disorders. The review focused on major depressive disorder, schizophrenia, Alzheimer's disease, and Parkinson's disease, with particular emphasis on clinical presentation, underlying mechanisms, and potential diagnostic relevance.

A literature search was conducted using electronic databases, including PubMed and Google Scholar, to identify relevant studies published in English. Additionally, selected sources not indexed in PubMed were identified through manual searches and reference screening. The search strategy combined terms related to olfactory function (e.g., olfactory dysfunction, hyposmia, anosmia, odor identification, olfactory testing) with terms referring to the selected disorders (e.g., major depressive disorder, schizophrenia, Alzheimer's disease, Parkinson's disease). Reference lists of included articles were also screened to identify additional relevant publications.

No strict lower time limit was applied. However, the review predominantly included studies published from 2018 onwards, reflecting the most recent developments in the field. Earlier publications were considered selectively when they provided essential background or widely cited findings relevant to olfactory dysfunction. The search was conducted up to March 2026.

Eligible sources included original research articles, systematic reviews, and meta-analyses addressing olfactory function in the context of the examined conditions. Particular attention was given to studies evaluating different domains of olfactory performance, such as odor threshold, discrimination, and identification, as well as to studies exploring neurobiological correlates and longitudinal changes.

Studies were selected based on their relevance to the aim of the review and their contribution to understanding similarities and differences between psychiatric and neurodegenerative disorders. Studies not directly addressing olfactory function, not related to the selected conditions, or lacking sufficient methodological clarity were excluded. In addition, non-English publications and conference abstracts without full-text availability were not considered.

Due to the narrative nature of the review, no formal quality assessment or meta-analytic procedures were applied. The collected data were analysed qualitatively, with a focus on identifying recurring patterns, disorder-specific characteristics, and potential clinical implications of olfactory dysfunction. It should be noted that variability across studies, including differences in methodology and study populations, may influence the comparability of findings.

3. Olfactory Dysfunction in Psychiatric Disorders

3.1 Olfactory Dysfunction in Major Depressive Disorder

Major Depressive Disorder (MDD) is a leading cause of disability worldwide. Globally, approximately 300 million individuals are estimated to be living with the disorder, and prevalence rates continue to grow. The disorder is characterized by a broad spectrum of psychological and somatic symptoms, including persistent low mood, fatigue, and anhedonia. [8–10] In recent years, growing evidence has suggested that MDD is also associated with disturbances in olfactory function. Investigating these changes may provide valuable insight into the relationship between sensory processing and affective regulation in depression. [11–15]

One of the earlier lines of research focused on identifying structural correlates of olfactory impairment in MDD. This study has shown that patients experiencing acute episodes of major depression exhibit significantly reduced olfactory sensitivity, accompanied by decreased olfactory bulb volumes. Furthermore, smaller olfactory bulb volume has been associated with higher depression severity scores, suggesting that structural changes within early olfactory pathways may parallel the intensity of affective symptoms. These findings indicate that olfactory dysfunction in MDD may have measurable neurobiological correlates. [11]

Further evidence suggests that disturbances in olfactory function in MDD appear to vary according to the clinical phase of the illness. Comparisons between symptomatic and remitted states show that olfactory deficits are most evident during active depressive episodes. When symptoms subside, olfactory performance tends to improve, suggesting that these alterations are not fixed but potentially reversible. This pattern supports the view that olfactory dysfunction in depression is more likely linked to transient functional changes within neural circuits rather than to irreversible structural damage of the sensory system. [12]

Longitudinal population-based research further clarifies the temporal dynamics of this relationship. Studies in older adults have shown that individuals with impaired olfactory function are more likely to report depressive symptoms at the same assessment point. More importantly, prospective follow-up over several years has revealed that baseline olfactory impairment predicts an increased likelihood of developing depressive symptoms, whereas initial depressive symptoms do not appear to predict later olfactory decline. This directional association suggests that, in certain populations, olfactory dysfunction may precede and potentially signal vulnerability to depression. Such findings highlight the clinical importance of depression screening in patients presenting with unexplained olfactory deficits. [13]

