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Speech and language biomarkers for Parkinson's disease prediction, early diagnosis and progression

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Parkinson's disease (PD), a multifaceted neurodegenerative disorder, can manifest as an array of motor and non-motor symptoms. Among these, speech and language impairments are particularly prevalent, often preceding motor dysfunctions. Emerging research indicates that these impairments may serve as early disease indicators. In this narrative review, we synthesised current findings on the potential of speech and language symptoms in PD identification and progression monitoring. Our review highlights convergent, albeit preliminary, lines of evidence supporting the value of speech-related features in detecting early or prodromal PD, even across language groups, especially with sophisticated analytical techniques. Distinct speech patterns in PD subtypes and other neurological disorders may assist in differential diagnosis and inform targeted management efforts. These features also evolve over the disease course and could effectively be utilised for disease tracking and guide management plan modifications. Advances in digital voice processing allow cost-effective, remote and scalable monitoring for larger populations.

Parkinson's disease (PD) is a complex neurodegenerative disorder characterised by intracellular deposits of α-synuclein and progressive loss of dopaminergic neurons in the substantia nigra pars compacta[1]. It is the fastest-growing and second-most common neurological disease currently affecting approximately 10 million individuals worldwide with the figure expected to double by 2050[2]. While the principal manifestations include impaired motor functions (e.g., resting tremor, rigidity and bradykinesia), a multitude of non-motor symptoms occur concomitantly throughout the disease course[1,3,4], further contributing to the overall disease burden and poorer quality of life for people with PD (PwPD) and their caregivers and loved ones.

There is a recent shift to a biological definition of PD integrating pathogenesis, genetics, biomarkers and clinical components of both motor and non-motor features[5,6]; however, these newly proposed criteria are intended exclusively for research purposes. Clinically, a diagnosis still relies primarily on motor dysfunctions, specifically the presence of bradykinesia combined with rigidity and/or resting tremor[1]. By this point, ~50–60% of substantial nigra dopaminergic neuron loss and up to 70% of striatal dopamine depletion have likely occurred[7,8], which significantly limits the effectiveness of any neuroprotective or disease-modifying therapies aiming to slow or halt neurodegeneration[9–11]. Sensitive and reliable biomarkers of PD at or before symptom onset are therefore urgently needed for such interventions to be introduced early to achieve the optimal treatment outcome.

Rapid eye movement (REM) sleep behaviour disorder (RBD), a parasomnia characterised by dream-enactment behaviours during loss of REM sleep muscle atonia, is considered a key prodromal stage of α-synucleinopathies[12]. However, RBD is not a specific or sensitive marker for PD as it also occurs in other neurodegenerative disorders such as dementia with Lewy bodies (DLB) and multiple system atrophy (MSA)[12,13], and its prevalence in PD is relatively low (~ 24–42%)[14,15]. Moreover, the need for a polysomnographic confirmation[12,16] further restricts its use at the populational level.

Speech impairments, on the other hand, are particularly prevalent, affecting up to 90% of PwPD[17,18]. Growing evidence indicates that speech and language alterations often precede the defining motor signs and PD diagnosis by as much as a decade[4,19–23]; consequently, several guidelines recommend incorporating speech and language pathology/therapy (SLP) as a crucial component of PD care and rehabilitation from diagnosis[24]. Recent research highlights the value of objective acoustic speech markers in detecting PD in the initial or even prodromal (e.g., RBD) stages[23,25,26]. This implicates a potential window for timely interventions, such as monoamine

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oxidase B inhibitors, anticholinergics and future novel therapies that may confer improved efficacy in early PD stages[9,11]. Speech and language features might also be used as a proxy measure for tracking disease progression and status as they evolve over the course of the disease[25,27–31]. Moreover, specific patterns of speech impairment have been linked to the presence of varying disease subtypes characterised by distinct underlying pathologies[23,29] and have been shown to differentiate PD from other basal ganglia disorders[32] and synucleinopathies[23,33–35] as well as between PD subtypes[36,37].

To reflect the current state of knowledge and inform future investigations, we conducted a narrative review synthesising current evidence pertinent to the value of speech and language biomarkers in PD prediction, early detection and progression. Common speech and language difficulties in PD and recommended speech tasks and measurement tools were only briefly described as multiple reviews have addressed these topics[3,4,38–41].

