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Review

Exploring the Application Potential of α-Synuclein Molecular Probes in Early Diagnosis of Parkinson's Disease: Focus on Imaging Methods

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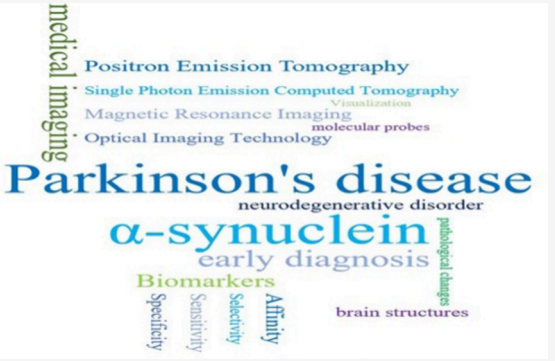
ABSTRACT: This review aims to explore the potential application of α-synuclein (α-syn) molecular probes in the early diagnosis of Parkinson's disease (PD), particularly through systematic evaluation using medical imaging methods. In recent years, The abnormal aggregation of α-syn within the central nervous system is now recognized as a central driver of PD pathophysiology, solidifying its role as a critical diagnostic and prognostic biomarker. Early diagnosis of PD is critical for enabling precision therapeutic interventions and mitigating neurodegenerative progression, thereby enhancing long-term functional outcomes and the quality of life. However, challenges remain in clinical practice, particularly concerning the late timing of diagnosis and the lack of specific biomarkers. By analyzing the existing literature, we will assess the effectiveness of different imaging techniques combined with α-syn probes and discuss their advantages and limitations in clinical applications. These imaging methods can provide visualization of early pathological changes, helping to improve the recognition rate of PD. Finally, we emphasize the importance of future research to explore new molecular probes and imaging technologies that can improve early diagnosis rates and treatment outcomes for PD.



KEYWORDS: *Parkinson's disease, α-synuclein, medical imaging, molecular probes, biomarker*

1. INTRODUCTION

1.1. Epidemiological and Clinical Characteristics of Parkinson's Disease. Parkinson's disease (PD) is a common neurodegenerative disorder, and epidemiological studies show that the incidence is rising annually worldwide, particularly among the elderly population.[1,2] According to recent research, the prevalence of PD varies across different regions; for instance, studies in China indicate that the incidence of the disease has significantly increased over the past 40 years, reflecting the impact of an aging population.[3] Clinically, PD is characterized by a spectrum of motor and nonmotor symptoms, including bradykinesia, rigidity, tremors, and various cognitive and psychiatric disturbances. Notably, respiratory dysfunctions and dysphagia are also frequently encountered among PD patients.[4,5] These features not only affect the quality of life of patients but also impose a burden on families and society. Therefore, understanding the epidemiological characteristics of PD is crucial for formulating effective public health policies and intervention measures.[1,6]

1.2. Biological Functions of α-Synuclein and Its Role in PD. α-Synuclein (α-syn) is a small neuron-specific protein that plays a significant role in neuronal synapses.[7] Research has found that α-syn is critical in neurotransmitter release and synaptic plasticity.[8] However, in patients with PD, the abnormal aggregation of α-syn forms Lewy bodies, leading to neuronal damage and death, which triggers the onset of motor and nonmotor symptoms.[9−11] At this point, 50−80% of the dopaminergic neurons in the brain have already died, indicating that the disease is in the mid to late stages.[12] In recent years, therapeutic strategies targeting α-syn have gradually become a research hotspot, including the development of immunotherapy and small molecule drugs.[13,14] While the amyloid hypothesis has historically dominated discussions on α-syn aggregation in PD, emerging evidence underscores the critical role of transient, neurotoxic oligomers and lipid interactions in disease pathogenesis.[15,16] The molecular pathogenesis of PD centers on the conformational transition of α-syn from soluble monomers to neurotoxic oligomers and protofibrils. Under oxidative stress or lipid membrane interactions, α-syn undergoes nucleation-dependent polymer-

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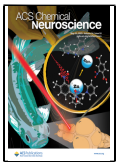

ization, forming β-sheet-rich intermediates that disrupt synaptic vesicle trafficking and mitochondrial function. The formation of intracellular α-syn fibrils is intricately associated with neurodegenerative mechanisms, while the dissemination of α-syn aggregates within the brain is believed to underlie the pathological progression of disease. This underscores the importance of α-syn assembly as both a diagnostic and staging biomarker, as well as a potential target for therapeutic intervention.[17,18]