The relationship between olfactory function and depressive symptoms appears not only predictive but also dynamic. Studies examining changes over time have demonstrated that

improvements in olfactory performance correlate with reductions in depressive symptom severity, particularly among individuals who initially present with measurable olfactory impairment (dysosmia). In these patients, significant gains have been observed in odor identification, detection threshold, and overall olfactory performance across repeated assessments. The stronger association between sensory improvement and mood reduction in dysosmic individuals suggests that baseline olfactory status may influence the trajectory of clinical recovery. These findings point toward a bidirectional interplay between sensory processing and affective regulation. [14]

Finally, recent meta-analytic evidence confirms that, overall, individuals with depression exhibit statistically significant impairments in olfactory functioning compared to healthy controls. The largest discrepancies are typically observed in odor identification tasks, supporting the view that depression predominantly affects higher-order central processing rather than peripheral olfactory sensitivity. [15]

Taken together, olfactory dysfunction in MDD appears to reflect predominantly functional alterations within central neural networks rather than irreversible structural damage. Its dynamic nature, including partial reversibility and association with clinical state, suggests a close link between olfactory processing and affective regulation. Moreover, longitudinal findings indicating that olfactory impairment may precede the onset of depressive symptoms highlight its potential role as a marker of vulnerability in selected populations.

3.2 Olfactory Dysfunction in Schizophrenia

Schizophrenia is a chronic and highly disabling psychiatric disorder affecting approximately 1% of the population worldwide. It is characterized by positive symptoms such as hallucinations and delusions, negative symptoms including diminished motivation and affect, and significant cognitive deficits. [16]

Apart from its primary psychopathological features, schizophrenia is increasingly recognized as involving alterations in sensory function, especially in the domain of olfaction. [17–22]

To better understand olfactory dysfunction in schizophrenia, it is important to first consider the structural and functional brain abnormalities associated with the disorder that may contribute to impaired olfactory processing. Neuroimaging studies consistently demonstrate widespread alterations affecting multiple regions, particularly the prefrontal and temporal cortices, the hippocampus, and large-scale connectivity networks. These structures are closely involved in higher-order olfactory processing through their connections with the orbitofrontal cortex and

medial temporal regions. Disruption within these circuits may therefore contribute to the olfactory deficits observed in schizophrenia. [17,18]

At the clinical level, a clear association between schizophrenia and olfactory dysfunction has also been demonstrated. In patients hospitalized during an acute psychotic episode, significant impairments were observed in odor threshold, discrimination, and identification compared to controls. Hospitalization duration was correlated with overall olfactory performance and odor discrimination, with longer inpatient stays corresponding to lower smell scores. However, no significant associations were found between olfactory performance and clinical symptom severity. This study may suggest that poorer olfactory performance reflects overall illness burden, as indicated by longer hospitalization, rather than momentary symptom intensity. [19]

The most recent and comprehensive meta-analysis further confirms the presence of selective olfactory deficits in schizophrenia-spectrum disorders. Specifically, impairments were consistently observed in higher-order olfactory tasks, such as odor identification and discrimination, whereas basic odor sensitivity remained largely unaffected. This pattern supports the notion that olfactory dysfunction in schizophrenia predominantly reflects disturbances in central processing rather than peripheral sensory impairment. Importantly, reduced odor identification performance was associated with longer illness duration, lower educational attainment, and greater severity of negative symptoms, suggesting that higher-order olfactory deficits may be linked to cognitive decline and illness progression. [20]

Beyond well-established findings in chronic schizophrenia, olfactory function has also been examined in the early and prodromal stages of psychosis. In this context, odor identification deficits were observed in individuals with first-episode schizophrenia and in those at ultra-high clinical risk compared to healthy controls, whereas participants with genetic risk alone did not show similar impairments. Importantly, within the ultra-high-risk group, poorer baseline odor identification was found in individuals who later transitioned to psychosis. Olfactory performance was also associated with cognitive functioning, suggesting that higher-order smell deficits may reflect broader neurocognitive alterations present in early psychosis. These findings indicate that impaired odor identification could represent a potential early marker of psychosis onset. [21]

