REVIEW ARTICLE

Non-linear analysis of heart rate variability as a biomarker for autonomic dysfunction in parkinson's disease: A scoping review

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Abstract

Parkinson's Disease (PD) is a neurodegenerative disorder that impacts both motor and autonomic systems, leading to complex autonomic dysfunction evident in various parameters of Heart Rate Variability (HRV). While traditional linear HRV analyses measure overall autonomic activity, they may overlook subtle irregularities associated with the disease. Non-linear HRV metrics, such as Detrended Fluctuation Analysis (DFA), Approximate Entropy (ApEn), Sample Entropy (SampEn), and recurrence plot analysis, provide a more nuanced perspective on HRV dynamics. This scoping review examines studies on non-linear HRV metrics in PD to map the existing research, highlight methodological considerations, their utility as clinical biomarkers and identify knowledge gaps. Pubmed, Google scholar and Cochrane databases were searched and studies were included covering PD patients in various stages and comparing them with healthy controls and other autonomic conditions like Multiple System Atrophy (MSA). Findings indicate that non-linear HRV metrics reveal significant reductions in HRV complexity and predict disease-specific autonomic dysfunction, particularly in early-stage PD, with some metrics differentiating PD from MSA. These findings suggest that non-linear HRV analysis holds promise for identifying early autonomic changes and tracking disease progression in PD. However, further research with larger cohorts and standardized HRV measurement protocols is necessary to establish non-linear HRV analysis as a reliable clinical tool.

Keywords: non-linear parameters, heart rate variability, Parkinson's disease, autonomic function

Introduction

Heart Rate Variability (HRV) refers to the natural variation in time intervals between consecutive heartbeats and has evolved over the last few decades as an indirect measure of autonomic function. Extremely complex neural mechanisms are responsible for these fluctuations which reflect the dynamic balance between the sympathetic and parasympathetic branches of the ANS. The influence of parasympathetic activation is quick and transient whereas sympathetic stimulation develops more slowly but is of higher amplitude [1,2].Traditionally, HRV has been analyzed using linear methods, which include time-domain and frequency-domain analyses. Time-domain measures quantify the amount of variability in the time intervals between heartbeats [e.g., Standard Deviation of NN intervals (SDNN), and Root Mean Square of Successive Differences (RMSSD)]. Frequency-domain methods decompose the HRV signal into its component frequencies, including Very Low Frequency (VLF), Low Frequency (LF), High Frequency (HF), and Ultra Low Frequency (ULF) bands, each reflecting different aspects of autonomic regulation. LF band (0.04–0.15 Hz) is associated with both sympathetic and parasympathetic activity, whereas the HF band (0.15–0.40 Hz) primarily reflects parasympathetic (vagal) influence. The VLF band (0.0033–0.04 Hz) is thought to be linked to thermoregulatory and neurohormonal mechanisms, while the ULF band (<0.0033 Hz) represents longer-term regulatory processes, including circadian rhythms and core body temperature fluctuations [3-4]. While these methods provide valuable insights into overall HRV, they are limited in their ability to capture the complex, non-linear dynamics of autonomic regulation.

Non-linear analysis techniques have emerged as complementary tools for examining HRV and enhancing understanding of the intricate patterns and irregularities inherent in autonomic control. Non-linear methods are capable of detecting subtle alterations in autonomic functions that might be missed by linear approaches.These techniques include Approximate Entropy (ApEn), Sample Entropy (SampEn), Detrended Fluctuation Analysis (DFA), fractal analysis, and Recurrence Quantification Analysis (RQA), among others [5-7]. For example, ApEn and SampEn are measures of the complexity and unpredictability of HRV signals, with lower entropy values indicating more regular and predictable patterns, often seen in physiological and pathological conditions such as aging, atrial fibrillation, and congestive cardiac failure [8-10]. DFA and fractal analysis assess the presence of long-range correlations and self-similarity in the HRV signal. RQA provides a quantitative assessment of the recurrence of dynamic patterns in the data [11-13].

Parkinson's Disease (PD) is a prototypical neurodegenerative disorder primarily associated with the depletion of dopaminergic neurons in the substantia nigra, resulting in striatal dopamine deficiency [14]. While PD is traditionally recognized for its motor symptoms—including tremor, bradykinesia, and rigidity—growing evidence highlights the significant burden of non-motor manifestations, particularly autonomic dysfunction. Dysautonomia in PD arises from widespread neurodegeneration affecting multiple autonomic regulatory centers, including the locus coeruleus, dorsal motor nucleus of the vagus, raphe nuclei, and hypothalamus [15-17].