1.3. Importance of Early Diagnosis and Its Impact on Treatment. Early diagnosis is crucial for the treatment of PD. Studies show that early identification and intervention can significantly improve patient prognosis and slow disease progression.[19] With advancements in medical imaging and biomarker technologies, methods for early diagnosis have become increasingly diverse. For example, brain imaging examinations (such as PET and MRI) can help identify early neurological functional changes, enabling early intervention.[20] Additionally, early diagnosis can assist patients and families in better planning future care and support, alleviating the disease's impact on quality of life. Therefore, developing effective early screening methods is a vital area of research in PD.

2. THE RELATIONSHIP BETWEEN α-SYN AGGREGATION AND PD

2.1. Pathological Features and Neurodegenerative Changes. α-syn is a core component of the pathological features of PD, with its aggregation forming Lewy bodies, which are hallmark pathological changes of the disease.[21] Research indicates that the abnormal aggregation of α-syn within neuronal cells leads to cellular dysfunction and neurodegenerative changes, resulting in the loss of motor function and the emergence of other nonmotor symptoms.[22] The aggregation of α-syn not only affects the survival of dopaminergic neurons but also may exacerbate neuronal damage through neuroinflammatory pathways. Furthermore, the aggregation of α-syn is closely related to various cellular pathological processes, including mitochondrial dysfunction, endoplasmic reticulum stress, and apoptosis, all of which contribute to the progression of PD. In terms of imaging, techniques such as MRI and PET have been applied to study changes in brain structure and function in PD patients, revealing microstructural changes in brain regions associated with α-syn aggregation, such as the substantia nigra and striatum, which correlate with the severity of clinical symptoms.[23−25] α-syn pathology follows a caudo-rostral gradient per Braak staging: initial aggregation in the dorsal motor nucleus of the vagus (Stage 1) progresses to locus coeruleus (Stage 2), substantia nigra (Stage 3), limbic cortex (Stage 4), and ultimately neocortex (Stages 5 and 6). This predictable anatomical spread creates distinct windows for imaging biomarker intervention: early stages (1−3) are detectable 10−15 years before motor onset, while later stages correlate with cognitive decline.[18,26]

In addition, studies have shown that abnormal aggregates of α-syn are present in the majority of sporadic PD patients, and their distribution and quantity are related to clinical symptoms and disease progression.[27−29] However, this pathological feature is not universally observed in genetic subtypes of PD: cases associated with LRRK2 (PARK8) or Parkin (PARK2) mutations frequently lack Lewy body pathology, indicating distinct molecular mechanisms in these cohorts.[30]

2.2. The Potential of α-syn as a Biomarker. With the in-depth study of the mechanisms of α-syn aggregation, its potential as a biomarker has gradually gained attention. Research has found that the levels of α-syn in cerebrospinal fluid are closely related to the clinical features and disease progression of PD, providing important clues for early diagnosis.[31] The aggregation state of α-syn can reflect neurodegenerative changes in patients, thereby helping to assess the severity and prognosis of the disease. Additionally, changes in the concentration of α-syn in serum and cerebrospinal fluid are also considered potential biomarkers that can distinguish PD from other neurodegenerative diseases.[32,33] The syn amplification assay technology provides a breakthrough tool for the early diagnosis and precise classification of PD by dynamically tracking the conformational conversion ability of pathological α-syn seeds.[34,35] While serum and cerebrospinal fluid α-syn levels show diagnostic potential (AUC = 0.78−0.85), the real-time quaking-induced conversion (RT-QuIC) assay revolutionizes detection by amplifying trace pathogenic α-syn seeds. Using recombinant α-syn substrate, RT-QuIC achieves 95% sensitivity and 98% specificity in differentiating PD from controls.[36] In clinical applications, research on using α-syn as a biomarker is continuously advancing, with related detection technologies such as electrochemiluminescence and immunoassays being optimized to improve diagnostic accuracy and sensitivity. In summary, the potential of α-syn as a biomarker not only provides new ideas for the early diagnosis of PD but also lays the foundation for the development of personalized treatment strategies.

