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Utility and Diagnostic Specificity of Dopamine Transporter (DAT) Scan in Parkinson's Disease and Lewy Body Dementia: A Literature Review

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Abstract

The dopamine transporter (DAT) can be imaged, most often with 123I-ioflupane SPECT, a technique that allows visualization of presynaptic nigrostriatal dopaminergic terminals. It is widely used to aid in the diagnosis of neurodegenerative Parkinsonism, primarily to differentiate Parkinson's disease (PD) from non-degenerative conditions that resemble it. It has also been used to help with the diagnosis of dementia with Lewy bodies (DLB). This review covers peer-reviewed literature published between 2021 and 2026, identified via comprehensive searches of PubMed, MEDLINE, and EMBASE using the terms 'dopamine transporter imaging', 'DAT-SPECT', 'Parkinson disease', 'dementia with Lewy bodies', and 'diagnostic specificity'.

The studies selected were clinical trials, meta-analyses, and cohort studies that focused on the diagnostic validity, clinical usefulness, and limitations of DAT imaging specificity in the context of Lewy body diseases. The review also examines research on the effectiveness of DAT imaging in prodromal synucleinopathy and atypical parkinsonian syndromes, which are most often mistaken for PD and DLB. DAT imaging has significant clinical value because it changes management in about half of patients evaluated and leads to a different diagnosis in nearly one-third of cases. There is particularly strong evidence for being able to distinguish PD from essential tremor and for supporting the diagnosis of DLB rather than that of Alzheimer's disease. The main limitation of DAT imaging is not its sensitivity but its specificity, especially when considering the broader group of degenerative parkinsonisms.

Keywords: Dopamine transporter imaging; DAT-SPECT; Parkinson disease; Dementia with Lewy bodies; Diagnostic specificity; Movement disorders

Introduction

The technique most commonly employed to perform Dopamine Transporter (DAT) imaging is 123I-ioflupane Single-Photon Emission Computed Tomography (SPECT), a procedure referred to as DaTscan; however, it is more commonly performed using Positron Emission Tomography (PET) tracers. DAT imaging enables observation of presynaptic nigrostriatal dopaminergic terminals. A reduced level of tracer binding in the striatum indicates degeneration of the nigrostriatal pathway. In a clinical context, DAT imaging is used to aid in the diagnosis of neurodegenerative parkinsonism and to differentiate Parkinson's Disease (PD) from non-degenerative disorders such as Essential Tremor (ET) and drug-induced parkinsonism. It has also proved useful in diagnosing Dementia with Lewy Bodies (DLB) since 2022 **[1-15].** The review under consideration in this article focuses on the diagnostic validity, clinical usefulness and limitations of DAT imaging across the whole of the Lewy body disease spectrum.

Pathophysiology and Rationale for Imaging

Parkinson's disease and dementia with Lewy bodies share the same fundamental pathological process, namely the progressive degeneration of the dopaminergic neurons in the substantia nigra pars compacta along with the accumulation of misfolded α-synuclein into Lewy bodies and Lewy neurites; as the neurons which make up the nigrostriatal projection system are lost, the presynaptic dopamine transporters — membrane proteins whose role is to take up dopamine at the striatal synapse — also vanish, resulting in a measurable reduction in radiotracer binding on SPECT or PET scans which corresponds both to the severity and the asymmetry of the nigrostriatal degeneration. In various Lewy body disorders, a degenerative process is present. Still, it is not observed in non-degenerative conditions such as essential tremor, drug-induced parkinsonism, and functional movement disorders. Hence, DAT binding serves as a biological marker that can distinguish true nigrostriatal degeneration from clinical mimics.

Diagnostic Validity plus Clinical Use in Parkinson Disease

A systematic review and meta-analysis that pooled data from 20 studies (13 of these having provided quantitative data for 950 and 779 patients, respectively) showed that DAT imaging resulted in a change in patients' management in 54% of cases (95% CI, 47%–61%) and caused a modified diagnosis in 31% of cases (95% CI, 22%–42%) **[1]**. Nevertheless, the substantial variation in these outcomes has given rise to considerable controversy regarding the reliability and reproducibility of DAT imaging across diverse clinical groups and research methods. Although previous studies have shown that DaTscan achieves raw diagnostic performance above 90% in both sensitivity and specificity when distinguishing neurodegenerative parkinsonism from non-dopaminergic conditions, there is still disagreement about how to apply the imaging results in clinical decision-making. Many clinicians tend to rely on their own clinical judgment and on more thorough longitudinal evaluations rather than simply on imaging biomarkers, a position that reflects ongoing concerns about becoming overly dependent on such diagnostics. There is also debate over the use of quantitative software and machine learning techniques, which are intended to increase interpretive objectivity and reduce inter-rater