According to the modified Braak hypothesis, alpha-synuclein pathology may originate in peripheral sites, such as the enteric and olfactory nervous systems, before propagating centrally, potentially contributing to autonomic disturbances [18-20]. Among these, cardiac autonomic dysfunction is particularly concerning due to its strong association with adverse cardiovascular outcomes, including an increased risk of sudden cardiac death [21]. This impairment is evident through various cardiovascular abnormalities, such as orthostatic hypotension, supine hypertension, and altered HRV, indicative of disrupted autonomic regulation [22-24].

Numerous studies have shown that HRV metrics can identify early autonomic changes in PD, even before noticeable cardiovascular symptoms appear [25-26]. As the disease advances, patients often experience worsening autonomic symptoms alongside motor decline [27-28]. Additionally, HRV metrics might provide insights into treatment response, particularly with dopaminergic medications commonly used in PD management. Dopaminergic therapy has been shown to influence autonomic function and aggravate dyskinesias and monitoring HRV could help assess the impact of treatment on both motor and non-motor symptoms [29-30]. Despite growing interest in non-linear HRV analysis, there is currently no comprehensive synthesis of the available literature on its application in PD. Given the complexity of non-linear HRV parameters and their varying interpretations, a scoping review is essential to map the existing research, highlight methodological considerations, their utility as clinical biomarkers and identify knowledge gaps,.

Material and Methods

This scoping review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and its extension for scoping reviews.The purpose of this review was to present the available literature on non-linear HRV analysis in PD to focus on its application in detecting autonomic dysfunction and monitoring disease progression [31-33].

Search strategy: A comprehensive literature search was conducted in three electronic databases: PubMed, Google Scholar and Cochrane. The search included studies published from the earliest available data up to December 2024. The search strategy utilized combinations of the following keywords: “Parkinson's disease” “non-linear” and “heart rate variability”. The full Boolean search string was as follows: Pubmed: ((non linear) AND (heart rate variability)) AND (P D): 487; Google scholar: non linear, heart rate variability, Parkinson: 888; Cochrane: "non-linear" AND “heart rate variability” AND "Parkinson": 1

Studies investigating “non-linear HRV analysis” in individuals with “PD”; Studies assessing the “relationship between HRV” and “autonomic dysfunction” or “disease progression”; articles published in “peer-reviewed journals”; studies in “English”; both “cross-sectional” and “longitudinal studies” were included. Review articles, case reports, editorials and opinion pieces; studies that only used “linear HRV methods” without non-linear analysis; articles not assessing HRV in relation to autonomic function in PD were excluded.

Screening and data extraction: After the initial database search, all identified articles were exported to “Rayaan” reference management software, where duplicates were removed. Titles and abstracts of the remaining articles were screened independently by two reviewers to assess their relevance to the research question. Full texts were retrieved for articles that met the inclusion criteria based on the abstract. Discrepancies between reviewers were resolved through discussion [34-36]. Data extraction was conducted using a standardized form that included the following information: Study design and methodology; participant characteristics (age, gender, disease duration, medications); HRV metrics (non-linear measures such as ApEn, SampEn, DFA and chaotic global metrics); “outcomes” related to autonomic dysfunction, motor symptoms and non-motor symptoms in PD; “key findings” related to the role of non-linear HRV in tracking autonomic dysfunction and disease progression.

Results

Study selection

The studies reviewed were selected for their focus on nonlinear HRV metrics in PD and their contribution to understanding autonomic dysfunction in PD through advanced HRV analysis techniques. Each study implemented nonlinear HRV metrics, though they varied in methods, sample sizes, and statistical approaches thus providing diverse perspectives on their clinical relevance. A total of 14 key studies were identified, including a recent study utilizing Multiscale Entropy (MSE) and SampEn by Valente *et al*. (2024). The objectives of the study, details of methodology, the non-linear metrics used and findings of the study are summarized in Table 1 [37-50].