3. OVERVIEW OF MEDICAL IMAGING TECHNOLOGY

Medical imaging technology is an indispensable part of modern medicine, providing crucial support for the diagnosis, treatment, and monitoring of diseases. With continuous technological advancements, the application scope of medical imaging is also expanding, covering various aspects, from basic image acquisition to complex image processing and analysis. The following details three main medical imaging technologies: positron emission tomography (PET), single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), and optical imaging technology.

3.1. Application of α-syn Probes in PET and SPECT. Existing radioactive tracers such as [^{123}I]FP-CIT SPECT and [^{18}F]FDOPA PET have high sensitivity and specificity in detecting dopaminergic neuron damage, but they cannot distinguish α-synucleinopathies from other diseases in the early stages.[37,38] In recent years, α-syn has attracted widespread attention as an important neuropathological marker due to its role in PD and other neurodegenerative diseases. Advances in PET and SPECT technology have provided new possibilities for imaging α-syn.[39] Currently, several PET probes targeting α-syn have entered the clinical research stages. Studies have shown that these probes can effectively identify and quantify α-syn aggregates in the brain, providing important tools for early diagnosis and monitoring of disease progression (Table 1).

A series of probes for imaging α-syn include PET or SPECT radiotracers, such as phenothiazine derivatives, benzothiazole and benzimidazole derivatives, bisquinoline derivatives, [^{11}C]-MODAG-001, DABTA derivatives including [^{18}F]d2, [^{18}F]d4, [^{18}F]d6, and [^{18}F]d8, as well as ^{18}F-SPAL-T-06, among others. They demonstrate high affinity and good selectivity for α-syn aggregates, showing potential in the development of PET tracers targeting neurodegenerative diseases.[40−45]

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Table 1. Affinity and Selectivity of PET/SPECT Molecular Probes for α-syn

Biomarkers	K_i Values	Affinity	Selectivity
[^{18}F]-F0502B	10.97 nM	high	high
^{18}F-C05-05	1.5 nM	high	high
[^{3}H]MODAG-001	0.6 ± 0.1 nM	high	high
^{11}C-PIB	4 nM	high	
^{18}F-BF227	9.63 nM	high	
[^{18}F]ACI-12589	17 nM	high	
[^{125}I]PHNP-3	6.9 nM	high	high
Phenothiazine Derivatives			
11b	32.10 ± 1.25 nM	high	
11d, 16a, and 16b	50−100 nM	moderate	
SIL23	148 nM	moderate	low
Bisquinoline (BQ) Derivatives			
BQ1	17.0 ± 3.5 nM	high	
BQ2	11.6 ± 2.6 nM	high	
Diphenyl Derivatives			
IDP-3	23 nM	high	
IDP-4	5.4 nM	high	low
Benzimidazole (BI) Derivatives			
BI-1	485 ± 160 nM		high
BI-2	99.5 ± 20.8 nM	high	high
BI-3	874 ± 169 nM		high
3-(Benzylidine)indolin-2-one Derivatives			
46a	2.1 nM	high	high
Disarylbisthiazole (DABTA) Derivatives			
d2	1.22 nM	high	high
d4	0.66 nM	high	high
d6	1.21 nM	high	high
d8	0.10 nM	high	high
Imidazo[2,1-*b*][1,3,4] Thiadiazole Derivatives			
[^{125}I]ITA-3	IC_{50} = 55 nM	moderate	
[^{18}F]FITA-2	IC_{50} = 245 nM		

Endo et al.'s research team has developed a new positron emission tomography (PET) imaging agent, ^{18}F-C05-05, which for the first time enables real-time imaging of α-syn deposits in patients' brains, providing new opportunities for early diagnosis. This imaging agent has shown a correlation with the severity of motor symptoms in PD patients, laying the groundwork for future disease monitoring and treatment efficacy assessment.[18]