variability, since their true clinical effectiveness will ultimately depend on confirmation across a range of patient groups and in external settings. For instance, a multicenter cohort study with 303 patients found that the optimal DaTQUANT thresholds, especially those for posterior putamen binding in the more affected hemisphere, were just as effective as more complex multivariable methods in predicting both DLB and the parkinsonian syndromes [7]. Likewise, analyses that recommend specific cutoff values for the binding ratio, z-score, and percent deviation of the posterior putamen alone (with an accuracy of 84%–95%) have provoked discussion due to uncertainties about their use inside heterogeneous clinical populations [13]. These pending issues show that even with improvements in quantitative indicators, agreement on their generalizability remains lacking. Longitudinal studies, such as those conducted by the Parkinson's Progression Markers Initiative (PPMI), have demonstrated that regional decreases in DAT signal correspond to the progression of motor symptoms [3]. Yet, even these data do not entirely clarify the best approach to incorporating DAT imaging into the development of clinical algorithms. The 2022 expansion of the regulatory indications for DAT imaging in dementia with Lewy bodies has also intensified the debate about the evidence base and the most suitable manner of integrating imaging into clinical practice, proving that controversies concerning its usefulness, implementation, and interpretation remain at several levels in the field. DLB is the second most common type of neurodegenerative dementia following Alzheimer's disease and is thought to affect about 1.4 million people in the United States; yet approximately 20% of cases of DLB are incorrectly diagnosed as being Alzheimer's disease by neurologists [15], which shows that there is a serious defect in diagnostic validity.

In the United States, access to DAT scans may be hindered by numerous factors, including inadequate insurance coverage, high scan costs, and geographic disparities, all of which can cause delays or, in some cases, prevent patients from receiving appropriate imaging. The effect of these barriers is particularly serious for people in low-income groups, members of racial and ethnic minority groups, and those who live in rural or medically underserved areas, since it exacerbates existing health inequalities. Consequently, individuals from these groups who may have DLB often go through long periods of diagnostic uncertainty, are diagnosed at a later stage, or receive care that is less good than that received by people who have more resources or who have access to specialist centers. The ongoing failure to ensure equal access to diagnostic imaging continues to perpetuate health inequalities by preventing early intervention. It leads to differences in functional outcomes, quality of life, and caregiver burden within these communities. Additionally, these problems may cause disadvantaged groups to be systematically underrepresented in clinical research cohorts, thereby decreasing the external validity and transferability of the study findings. Systemic policy changes, therefore, need to be implemented to eliminate these disparities, for example, by extending insurance coverage, improving reimbursement for providers, and increasing the availability of specialized imaging in remote areas. Moreover, even though autopsy data remain limited, they are growing more accessible; for instance, recent longitudinal studies in patients with autopsy-confirmed Lewy body disease have found that a putamen z-score cutoff of -1 reliably predicts the pathology identified at autopsy [11].

Differentiating Parkinson's Disease from Essential Tremor

A primary reason for performing DAT imaging is to tell the difference between Parkinson's disease, which is characterized by, and essential tremor. Even though software that provides quantitative data and is used alongside machine-learning classifiers continues to help reduce variability among observers who assess the scans visually, the scans themselves remain unclear. Transcranial sonography has been found to have diagnostic validity for distinguishing early-stage PD from ET, with a validity similar to that of DAT imaging, suggesting it could serve as a more cost-effective alternative in cases where reimbursement is limited, or access is difficult [5,6]. Methods based on acceleration and posture have reported sensitivities and specificities between 75% and 83% when making this distinction—figures less accurate than those achieved with DAT imaging—thus corroborating its present role as the more discriminating test in unclear cases [10].