Table 1: Non-linear parameters of heart rate variability in PD patients

Study	Objective	Methodology	Non-linear HRV Metrics Used	Key Findings
Haapaniemi *et al*., (2001) [37]	To evaluate diurnal HR V autonomic regulation in untreated PD patients.	Fifty-four untreated PD patients and 47 controls assessed with 24-hour ECG.	Spectral HRV, SD1, SD2, power law slope	Poincare SD1 and SD2 did not differ significantly in patients from controls. Slope of power law correlated with severity of hypokinesia.
Kallio *et al*., (2002) [38]	To compare nonlinear HRV analysis in untreated PD patients and controls to identify autonomic dysfunction.	Thirty-two untreated PD patients and 24 healthy controls were assessed using HRV measures.	DFA, ApEn, FD; SD1 and SD2; SD1/SD2.	PD patients showed a significant reduction in HRV complexity measures. FD had significant correlation with all time domain measures; SD2 correlated with spectral and time domain measures.
Pursiainen *et al*., (2002) [39]	To examine circadian HRV fluctuations in untreated PD patients.	Forty-four PD patients and 43 controls assessed with 24-hour ECG recordings.	ApEn, DFA, SD1, SD2	Night-time HRV suppression was more pronounced in PD, reflecting impaired parasympathetic regulation.
Kallio *et al*., (2004) [40]	To evaluate nocturnal HRV in PD patients and identify ANS dysfunction during sleep phases.	Examined HRV in PD patients and controls during sleep using ECG recordings, focusing on nighttime HRV metrics.	FD	FD did not differentiate the patients from controls in any of the sleep stages. Findings did not show significant autonomic differences.
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Kallio *et al*., (2004) [40]	To evaluate nocturnal HRV in PD patients and identify ANS dysfunction during sleep phases.	Examined HRV in PD patients and controls during sleep using ECG recordings, focusing on nighttime HRV metrics.	FD	FD did not differentiate the patients from controls in any of the sleep stages. Findings did not show significant autonomic differences.
Brisinda *et al*., (2015) [41]	To evaluate the effectiveness of nonlinear HRV in differentiating PD from multiple system atrophy (MSA).	Fifty-one patients (25 PD, 9 MSA, 17 uncertain diagnosis) were assessed with HRV parameters.	Recurrence plot analysis, SD1, SD2, entropy, DFA, Correlation Dimension	Nonlinear HRV, particularly recurrence plot analysis, provided 76.5 % accuracy in distinguishing MSA from PD, supporting its potential for early diagnostic differentiation.
Valenza *et al*., (2017) [42]	To introduce complexity variability using Lyapunov exponents in PD patients compared to controls.	Thirty PD patients and 29 healthy controls; 10-minute ECG during rest.	Lyapunov Exponents, Complexity Variability Index (CVIDLE)	PD patients exhibited higher complexityvariability compared to controls, suggesting subtle ANS alterations.
Porta *et al*., (2020) [43]	To assess symbolic markers' effectiveness in identifying autonomic dysfunction in PD patients.	Twelve PD patients and 12 healthy controls; ECG and SAP measurements during rest and tilt.	Symbolic dynamics (0V%, 1V%, 2UV%).	Symbolic markers, especially 2UV%, showed increased complexity in PD during head-up tilt, highlighting subtle autonomic control differences compared to healthy controls.
Brisinda *et al*., (2021) [44]	To assess HRV parameters for early differentiation of PD and MSA during wakefulness and sleep.	Sixty-six PD (34 with confirmed diagnoses of MSA or PD) and 52 healthy controls.	Recurrence Plot Parameters, VLF Power	Recurrence plot metrics and VLF power differentiated PD and MSA with 88.2% predictive accuracy, aiding in early prognostic stratification and diagnostic refinement.