Zeng et al.'s research indicates that new imidazo[2,1-*b*][1,3,4]thiadiazole derivatives serve as novel candidate molecules for α-syn PET imaging, effectively recognizing and labeling α-syn aggregates, thereby enhancing the contrast and specificity of the imaging.[46] However, some probes (such as ^{11}C-PIB and ^{18}F-BF227) show binding affinity for α-syn aggregates (the K_d value of ^{11}C-PIB is 4 nM, and the K_d of ^{18}F-BF227 is 9.63 nM), but lack selectivity and fail to demonstrate specific binding to α-synaggregates in the brain tissue of PD patients.[47,48] Xiang et al.'s study reveals a newly developed PET tracer F0502B, which has high selectivity and affinity specifically for recognizing α-syn aggregates and can effectively image in mice and nonhuman primates. The structure of the α-syn fiber-F0502B complex, analyzed through cryo-electron microscopy, provides new insights into the binding mechanism of F0502B, enhancing our diagnostic and research capabilities for such diseases.[49] Kaide et al.'s research shows that a ^{125}I-labeled chalcone analogue called [^{125}I]PHNP-3 exhibited high affinity (K_d = 6.9 nM) and selectivity for α-syn aggregates in in vitro binding assays, and showed modest brain uptake (0.78% ID/g at 2 min) in a biodistribution study in normal mice.[50] Another class of compounds, N,N-dibenzylcinnamamide (DBC) derivatives, were also identified as novel α-syn ligands with high affinities (KD < 10 nM) through a high-throughput screening system based on surface plasmon resonance (SPR) technology, and a high-affinity F-labeled DBC compound (5-41) with a KD of 1.03 nM was obtained as a potential PET radiotracer candidate.[51] Disarylbisthiazoles (DABTAs) have also been shown to have high affinity and selectivity toward α-syn aggregates, and their characterization within competition binding assays, autoradiography, and pharmacokinetic studies is ongoing to evaluate their potential as α-syn PET tracers.[52] The discussion of Smith's this study emphasizes the ability of [^{18}F] ACI-12589 as an innovative biomarker to identify α-syn pathology, distinguishing early diagnosis of α-syn-related diseases.[53] Wurster et al.'s research shows that patients with triple repeats of the SNCA gene have significantly elevated levels of α-syn in their cerebrospinal fluid. Combined with positron emission tomography and magnetic resonance imaging (PET-MRI) technology, studies indicate reduced metabolism and atrophy in the frontal, parietal, and occipital regions of the brain, providing new insights into the critical role of α-syn in neurodegenerative diseases.[54]

In Braak Stage-specific tracer uptake patterns, recent PET studies demonstrate stage-dependent tracer retention: [^{18}F]ACI-12589 shows 3.7-fold higher binding in medulla oblongata vs cortex during Stage 2, while limbic-predominant retention in Stage 4 correlates with Montreal Cognitive Assessment scores.[55] Dual-tracer studies combining α-syn and tau probes (e.g., [^{18}F]MK-6240) reveal spatiotemporal competition—cortical α-syn deposition delays tau spread by 4.2 years in PD dementia cohorts.[56]

Additionally, clinical trials have demonstrated that these probes can provide imaging information related to pathological states in PD patients, offering a basis for the development of personalized treatment plans. With the continuous advancement of technology, it is likely that more PET probes targeting α-syn will gain clinical application in the future, further promoting the diagnosis and treatment of neurodegenerative diseases.

3.2. Application of α-syn Probes in MRI. MRI is a noninvasive imaging technology with superior soft tissue contrast, capable of clearly displaying brain structures and lesions, especially important in the study of neurodegenerative diseases.[57] In PD research, MRI can be used not only to observe structural changes in specific areas of the brain but also to assess changes in neural network function and microstructure by combining quantitative techniques such as diffusion tensor imaging (DTI), diffusion kurtosis imaging (DKI), quantitative susceptibility imaging (QSM), and functional MRI (fMRI).[58−61] Advances in these technologies have made MRI significantly promising for early diagnosis and disease monitoring in PD.

In recent years, innovations in MRI technology have provided new possibilities for the application of α-syn probes. Researchers have developed novel MRI probes that can specifically bind to α-syn, thereby improving the accuracy of early diagnosis. After surface modification, MRI probes