Methods

We searched PubMed, Google Scholar and Web of Science databases using the search terms Parkinson's disease" OR "Parkinson disease" OR "PD" AND "language" OR "linguistic" OR "speech" OR "acoustics" OR "voice" OR "fluency" OR "intelligibility" OR "communication." Reference lists from identified publications were also searched. Papers were reviewed and selected based on their relevance to the focus of the review.

Speech and language assessment

The evaluation of speech and linguistic functions encompasses a set of standardised tests that are applicable across various disciplines, including conditions like PD and other movement disorders[38–41]. The recommended and widely employed tests are 1) sustained phonation of the vowel /a/ in a single breath, which helps assess breath control, vocal fold function and vocal quality; 2) rapid repetition of syllables such as /pa/, /ta/ and /ka/ to evaluate consonant and vowel articulation, articulation rate and regularity, coordination and speech timing; 3) reading a passage that assesses articulation, prosody and resonance and 4) verbal fluency test (phonemic and semantic naming) to assess lexicon access, verbal functioning and executive control[42,43] 5) picture description and/or spontaneous monologue, which provides insight into fluency, language formulation at the lexical-semantic, morpho-syntactic and discourse-pragmatic levels and overall speech and language abilities[38,39,41].

Following the administration of these tests, speech recordings are analysed either perceptually by a qualified speech and language pathologist or objectively through acoustic and linguistic analyses. Perceptual analysis involves the use of standardised protocols to systematically describe speech characteristics (e.g., voice quality, articulation, rate and rhythm), the severity of dysarthria, overall intelligibility and naturalness of speech; these can help gauge the functional aspects of communication deficits[17,38,44]. Objective analyses, on the other hand, utilise specialised software or digital interfaces to quantify various acoustic parameters related to spectral characteristics of voice signals and linguistic features from speech transcripts, providing a more in-depth and sensitive approach to assessing an individual's speech and language abilities[4,38,41]. With automated signal processing, these objective tools are also more accessible and scalable, allowing for remote monitoring.

Consideration of self-perception of voice, speech and language impairment is advocated as can provides important insights into the impact of PD on functional communication in real-world contexts[45–49]. Example tools used in this context include the Voice Handicap Index[45], the Dysarthria Impact Scale[50] and the Dysarthria Impact Profile[48]. They provide valuable information on the subjective perception of impact; however, they are less sensitive to minor fluctuations in function and may be affected by flooring and ceiling effects inherent to the evaluation scales employed.

Voice, speech and language alterations in PD

Impaired speech in PD can result from disruption to some or all subsystems involved in speech production, including phonation, articulation, prosody, respiration and resonance. These impairments are typically characterised by diminished loudness reflected by a soft or asthenic voice[51], reduced variability in loudness and pitch resulting in a monopitch and monoloudness[25,26,30,51], a harsh and/or breathy voice quality[17,32] and imprecise articulation[25,52], all contributing to decreased intelligibility[17,53]. Inappropriate pauses and inconsistent speech rates such as abrupt deceleration or acceleration of speech have also been reported[4,26,54,55], which collectively can be classified as "hypokinetic dysarthria"[53]. These perceptual changes are reflected in objective acoustic features including reduced range and variation in voice intensity and fundamental frequency (*f0*), shorter maximum phonation time, lower harmonics-to-noise ratio (HNR) and cepstral peak prominence (CPP), restricted vowel space area (VSA) and lower vowel articulation index (VAI), longer voice onset time (VOT), increased perturbations in the amplitude and frequency of sound waves described as jitter and shimmer, respectively, slower and irregular diadochokinetic rate and prolonged pause intervals[3,19,30,37,56].

While most communication research in PD has focused on motor speech functions, impaired language is associated with PD. The verbal output of PwPD relative to individuals without PD is often less informative[23,31,57], concise[58], grammatically intact[31] and complex[58,59], relying more on content words rather than functional words (e.g., prepositions and conjunctions)[23] during narrative or other structured tasks. At the conversational level, word-finding difficulties or "tip-of-the-tongue" phenomenon and challenges in initiating and maintaining a topic have been observed[4,60]. PwPD can also have difficulties recognising and interpreting non-verbal cues such as emotion expressed through facial expression or tones[61–63], in addition to reduced body gestures and flattened affect[3,60,63], making it harder for them to engage in conversations.