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Carricarte Naranjo *et al*., (2021) [45]	To evaluate deceleration capacity (DC) as a marker of cardiac autonomic dysfunction.	Twenty PD patients (>60 years) and 27 controls with 7-min ECG.	DC, Spectral HRV, Multiscale Entropy.	DC was significantly reduced in older PD patients, indicating impaired vagal modulation and autonomic dysfunction.
Valente *et al*., (2022) [46]	To analyze autonomic and cardiorespiratory responses to tilt testing in PD patients.	Twenty-five PD patients and 23 controls evaluated via active tilt test using linear and non-linear HRV measures.	SD1, SD2, SD1/SD2, rMSSD, LF/HF ratio	Reduced parasympathetic response and H RV complexity in PD patients during tilt test, indicating impaired autonomic modulation.
Lazzeri *et al*., (2022) [47]	To compare cognitive and autonomic profiles in PD and MSA.	Twenty MSA patients (subtypes: MSA-P, MSA-C).	Symbolic HRV (0V%, 2UV%).	HRV parameters were comparable between MSA-P and MSA-C, highlighting autonomic similarities across subtypes. Focused on MSA subtypes, not PD
Dorantes-Méndez *et al*., (2022) [48]	To classify PD patients using symbolic dynamics and multiscale entropy measures.	Twenty-four volunteers (12 PD patients, 12 controls) performing cardiorespiratory maneuvers.	Symbolic dynamics, MSE	Symbolic dynamics achieved over 95% classification accuracy, identifying reduced HRV complexity in PD.
Valente *et al*., (2024) [49]	To examine and compare autonomic responses in PD patients and controls during rest and active tilt table test.	Twenty-three PD patients and 23 controls were assessed with HRV parameters.	Five entropies and DF A, Three chaotic global metrics and seven permutations (hsCFP1 to hsCFP7)	At rest, PD group exhibited lower values of hsCFP3 and sample entropy. During the tilt table test, PD group demonstrated lower values of ApEn (Approximate entropy)
Nigam *et al*., (2024) [50]	To assess HRV and COMPASS-31 in identifying autonomic dysfunction in PD patients.	One hundred and thirty seven PD patients evaluated via HRV metrics and COMPASS-31 questionnaire.	SD1, SD2	Astatistically significant association of age with time domain parameters of HRV (SDNN and SD2)

Participant characteristics

The participant demographics across studies consistently included middle-aged to older adults diagnosed with PD, often exhibiting autonomic symptoms. Sample sizes varied significantly, ranging from small cohorts of 12–20 participants to larger studies involving more than 50 individuals [44,50]. Several studies incorporated mixed cohorts to allow direct comparisons of HRV metrics between PD, MSA and Parkinsonian syndromes of uncertain origin. This approach provided a broader understanding of disease-specific autonomic dysfunction [41,47]. Most participants across these studies were in the mild to moderate stages of PD, generally aligning with Hoehn-Yahr stages 1–2.5, making the findings particularly applicable to early and mid-stage cases [41,54].

Studies focusing on untreated PD patients provided key insights into autonomic dysfunction patients before dopamine therapy. For instance, Haapaniemi *et al*. (2001) studied 54 untreated PD patients with a mean age of 64.2 years and 47 age-matched healthy controls, analyzing 24-hour HRV to evaluate diurnal autonomic regulation [37]. Pursiainen *et al*. (2002) examined circadian HRV variations in 44 untreated PD patients and 43 controls, identifying impaired parasympathetic regulation [39].

In another study, Carricarte-Naranjo *et al*. (2021) found significantly lowered HRV in a sub-cohort of PD patients older than 60 years, emphasizing the relevance of age-related reductions in Deceleration Capacity (DC), a novel marker of cardiac autonomic dysfunction [45]. Short-term cardiovascular dynamics during rest were also evaluated, with Valenza et al. (2017) analyzing 30 PD patients and 29 healthy controls using short-term ECG recordings to identify subtle alterations in autonomic control [42]. The heterogeneity of patient groups and variations in HRV measurement protocols improves applicability of the finding. However it can introduce confounding factors, potentially limiting the comparability of results and complicating the interpretation of autonomic dysfunction across studies.

Non-linear HRV metrics

The studies applied a variety of non-linear HRV metrics, highlighting the diversity of methods available and their specific strengths. Haapaniemi et al. (2001) employed spectral measures, Poincaré plot analysis (SD1 and SD2) and power law relation slopes, revealing no significant difference in values in PD patients compared to controls [37]. "ApEn" and "DFA" were the most frequently employed metrics. Kallio *et al*. (2002) found that these measures could not effectively capture reduced HRV complexity in PD patients. They suggested that non-linear parameters describe long-term regulation mechanisms and reliable estimation would require long data sets [38]. Pursiainen *et al*. (2002) demonstrated that SD1 of the Poincare was suppressed during the daytime and at night, reflecting diminished parasympathetic regulation and disrupted long-term H RV patterns [39]. Brisinda *et al*. (2015) expanded on this by using "recurrence plot (RP) metrics", "correlation dimension" and "Poincaré plot parameters", showing that RP metrics could differentiate PD from MSA with a high degree of accuracy. Discriminant Analysis (DA) was used to evaluate if HRV parameters were adequate to provide a separation between PD and MSA patients. DA applied to non linear HRV parameters had a high degree of accuracy (above 80 %), a finding that suggests potential diagnostic utility for these metrics [41].