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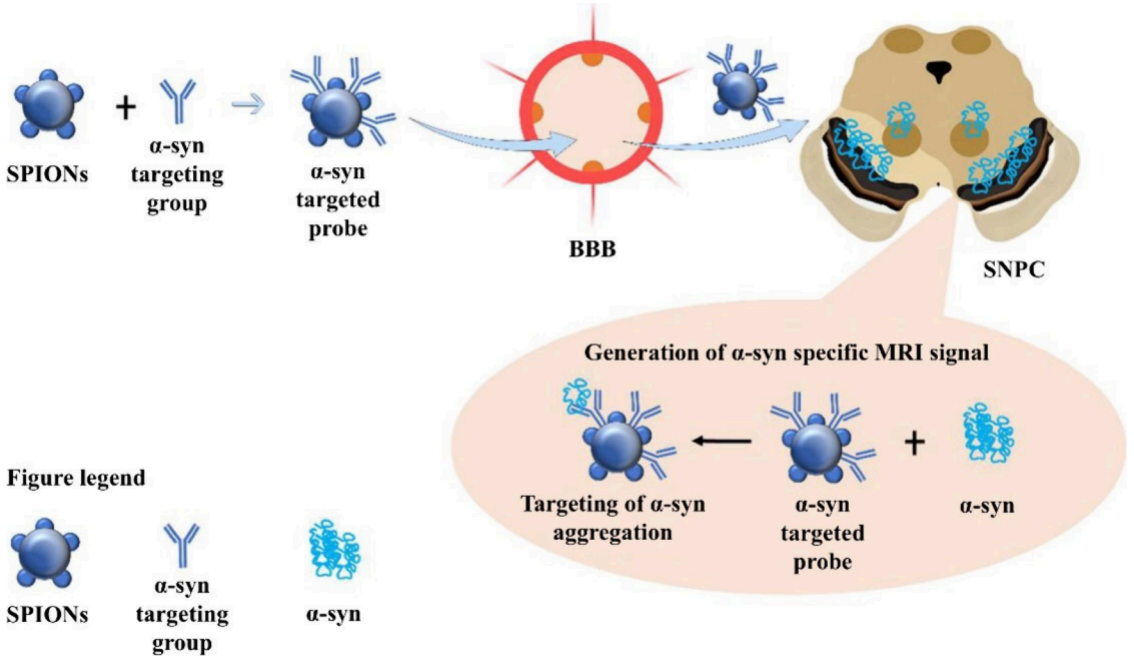

Figure 1. After surface modification, Superparamagnetic iron oxide nanoparticles (SPIONs) are coupled with α-targeting groups to form α-syn targeting probes, which cross the blood−brain barrier (BBB) and bind to the abnormally aggregated α-syn in substantia nigra pars compacta neurons (SNPCs) through intermolecular interactions, indirectly reflecting the level of α-syn deposition in the brains of PD rats through MRI imaging.

combine with α-syn targeting groups to form α-syn-targeted probes, which can cross the blood-brain barrier and bind to abnormally aggregated α-syn in neurons through intermolecular interactions, indirectly reflecting the level of α-syn deposition in the brains of PD patients, observed by using MRI imaging technology (Figure 1). Chen et al.'s study demonstrated a T1-T2 switchable nanoprobe (ASOSN) driven by α-syn oligomers, which can provide clear signal changes in MRI imaging, helping to identify early signs of PD.[62] Sun et al.'s research confirms that the application of dual-target molecular magnetic resonance imaging probes can noninvasively analyze pathological α-syn and microglial proliferation in mouse models, further advancing the early diagnosis and pathological research of diseases such as PD.[63]

Additionally, with advancements in technology, the imaging resolution and contrast of MRI have significantly improved, making the application of probes more widespread. Combined with emerging technologies, such as deep learning, the prospects for MRI in neuroimaging are becoming increasingly broad.

3.3. Applications of α-syn Probes in Optical imaging. Optical imaging technology is a technique that utilizes optical principles for imaging and has been widely applied in the biomedical field in recent years. Optical imaging technology includes various forms such as fluorescence imaging and photoacoustic imaging, which can provide high-resolution information about tissue structure and function. With continuous technological advancements, the application potential of optical imaging technology in biological detection, disease diagnosis, and treatment monitoring is enormous, and it is expected to play a greater role in personalized medicine in the future.

α-syn probes are molecular tools based on optical imaging technology, typically composed of targeting components (such as antibodies, aptamers, or small molecule ligands) that specifically recognize α-syn coupled with optical signal markers (such as fluorescent dyes, quantum dots, or near-infrared probes). In PD, abnormal aggregation of α-syn forms Lewy bodies, and the probes selectively bind to pathological α-syn aggregates through the targeting components, triggering enhanced fluorescence or scattering signals from the optical markers. Techniques such as confocal microscopy, two-photon imaging, or in vivo near-infrared fluorescence imaging can noninvasively detect α-syn pathological features in brain tissue or peripheral biological samples (such as cerebrospinal fluid or blood), enabling early diagnosis of the disease or monitoring of pathological progression.