A short glossary of speech and language terminologies used in this study is outlined in Table 1. A schematic illustrating the strategic integration of speech and language markers across the PD continuum to facilitate clinical decision-making and better management of the disease is depicted in Fig. 1.

Preclinical or prodromal speech and language markers for early PD detection and prediction

In the PD progression trajectory proposed by Braak et al.[64], Lewy body pathology in Stages 1–2 is confined to the brainstem, affecting the glossopharyngeal and vagal nerves, which innervate the laryngeal and pharyngeal musculature and coordinate articulatory and respiratory activities[19,21,65], and olfactory regions before reaching the substantia nigra. In accordance with Braak's staging, Selby[66] also hypothesised a caudorostral symptom progression in PD, starting with failure in speech-related respiratory control and then articulation involving the larynx, pharynx, tongue and lips. Converging evidence now suggests that voice and speech alterations, along with abnormalities in swallowing and smell, are among the earliest signs of PD and may serve as early markers for diagnosis and prediction.

Dysprosody was consistently observed in the early and even prodromal stages of the disease across different languages. In a multicentre cohort study administered in Czech, English, German, French and Italian languages, monopitch differentiated groups, even in the prodromal phase of PD[25]. In this study, early speech markers were explored in 150 participants with idiopathic RBD, 149 with early-stage PD (mean disease duration 1.7–2.5 years) and 149 controls. Four speech tasks including sustained phonation, fast syllable repetition (/pa//ta//ka/), text reading and narration were administered at baseline and 12-month follow-up. A significant difference was noted in monopitch, prolonged pauses and imprecise consonants between PD and control participants, resulting in an area under the curve (AUC) of 0.80 for group classification. Monopitch and prolonged pauses were also different between RBD and PD, with an AUC of 0.72 when combined with extra features including harsh voice and articulation rate. Similarly, monopitch separated RBD subjects from controls, though with a smaller AUC of 0.65, by incorporating the same additional features.

The relationship between prominent speech features like prosody in prodromal PD and other markers of the disease such as altered olfactory functions and nigrostriatal system have also been investigated in Czech[67].

Table 1 | Glossary of speech and language terminologies in this review

Term	Definition
Asthenic voice	A perceptual measurement indicating weakness or lack of energy during phonation.
Breathy voice	A voice quality characterized by an airy or breathy sound, due to incomplete closure of the vocal folds.
Cepstral peak prominence (CPP)	A measure of the prominence of the highest peak in the cepstrum of a voice signal, indicating voice clarity and quality.
Content density	Proportion of content words relative to functional words, which measures the amount of meaningful information in a given amount of language output.
Content words	Words that convey meanings (e.g., nouns, verbs, adjectives and adverbs).
Diadochokinetic rate	The rate at which an individual can repeat rapidly alternating syllables (e.g., /pa//ta//ka/) without semantic meaning.
Discourse-pragmatic	It examines how the context influences the meaning of the discourse produced.
Functional words	Words that serve primarily grammatical purposes (e.g., prepositions, conjunctions and articles).
Fundamental frequency (*f0*)	The frequency at which the vocal folds vibrate when voiced speech sounds are made.
Harsh voice	A voice quality that sounds rough or strained.
Harmonics-to-noise ratio (HNR)	The ratio of harmonic components to noise components in a voice signal, reflecting voice quality.
Intelligibility	The degree to which speech is understandable to listeners.
Jitter	Variability of fundamental frequency (*f0*) from one cycle to the next.
Lexical-semantic	It examines linguistic ability at the word (vocabulary or lexicon) and content (their meanings) levels.
Monoloudness	Speech characterised by constant loudness with no variation.
Monopitch	Speech characterised by constant pitch with no variation.
Morpho-syntactic	It examines how the form of words (morphology) and their grammatical functions (syntax) interact to contribute to sentence structure and meaning.
Phonemic naming	List words by phonemes or sounds (e.g., words start with letter "D").
Prosody	The rhythm, stress and intonation of speech.
Resonance	The voice quality produced by vibrations of the vocal tract, including the throat, mouth and nasal cavities.
Semantic naming	Name words based on their meanings (e.g., naming animals).
Shimmer	Variability of amplitude of sound waves from one cycle to the next.
Syntactic boundary	It indicates where one grammatical unit ends and another begins.
Vowel articulation index (VAI)	An acoustic measure of derived from vowel formant frequencies.
Voice onset time (VOT)	The time between the release of a plosive consonant and the onset of voicing.
Vowel space area (VSA)	An acoustic measure calculated as the area of the polygon formed by the formant frequencies of the corner vowels.
Voice tremor	A "shaky" or "unsteady" voice quality caused by rhythmic, involuntary contractions of the laryngeal muscles.