Valente *et al*. employed five distinct entropies (Approximate, Sample, Shannon, Renyi and Tsallis), DFA and chaotic global HRV techniques (hsCFP1 to hsCFP7). Lower entropy measures correlate with diminished adaptability in autonomic regulation. This multi-metric approach highlights how non-linear metrics can collectively provide a comprehensive assessment of autonomic health in PD [49].

Valenza *et al*. (2017) introduced the concept of "complexity variability", a novel framework that quantifies the variance of instantaneous Lyapunov spectra over time. This method addresses the limitations of traditional single-point complexity measures, which average data over a time window and may miss transient changes in physiological dynamics. They demonstrated that complexity variability was significantly increased in PD patients compared to healthy controls, pointing to subtle autonomic changes that may accompany or precede clinical manifestations of autonomic dysfunction [42].

The authors emphasized that such variability could serve as a putative biomarker for PD, offering improved sensitivity for detecting disease-related changes in cardiovascular dynamics. These findings challenge the conventional notion that reduced HRV complexity alone characterizes PD. Instead, the increase in complexity variability may reflect an unstable autonomic control system, where transient fluctuations in HRV complexity occur due to disrupted autonomic regulation. The inclusion of novel metrics such as complexity variability thus broadens the scope of non-linear HRV analysis, which can be a more dynamic and sensitive tool for detecting subtle autonomic alterations in PD. Carricarte-Naranjo *et al*. (2021) introduced the DC as a novel measure of vagal modulation. DC was significantly reduced in PD patients over the age of 60, suggesting it as a sensitive marker for cardiac autonomic dysfunction, potentially linked to the risk of sudden cardiac death in this population [45]. These results indicate the importance of age-specific evaluations of HRV in PD patients. Dorantes-Méndez *et al*. (2022) applied symbolic dynamics and multiscale symbolic entropy, finding a significant decrease in HRV signal complexity among PD patients during controlled breathing maneuvers. These symbolic metrics achieved over 95% classification accuracy between PD patients and controls, emphasizing their diagnostic potential in early-stage PD [48]. While most studies aligned with the objective of identifying autonomic dysfunction in PD, a few, such as Kallio *et al*. (2004) and Lazzeri *et al*. (2022), either showed no significant HRV differences or primarily focused on non-PD cohorts, thereby limiting their direct relevance. The collective findings demonstrate the robust capabilities of non-linear HRV metrics in identifying subtle and dynamic autonomic alterations in PD. The inclusion of novel measures like complexity variability, symbolic entropy and DC expands the utility of HRV analysis, making it an invaluable tool for early diagnosis and monitoring in PD.

Nonlinear HRV metrics and clinical correlations

Nonlinear HRV metrics demonstrated consistent correlations with clinical parameters such as motor symptom severity and the extent of autonomic dysfunction, highlighting their potential as biomarkers for PD. Kallio *et al*. (2002) found that among the nonlinear parameters, the Fractal Dimension (FD) showed the strongest correlation with all time domain and absolute measures, indicating its relevance in capturing parasympathetic and sympathetic function [38].

Valenza *et al*. (2017) demonstrated that increased complexity variability in PD patients reflected the unstable nature of autonomic control, likely tied to ongoing neurodegeneration within the autonomic nervous system, even in early disease stages [42]. The clinical significance of symbolic dynamics and entropy-based metrics was demonstrated by Dorantes-Méndez *et al*. (2022), who reported that these metrics could achieve over 95% classification accuracy between PD patients and controls. These findings reinforce the potential of nonlinear HRV analysis in early detection and tracking of autonomic dysfunction [48].

Haapaniemi *et al*. (2001) reported significant reductions in spectral HRV measures, particularly in the low-frequency and high-frequency components. Moreover, the power-law slope showed a negative correlation with motor symptom severity, especially hypokinesia, emphasizing the clinical relevance of HRV metrics in monitoring motor symptom progression. These findings further underscore the interplay between autonomic dysfunction and motor symptomatology in PD [37].Nonlinear metrics also hold promise in distinguishing between PD and other neurodegenerative disorders.

Brisinda *et al*. (2015) demonstrated that recurrence plot analysis, correlation dimension, and other nonlinear parameters effectively differentiated PD from MSA, achieving high diagnostic accuracy. This distinction is crucial given the overlapping autonomic features of PD and MSA, with MSA often progressing more rapidly. Such differentiation supports timely and tailored interventions for these conditions [41].