Fluorescence imaging is an optical imaging technique that allows for the targeting of fluorescent probes, featuring high sensitivity, low cost, ease of operation, and intuitive visualization. However, the currently discovered α-syn fluorescent probes have not yet addressed issues such as low selectivity, short emission wavelengths, and inadequate imaging time for in vivo imaging.[64]

For instance, the α-syn fluorescent probes derived from chromone, created by Yushchenko,[65] and the α-syn fluorescent probes based on benzofuranone derivatives, developed by March,[66] both demonstrate strong affinity for α-syn in vitro; however, their utilization in in vivo studies remains constrained.[67] Near-infrared fluorescence imaging (NIRF) shows advantages over PET imaging in avoiding radiation damage, cost, and sensitivity. Various NIRF probes have been developed to specifically target protein aggregates related to Alzheimer's disease and PD, such as BD-Oligo and PTO-29 probes, which exhibit excellent in vivo imaging characteristics.[68] Zeng et al.'s study has obtained a series of D-π-A based trisubstituted alkenes, FPQXN and TQXN-2 which have acceptable optical properties and high binding affinity for α-syn fibrils. This facilitates the in vitro detection of α-syn aggregates and provides new prospects for the further development of α-

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syn fluorescent probes.[69] Previous researches show tha mono- and trimethine cyanine dyes and N-arylaminonaphthalenesulfonate (NAS) derivatives are more sensitive and versatile than traditional fluorescent probes (such as thioflavin T and Congo red), effectively monitoring α-syn aggregation associated with PD.[70−72] Porcu's research is focusing on three types of novel molecular probes, including Hydroxyl azobenzene (AZO-OH), dicyanovinyl bithiophene (DCVBT) and tetra-amino phthalocyanine (PcZnNH2), hoping to significantly enhance the detection accuracy of α-syn aggregation through the principle of two-photon excitation (TPE). By combination of innovative physical spectroscopy techniques with quantum chemical calculations, these molecules exhibit strong affinity, potentially paving the way for new diagnostic and therapeutic strategies to mitigate the impact of neurodegenerative diseases. In particular, the optical properties and biocompatibility demonstrated by DCVBT make it the most promising candidate for future biomedical applications.[73]

4. LIMITATIONS AND CHALLENGES

4.1. Limitations in Imaging Technology. α-syn plays a crucial role in PD and other neurodegenerative diseases, and the application of imaging technology provides new methods for its research.[74,75] However, existing imaging technologies still have significant limitations in terms of sensitivity and specificity.[76,77] First, insufficient selectivity of imaging probes may lead to the generation of nonspecific signals, thereby interfering with the detection of true biomarkers. Second, the spatial and temporal resolution of imaging technologies also limits their application in the detection of early lesions. In many cases, early pathological changes may occur at the cellular level, while existing imaging technologies often struggle to capture these subtle changes. Additionally, the stability and biocompatibility of imaging probes can affect their performance in vivo, leading to inconsistent results under different experimental conditions, which further complicates the research.

The clinical translation of α-syn molecular probes necessitates rigorous ethical scrutiny, particularly due to their potential cross-reactivity with structurally homologous proteins, such as tau and β-amyloid, in elderly populations with comorbid neurodegenerative pathologies. This nonspecific binding, observed in in vitro assays, risks diagnostic misclassification, inadvertently labeling patients with incidental Lewy body pathology as PD cases. This highlights the importance of the informed consent process, which should transparently communicate the uncertainties of the diagnosis to patients.

4.2. Future Research Directions and Improvement Suggestions. Accumulating evidence suggests that transient, neurotoxic oligomers—small, metastable prefibrillar aggregates—exhibit enhanced membrane permeabilization and induced oxidative stress, contributing to synaptic dysfunction and neuronal death.[15] Critically, these oligomers evade detection by conventional amyloid-centric probes, underscoring the need for imaging agents that target conformational epitopes unique to oligomeric species. Equally pivotal is the role of lipid environments in modulating α-syn aggregation. Interactions with phospholipid membranes, particularly at synaptic vesicles, stabilize α-syn in lipid-bound conformations that catalyze oligomerization.[16,78] Anionic lipid microdomains, such as those rich in phosphatidylserine or polyunsaturated fatty acids, further regulate α-syn membrane affinity, phase separation, and fibril nucleation.[79−81] Dysregulated lipid metabolism (e.g., sphingolipid imbalances or oxidized lipids) exacerbates α-syn toxicity by promoting membrane disruption and stabilizing β-sheet-rich oligomers.[82−84] Moreover, lipid-coated oligomers exhibit distinct biological activities, including enhanced cellular uptake and inflammasome activation.[85,86]