Furthermore, another study aimed to investigate whether olfactory dysfunction in schizophrenia varies according to symptom profile and sex. The results indicated that, after controlling for potential confounding factors, negative symptoms in male patients were significantly associated with poorer odor discrimination and identification, as well as reduced overall olfactory performance. In contrast, in female patients, positive and general psychopathology symptoms

were primarily linked to impaired odor identification. These results indicate that olfactory dysfunction may be differentially related to specific clinical dimensions and may exhibit sex-related patterns, which could be relevant when considering olfaction as a potential biomarker in schizophrenia. [22]

Taken together, olfactory dysfunction in schizophrenia is primarily characterized by impairments in higher-order processing, particularly odor identification and discrimination, reflecting disturbances within central neural networks. Its presence in early and prodromal stages, along with associations with cognitive dysfunction and negative symptom severity, suggests that olfactory impairment may represent a marker of broader neurocognitive and pathophysiological alterations underlying the disorder.

4. Olfactory Dysfunction in Neurodegenerative Disorders

4.1 Olfactory Dysfunction in Alzheimer's Disease

Alzheimer's disease (AD) is the most common cause of dementia and a progressive neurodegenerative disorder characterized by the accumulation of β-amyloid plaques and neurofibrillary tangles composed of hyperphosphorylated tau protein. These pathological processes lead to synaptic dysfunction, neuronal loss, and progressive brain atrophy, resulting in gradual cognitive decline. Clinically, AD most often begins with subtle memory impairment and progressively affects other cognitive domains, including language, attention, and executive functions. Importantly, neuropathological changes may develop many years before the onset of clear clinical symptoms, highlighting the need for early markers of the disease. [23]

Impairment of olfactory function is a common feature of Alzheimer's disease and may be detectable at very early stages of its course. Studies have shown that both odor discrimination and odor identification are already reduced in the prodromal phase, with further decline observed as the disease progresses. [24,25] Importantly, olfactory deficits may appear even before clear cognitive impairment becomes evident. Individuals reporting subjective cognitive decline, despite performing within normal ranges on standard cognitive tests, have been found to show poorer odor identification, suggesting that changes in olfactory function may precede measurable cognitive deterioration. [26]

Beyond their early occurrence, olfactory disturbances may also have clinical relevance in identifying individuals at risk of Alzheimer's disease. Certain olfactory measures, particularly odor identification and familiarity, have been associated with an increased risk of progression from mild cognitive impairment to Alzheimer's disease, in some cases more effectively than commonly used cognitive screening tools such as the MMSE. This effect appears especially

pronounced in individuals carrying the APOE ε4 allele.[27] Moreover, simplified olfactory tests based on selected odorants have demonstrated good diagnostic performance, supporting their potential use in clinical settings as a screening method for early-stage disease. [25]

The relationship between olfactory dysfunction and Alzheimer's disease is further supported by neurobiological findings. Neuroimaging studies have revealed reduced grey matter volume in regions associated with olfactory processing, including the piriform cortex, amygdala, entorhinal cortex, and hippocampus. These structures are also involved in memory processes and are known to be affected early in the course of neurodegeneration. [28] In addition, lower olfactory performance has been associated with poorer outcomes in neuropsychological testing and with the presence of β-amyloid pathology. Notably, individuals with amyloid deposition exhibit weaker olfactory function even when compared within the same stage of cognitive impairment, which suggests that olfactory deficits may reflect underlying molecular changes.[29]

Further evidence points to a link between olfactory impairment and tau pathology. Reduced performance in odor identification tasks has been associated with increased tau accumulation in medial temporal and olfactory-related regions of the brain. Longitudinal observations indicate that poorer olfactory function at baseline may be related to greater tau deposition over time, suggesting that these deficits may precede and potentially signal ongoing neurodegenerative processes. [30]

Taken together, olfactory dysfunction in Alzheimer's disease represents an early and clinically relevant feature closely linked to underlying neurodegenerative processes. Its association with β-amyloid deposition, tau pathology, and structural changes in olfactory-related brain regions suggests that olfactory impairment reflects ongoing molecular and neuroanatomical alterations. Importantly, its presence in preclinical and prodromal stages highlights its potential value as a non-invasive marker for early detection and monitoring of disease progression.