Similar to earlier work, data suggest that prosodic impairment can present prior to the appearance of nigro-putaminal dopaminergic deficits, with dysprosody and olfactory dysfunctions co-occurring. Reduced pitch variability was detected in people with RBD and hyposmia but not those with normal olfaction compared to healthy individuals[67]. Additionally, while monopitch at baseline was independent of putamen binding ratio captured by dopamine transporter single-photon emission computed tomography (DAT-SPECT), deterioration in impaired pitch variability was only seen in the RBD subgroup with hyposmia and abnormal DAT-SPECT at the 2-year follow-up.

Again, using RBD as a model for prodromal PD, a French-speaking cohort yielded similar outcomes in exploring voice characteristics from prodromal to early PD[26]. Both RBD and PD groups produced more monotonous speech alongside longer pause durations and an unsteady rhythm, compared to the control group[26]. Leveraging voice features extracted from automated acoustic analysis and supervised learning classifications, early PD was classified with 89% accuracy for males and 70% for females, while RBD detection achieved an accuracy of 63–70%. It is noteworthy that more pronounced prosodic deficits were observed during emotional encounters during task performance, implying that tasks with higher emotional demands could offer greater sensitivity in detecting early, nuanced speech alterations.

Vowel distortion is a key component of dysarthric speech. It is typically measured by exploring the distribution of the first and second formants[68]. There is some preliminary evidence to suggest composite measures of vowel production differ in PwPD prior to the commencement of therapy and matched controls[52]. These parameters include the VSA and VAI derived from connected speech tasks. It is also noted that spontaneous speech tasks (e.g., monologue), which are more complex with higher articulatory demands, better separated groups compared to non-spontaneous tasks (e.g., sentence repetition and passage reading)[52].

Vowel articulation deficits may also be present in the prodromal stage[69]. In a study exploring whether altered vowel articulation was a prodromal symptom of synucleinopathy in a larger male sample (60 RBD, 60 de-novo (newly diagnosed), untreated PD and 60 age-matched controls), both the RBD and PD groups exhibited significantly smaller VSA during passage reading than controls and lower VAI was found in PD compared to controls[69]. The results also revealed that imprecise vowels evaluated by both acoustic indices correlated with the Unified Parkinson's Disease Rating Scale (UPDRS) motor scores and the severity of bradykinesia and rigidity but not axial gait symptoms or tremor. Furthermore, a positive correlation was observed between the putamen binding ratio detected from DAT-SPECT and VSA in RBD, suggesting that nigrostriatal neurodegeneration might play a role in articulatory impairment.

Advances in digital voice processing and machine learning utilising speech signals have propelled research forward in the detection and prediction of PD. Sophisticated feature selection and classification models have been proposed to be able to effectively distinguish PwPD from healthy individuals[70–73], regardless of the presence of overt symptoms[74], and even people in prodromal PD (e.g., RBD)[75] with motor symptoms from those without[73], based on sets of simple speech tasks. More recent studies have also demonstrated the scalability and accessibility of these detection tools to a