Additionally, Carricarte-Naranjo *et al*. (2021) highlighted DC as a novel measure of vagal modulation, which correlated strongly with autonomic dysfunction in older PD patients. The reduction in DC underscores its potential as an age-sensitive marker for identifying cardiac autonomic dysfunction in PD[45].

Overall, these studies illustrate the utility of nonlinear HRV metrics in reflecting disease-specific autonomic patterns, distinguishing between neurodegenerative conditions, and tracking PD progression.

Discussion

The results of this scoping review provide valuable insights into the potential of nonlinear HRV parameters in understanding autonomic dysfunction in PD. Traditional linear HRV methods, while insightful, often lack the complexity needed to capture the irregularities and multidimensional nature of autonomic control seen in PD.

Non-linear HRV analysis addresses these limitations by uncovering subtle patterns and irregularities that reflect the complex interplay between the sympathetic and parasympathetic nervous systems.Nonlinear HRV metrics such as ApEn, SampEn, DFA, and MSE measure the complexity and irregularity of heart rate signals over time [51-53]. ApEn and SampEn provide estimates of HRV signal predictability, with lower entropy values indicating a more regular, less adaptable autonomic system—patterns commonly associated with PD. DFA examines long-term correlation properties and has shown that short-term variability measures (SD1) in DFA are often reduced in PD, reflecting a compromised parasympathetic system [38]. MSE, which examines complexity over various timescales, has highlighted the broader loss of adaptability within the autonomic system in PD patients [48]. Spectral HRV measures, Poincaré plots, and power-law relationships further highlight significant reductions in vagal modulation and overall HRV complexity, correlating strongly with motor symptom severity [37].

Key findings across studies consistently showed that non-linear HRV parameters, especially ApEn and hsCFP3, reveal significant reductions in HRV complexity in PD patients. These decreases in complexity suggest a loss of adaptive capacity within the autonomic nervous system, likely due to PD-related neurodegeneration in autonomic regulatory centers. Importantly, this complexity reduction is detected even in patients with early-stage PD who might not yet exhibit overt symptoms of autonomic dysfunction [42]. This indicates the potential utility of non-linear HRV metrics as early biomarkers, allowing clinicians to identify and monitor autonomic impairment before it manifests clinically. Moreover, some studies within this review have shown that certain non-linear HRV parameters can distinguish PD from MSA, a differential diagnosis that is often challenging due to overlapping symptoms. For instance, symbolic HRV analysis, which identifies parasympathetic and sympathetic autonomic activities through patterns such as 2UV% and 0V %, has demonstrated potential in differentiating PD from MSA subtypes. Metrics like DFA and fractal analysis were notably distinct in PD versus MSA groups, suggesting that non-linear HRV measures may assist in refining differential diagnoses. Finally, RQA, as used in recurrence plots, quantifies the number and duration of recurring patterns in HRV data, distinguishing PD from other conditions like MSA based on HRV dynamic patterns [54].

Innovative markers like DC have proven effective in detecting vagal modulation deficits, even in older PD patients, further underscoring the nuanced insights offered by non-linear HRV metrics [45]. Additionally, symbolic dynamics and MSE methods have demonstrated high classification accuracy, further supporting the application of advanced non-linear HRV metrics in identifying autonomic impairment.

The clinical application of non-linear HRV metrics in PD however faces several challenges. Differences in study designs, sample sizes, and H RV measurement protocols make it difficult to standardize findings across studies. Additionally, confounding factors such as medication, physical activity levels, and comorbidities can affect HRV outcomes and thus need to be carefully controlled in future research. Addressing these limitations through larger, well-designed studies could confirm the reliability and reproducibility of these metrics, enabling their integration into clinical practice.

Conclusion

Non-linear HRV analysis presents an innovative, non-invasive method for evaluating autonomic function in PD. Unlike traditional linear metrics, non-linear parameters such as entropy and fractal scaling better reflect the loss of physiological complexity associated with PD. The review supports their potential utility in early diagnosis, disease monitoring, and differentiation from related disorders like MSA. However, methodological inconsistencies and limited sample sizes across studies highlight the need for standardization and larger cohorts. With further validation, non-linear HRV may serve as a valuable clinical biomarker in PD management.

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