4.2 Olfactory Dysfunction in Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder traditionally defined by its motor manifestations, although it is now recognized that a wide range of non-motor symptoms may precede their onset. These early features, including sleep disturbances, autonomic dysfunction, and sensory deficits, are part of the prodromal phase of the disease. Among them, olfactory dysfunction is particularly common and may occur several years before clinical diagnosis, often remaining unnoticed despite its impact on daily functioning and quality of life. Because of its early onset and significant predictive value, impaired olfaction is now

considered an important marker of underlying neurodegenerative processes in PD and is incorporated into research criteria for prodromal disease. [31,32]

Beyond its role as an early symptom, olfactory dysfunction reflects structural and functional alterations within both peripheral and central components of the olfactory system. Current evidence suggests that pathological processes involving alpha-synuclein may originate in the olfactory bulb and subsequently spread to interconnected brain regions, leading to progressive disruption of odor processing. These changes are associated with impaired neural activity and connectivity within olfactory pathways, which contribute to deficits in odor detection, discrimination, and identification. Importantly, the severity of olfactory impairment varies among patients and may be related to differences in disease phenotype and progression, with some studies indicating a potential association with an increased risk of cognitive decline. [33]

A recent study further demonstrates that olfactory dysfunction differs between clinical subtypes of Parkinson's disease and is linked to alterations in brain network organization. Patients with the akinetic-rigid subtype tend to present with more pronounced olfactory deficits compared to those with the tremor-dominant form, as reflected in lower scores on standardized smell identification tests. These differences are accompanied by reduced functional connectivity within the olfactory network, including regions such as the hippocampus and posterior cingulate cortex, suggesting a relationship between olfactory performance and underlying neural connectivity. [34]

Complementary findings from clinical studies indicate that olfactory impairment in Parkinson's disease is not uniform across different domains of olfactory function. While patients with the akinetic-rigid subtype show greater impairment in odor detection threshold, differences in odor identification and discrimination appear less consistent between subtypes. These observations suggest that distinct components of olfactory processing may be differentially affected depending on the clinical phenotype, further supporting the heterogeneity of underlying pathophysiological mechanisms in Parkinson's disease. [35]

From a mechanistic perspective, the olfactory system may play a key role in the early spread of neurodegenerative processes due to its extensive neural connectivity. The propagation of pathology from the olfactory bulb to other brain regions is thought to be associated with alterations in neurotransmitter systems and abnormal accumulation of α-synuclein, which further disrupts synaptic function and contributes to disease progression. Ongoing research is focused on targeting these molecular pathways, including modulation of autophagy, oxidative stress, and neuroinflammation, although significant challenges remain in translating these approaches into effective therapies. [36]

Longitudinal studies indicate that olfactory function in PD tends to decline over time, although this process is not strictly linear and may fluctuate. Evidence suggests that deterioration of smell, particularly odor detection, may be more pronounced in the early stages of the disease. However, the relationship between olfactory impairment and other clinical features, such as motor severity, cognitive decline, or mood disturbances, remains inconsistent across studies. These observations imply that olfactory dysfunction may follow a partially independent trajectory, while still providing valuable information about disease evolution, especially in its early phases. [37]

Taken together, olfactory dysfunction in Parkinson's disease represents an early and heterogeneous feature reflecting both peripheral and central alterations within the olfactory system. It is closely linked to underlying neurodegenerative processes, including α-synuclein pathology and disrupted neural connectivity, and may emerge in the prodromal phase of the disease. Variability across clinical subtypes further highlights disease heterogeneity and supports the potential role of olfactory dysfunction as a non-invasive marker of early disease processes and progression.

5. Comparative Analysis

Across the examined conditions, olfactory dysfunction emerges as a shared but heterogeneous phenomenon, differing in its underlying mechanisms, clinical course, and potential diagnostic relevance. A key distinction can be observed between psychiatric and neurodegenerative disorders.