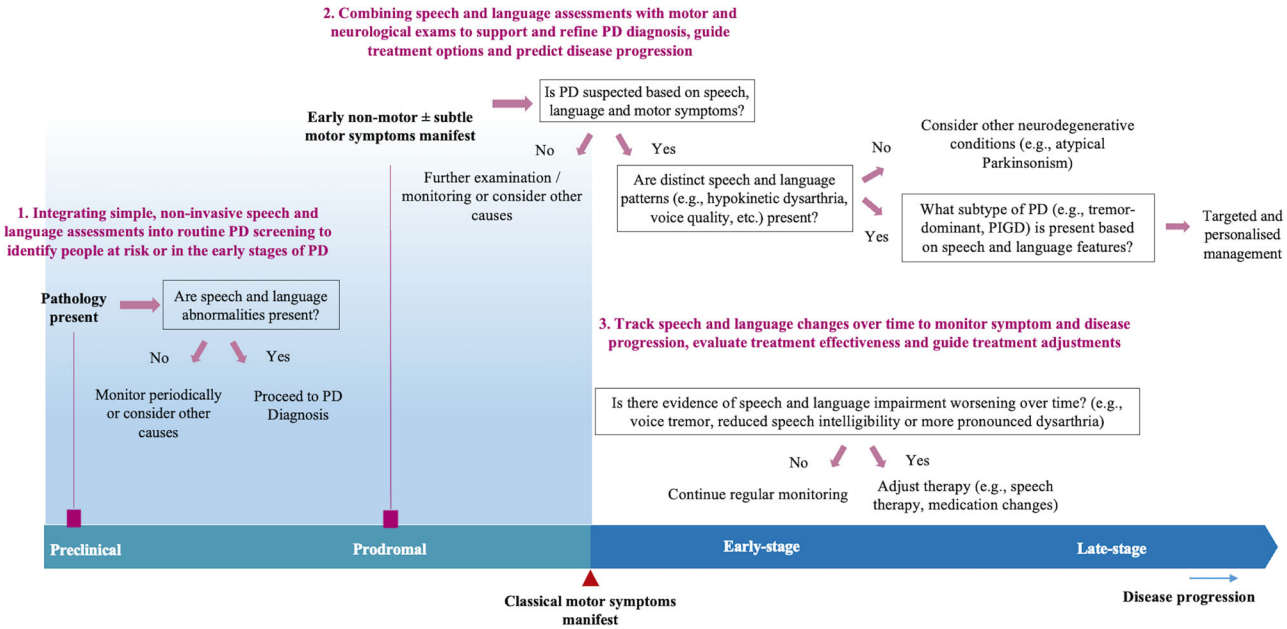

Fig. 1 | Integrating speech and language markers into clinical practice for Parkinson's disease screening, diagnosis, differential diagnosis, subtyping and monitoring. This schematic demonstrates how integrating speech and language markers into clinical practice across the Parkinson's disease (PD) continuum can enhance early detection, inform clinical decision-making and optimize disease management throughout its progression.

wider population with their capability of operating effectively on mobile devices[70,75–77]. Sustained vowel task, among other tests, was widely adopted[65,70–72,74]. Data suggest that ~99% discrimination accuracy can be achieved[65], using even just a handful of dysphonic measures by support vector machines[72]. However, overfitting is likely due to the model complexity and limited training samples, without validation on novel datasets. When the same technique was applied to a larger cohort (1078 PwPD and 5453 controls), the accuracy dropped to < 70%[78], though the reduced performance may also be linked to the poorer sound quality of phone calls[78] compared to controlled and standardised speech sampling[72].

While studies have underscored the value of speech features as early PD markers, especially with advanced analytics, these approaches come with their own set of advantages and challenges. Machine learning algorithms can uncover complex patterns and subtle voice and speech changes in early-stage PD that conventional models might miss, leading to more accurate and nuanced predictions. However, these advanced models often lack interpretability due to their "black box" nature, making it challenging to understand the decision-making processes that are crucial for clinical validation. Additionally, the transferability of these advanced models to clinical settings requires extensive validation to ensure they work across diverse populations and clinical settings.

Compared to motor speech features, fewer research efforts have been directed to early PD language and conversational limitations, and that on preclinical or prodromal language alterations remain scarce. However, there is evidence indicating that language deficits are detectable in prodromal PD and tasks with higher cognitive demands can distinguish RBD and PD with mild cognitive impairment (MCI) from controls as well as RBD and PD with intact cognition with an AUC of up to 0.82[79]. In this study, prodromal linguistic markers were investigated in 40 RBD cases and 40 de-novo PD cases without MCI, 14 RBD cases and 15 de-novo PD cases with MCI and 30 controls[79]. It is observed that both RBD groups had lower content density than controls during spontaneous discourse, whereas RBD and PD subgroups with MCI exhibited poorer lexical diversity and more frequent phrase repetitions than both subgroups without MCI and controls in a story narration task. The results also showed that only 7.5% of RBD subjects without MCI had an abnormal DAT-SPECT, implying that the presence of linguistic abnormalities might precede the substantia nigra degeneration.