These findings challenge the amyloid-centric diagnostic framework and highlight opportunities for next-generation probes. For instance, lipid-compatible imaging agents could detect membrane-associated oligomers or lipid peroxidation markers in early PD.[81,82] Similarly, oligomer-selective probes leveraging conformation-specific antibodies or amphipathic dyes may improve sensitivity to prefibrillar toxic species.[15,83] Addressing these mechanistic dimensions will enrich diagnostic strategies and align them with the multifaceted nature of α-syn pathobiology.

In response to the current limitations of imaging technology in detecting α-syn, future research should focus on improving the specificity and sensitivity of imaging probes.[87,88] First, developing new high-selectivity probes is an important direction; these probes should effectively distinguish α-syn from other biomolecules, reducing interference caused by nonspecific binding. Second, integrating artificial intelligence and machine learning technologies can enhance the analytical capabilities of imaging data, helping to identify subtle changes in biomarkers for early diagnosis. Furthermore, researchers should also pay attention to the combination of imaging technology with other biomarker detection methods, such as liquid biopsy techniques, to improve the comprehensiveness and accuracy of detection. Finally, establishing standardized research methods and protocols is also crucial, as this will aid in the comparability of results across different studies and provide stronger support for clinical applications. Through exploration and improvement in these directions, the imaging detection technology for α-syn is expected to play a greater role in the early diagnosis of neurodegenerative diseases in the future.

5. NEUROPROTECTION AND TREATMENT IN PD

With in-depth research on PD, various models have emerged (such as toxicological models, genetic models, stem cell models, and 3D organ models). These models not only help us better understand the pathological mechanisms of the disease but also provide a valuable platform for finding new neuroprotective therapies.[89] Emerging studies highlight the therapeutic potential of plant-derived compounds in mitigating PD pathology through multimodal neuroprotective mechanisms. Yadav et al. demonstrated that *Mucuna pruriens*, a leguminous plant, significantly reduced nitric oxide and lipid peroxidation levels in PD mice, thereby preserving dopaminergic neurons—a finding underscoring its dual antioxidative and neurorestorative properties.[90] Similarly, ursolic acid (25 mg/kg, optimal dose) ameliorated motor deficits in PD models by attenuating oxidative stress and enhancing neuronal survival, positioning it as a promising candidate for dose-refined therapeutic regimens.[91] *Withania somnifera* further exemplifies plant-based interventions, with its extracts suppressing apoptotic pathways (via upregulated Bcl-2 expression), reducing dopamine depletion, and dampening neuroinflammation through decreased GFAP expression, thereby synergistically targeting oxidative and inflammatory cascades.[92] Beyond phytochemicals, activation of the WNT-β-catenin signaling pathway by lithium chloride enhances

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neurogenesis and motor recovery, suggesting that pharmacological modulation of developmental pathways may complement antioxidant strategies.[93] These discoveries are bolstered by advancements in PD modeling, including toxin-induced, genetic, stem-cell-derived, and 3D organoid platforms, which collectively enable rigorous dissection of pathological mechanisms and preclinical validation of neuroprotective agents. Together, these studies advocate for integrating plant-derived compounds and pathway-targeted therapies into PD treatment paradigms, leveraging their pleiotropic actions against oxidative stress, apoptosis, and neuroinflammation, while emphasizing the need for standardized disease models to bridge translational gaps.

6. CONCLUSION

In this review, we discuss the importance of α-syn molecular probes in the early diagnosis of PD. With the continuous advancement of scientific research technology, the application of α-syn as a key pathological biomarker for PD provides new perspectives and tools for clinical early diagnosis. Looking ahead, by integrating the latest research findings from neurology, medical imaging, molecular biology, and other fields, we hope to promote the development of new diagnostic technologies. At the same time, strengthening clinical trials and data sharing will help validate the effectiveness and reliability of new technologies, thereby enhancing the accuracy of early diagnosis. We believe that it is possible to achieve early identification and intervention for PD in the near future, improving the quality of life and prognosis for patients.

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Notes

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