The debate about cases in which scans show no sign of a dopaminergic deficit (SWEDD) centers on whether such cases represent true false negatives in DAT imaging or instead reveal the heterogeneity found in Parkinsonism. The proportion of SWEDD cases among patients who have been clinically diagnosed with early PD ranges from 2% to 20%, the exact figure depending on the methods employed and the care taken with follow-up [9]. Some longitudinal studies have discovered that a part of the SWEDD cases subsequently develop abnormal DAT scans or clinical features consistent with Parkinson's disease, which implies that the initial negative results may be signs of prodromal or very early neurodegeneration [10-20]. Conversely, other studies that have used high-level imaging analyses have found ongoing clinical and imaging differences, supporting the idea that the majority of SWEDD cases constitute a biologically distinct, non-degenerative subgroup [2,8]. Importantly, when strict diagnostic guidelines and combined analytical methods are applied, the rate of SWEDD is substantially reduced, demonstrating that many of these cases are attributable to diagnostic and methodological factors rather than intrinsic limitations of the scan [14-22]. As a general rule, the literature shows that there is still a debate going on; even if some SWEDD cases are later found to indicate early PD, most are probably a part of distinct clinical entities, stressing the requirement for attentive longitudinal assessment and an in-depth examination of the imaging data at the diagnostic stage.

Discussion

An examination of the literature published between 2021 and 2026 indicates that DAT imaging remains a powerful and clinically significant method for confirming damage to the nigrostriatal dopamine system. The majority of studies agree on its high diagnostic value when distinguishing Parkinson's disease from essential tremor, both regarding the technique's ongoing relevance and its inclusion in diagnostic procedures. Furthermore, a careful examination of more recent research shows that although DAT imaging is reliable for differentiating neurodegenerative parkinsonism, its practical usefulness must be considered in light of ongoing methodological improvements and the broader clinical context. Since 2022, the differences in the SWEDD rates reported in various studies (ranging from 1.3% to 20%) when it comes to helping to diagnose DLB rather than Alzheimer's disease are most probably due to variations in diagnostic care

and the length of the follow-up period, not because of any intrinsic instability of the test [9,16]. When interpreting a negative scan in a case that is otherwise clinically convincing, clinicians should bear this point in mind. Methods that use quantitative software and machine learning could help improve reproducibility, but their application is limited because they primarily rely on internal validation with a single dataset [17,18]. The only kind of study that should be carried out if such tools are to be considered suitable for use in a clinical setting is a prospective study with external validation, although ongoing supervision is still required. In current clinical practice, these techniques should begin with DAT imaging to confirm nigrostriatal degeneration, followed by αSyn-SAA testing to identify the specific synucleinopathy, particularly when standard diagnostic criteria are unclear. It does not matter whether this approach is followed sequentially or in parallel, as it enables clinicians to combine structural imaging with protein-based biomarkers to increase diagnostic correctness, refine subtype differentiation, and inform individualized prognostic and therapeutic decisions. Through incorporating these advances, clinical pathways can gradually increase their use of evidence grounded in biological mechanisms and lower reliance on clinical criteria alone, thereby enabling earlier detection and more targeted management of Lewy body diseases.

Conclusion

DAT imaging retains a well-established, evidence-supported role in the diagnostic workup of Parkinson disease and dementia with Lewy bodies, particularly for distinguishing degenerative from non-degenerative parkinsonism and PD from essential tremor. Clinicians must realize that the main drawback of DAT imaging is the inability to tell Parkinson's disease apart from the atypical parkinsonian syndromes. In cases where the SWEDD results conflict, and they assume there is no neurodegeneration, they should take a personalized approach that includes conducting continuous longitudinal assessments. If SWEDD findings exist, it may be helpful to go beyond the standard guidelines by organizing a multidisciplinary review that incorporates the opinions of neuroimaging specialists, movement disorder experts, and, where possible, genetic counselors or biomarker researchers to improve the diagnostic process. Repeat imaging at regular intervals (usually once or twice a year) can be combined with new digital phenotyping tools or wearable technologies to objectively monitor the progression of motor symptoms, enabling the earlier identification of phenotypic changes that could assist with diagnosis. Moreover, it is advisable to begin discussing uncertainty surrounding the diagnosis and the possible role that further testing—such as tests based on emerging fluid or tissue biomarkers—might play early on, to encourage shared decision-making and lessen patient anxiety. In the future, the combination of quantitative-assisted analysis, AI-driven interpretation, and the expansion of biomarker platforms would deliver greater benefits when incorporated into an adaptive, patient-focused diagnostic algorithm. This detailed approach could make DAT imaging a flexible reference point in a constantly evolving set of tools, maximizing its impact on clinical outcomes and helping with diagnostic uncertainty.

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