In psychiatric conditions such as major depressive disorder and schizophrenia, olfactory deficits appear to be primarily related to functional alterations within central neural networks. These disturbances most consistently affect higher-order olfactory processes, including odor identification and discrimination, while basic sensory detection is often relatively preserved. Importantly, in depression, olfactory impairment may fluctuate in parallel with clinical status and, in some cases, improve following symptom remission, suggesting at least partial reversibility. In schizophrenia, deficits in higher-order olfactory processing seem to be more stable and are frequently associated with cognitive impairment and negative symptoms, indicating a link to broader disturbances in central information processing.

In contrast, in neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease, olfactory dysfunction is more closely associated with progressive structural and molecular pathology. In these conditions, impairment often appears in the early or even prodromal phase and tends to worsen over time. Olfactory deficits in neurodegeneration are not only more

persistent but also more strongly linked to underlying disease mechanisms, including protein aggregation, neuronal loss, and network degeneration within olfactory-related brain regions. Moreover, in both Alzheimer's and Parkinson's disease, olfactory dysfunction may precede the onset of core clinical symptoms, highlighting its potential value as an early marker of disease processes.

Another important difference concerns the clinical role of olfactory impairment. In psychiatric disorders, it may reflect current disease state or functional dysregulation of neural circuits, whereas in neurodegenerative diseases it may indicate ongoing neurobiological damage and disease progression. Despite these differences, a common feature across all examined conditions is the predominant involvement of higher-order olfactory processing, suggesting that complex central mechanisms play a critical role in the manifestation of olfactory dysfunction. However, inconsistencies across studies and methodological differences limit direct comparability of findings.

6. Conclusions

Olfactory dysfunction appears to be a common feature across both psychiatric and neurodegenerative disorders; however, its nature and clinical implications differ depending on the underlying condition. In psychiatric disorders, olfactory deficits seem to be largely related to functional alterations within central neural networks and may, at least in part, reflect dynamic changes associated with disease activity. In contrast, in neurodegenerative diseases, olfactory impairment is more closely linked to progressive structural and molecular pathology and often emerges in the early stages of disease development.

These differences highlight the complex nature of olfactory dysfunction and suggest that it should not be interpreted as a uniform clinical phenomenon. Instead, its significance appears to depend on the broader pathological context in which it occurs. The consistent involvement of higher-order olfactory processes across disorders indicates that central mechanisms play a key role in shaping olfactory impairment, regardless of etiology.

From a clinical perspective, the non-invasive and relatively accessible assessment of olfactory function may represent a useful complementary tool in both research and practice. In neurodegenerative disorders, it may contribute to early detection and identification of individuals at risk, while in psychiatric conditions it may provide additional insight into disease state and functional brain alterations. However, the variability observed across studies and conditions underscores the need for further research aimed at standardizing assessment methods and clarifying the specificity of olfactory deficits. Future studies should focus on longitudinal

and standardized assessments of olfactory function to better determine its clinical utility across different disorders.

This review has several limitations, including its narrative design and the heterogeneity of included studies, which may limit the generalizability of the findings.

Overall, a better understanding of olfactory dysfunction may enhance its clinical applicability and contribute to improved early detection strategies, as well as provide deeper insight into the neurobiological mechanisms underlying both psychiatric and neurodegenerative disorders.

Disclosure

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AI: AI was utilized for two specific purposes in this research. Text analysis of clinical reasoning narratives to identify linguistic patterns associated with specific logical fallacies. Assistance in refining the academic English language of the manuscript, ensuring clarity, consistency, and adherence to scientific writing standards. AI were used for additional linguistic refinement of theresearch manuscript, ensuring proper English grammar, style, and clarity in the presentation of results. It is important to emphasize that all AI tools were used strictly as assistive instruments under human supervision. The final interpretation of results, classification of errors, and conclusions were determined by human experts in clinical medicine and formal logic. The AI tools served primarily to enhance efficiency in data processing, pattern recognition, and linguistic refinement, rather than replacing human judgment in the analytical process.

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