Impaired linguistic function at the prodromal disease phase (RBD) might serve as a language-universal predictor for synucleinopathies. In one longitudinal study[23], a narration task was submitted to 180 idiopathic RBD subjects and 149 controls speaking Czech, English, German, French and Italian for elicitation of three linguistic (content richness, vocabulary range and sentence complexity) and two acoustic features (articulatory pace and pause durations) using an automated approach. The overall phenoconversion over a 5-year follow-up on average was linked to lower content richness, slower articulation rate and prolonged pauses. Among those who developed a certain synucleinopathy, the conversion of dementia and PD with MCI compared to PD without MCI was associated with greater baseline severity of linguistic impairment (odds ratio (OR) = 109.18). Specifically, lower content richness was linked to a higher risk of PD with MCI (OR = 7.46) and restricted vocabulary range was associated with higher risks of dementia (OR = 4.08) compared to PD alone. The across-languages applicability of language as well as acoustic markers is also reflected in dysarthria treatments. For instance, following Lee Silverman Voice Treatment, vocal intensity was increased in Cantonese, Japanese, French, Mandarin and Italian speakers with PD, while intonation was improved in Portuguese, German and Cantonese speakers[80]. Nonetheless, other features, such as VSA and rhythm, appeared to be language-specific, and further investigations are required.

Syntactic deficits might even be a preclinical sign of PD. In a small cohort comprising 33 people with sporadic PD without risk mutations, 8 with genetic PD (*PARK2* or *LRRK2* mutations), 9 asymptomatic first-degree relatives of people with genetic PD and 56 healthy controls with no familial history of PD[81], group comparisons revealed that both sporadic and genetic PD groups performed worse on all executive and language tasks (e.g., action semantics, object semantics and action naming) compared to controls. Of interest, asymptomatic mutation carriers displayed significantly poorer syntactic comprehension than controls, implicating the role *PARK2* or *LRRK2* mutations may have on language-processing mechanisms. Nonetheless, this preliminary evidence comes with caveats due to the extremely limited sample sizes, and replication in larger datasets is needed.

Other studies focused on early-stage PD have reported faster speaking rates characterised by short rapid output segments but longer hesitations and less word production[55], impairments in alternating semantic verbal fluency (e.g., naming animals and then furniture and then alternating back

and forth)[82] and pragmatic skills (the ability to adapt communication techniques in terms of language comprehension and production to different social contexts)[83]. However, whether these symptoms are manifested in the prodromal phases is uncertain and needs to be explored in future research.

Speech and language markers for differential diagnosis from other neurodegenerative conditions

PD and atypical Parkinson's syndromes such as MSA and progressive supranuclear palsy (PSP) present with overlapping clinical features[84], making accurate diagnosis challenging, especially on initial clinical evaluation. However, a few studies have highlighted that the distinct pathophysiology of atypical Parkinsonism results in unique speech symptom profiles, and detailed acoustic and language evaluation can help discriminate PD from MSA and PSP[33,85,86], even in the early disease process[34,35,87].

In comparison to PD, speech impairment in atypical Parkinsonism is generally more pronounced[34,35,85–88], possibly related to its more widespread and severe pathology and more rapid disease progression[84]. For instance, greater severity of imprecise consonants[33,85,86], articulatory decay[33,86] and diadochokinetic irregularity[33,86], slower diadochokinetic and speech rate[33,86] and longer pause times[34,86] are frequently observed in MSA and PSP compared to PD.

PD dysarthria presents mainly as hypokinetic[35,88], while dysarthria in atypical Parkinsonism, in particular MSA and PSP, is often mixed involving differing combinations of hypokinetic, spastic and ataxic components[86–88]. More specifically, the speech of people with MSA is predominantly hypokinetic-ataxic, characterised by strained-strangled voice quality[87,88], excessive pitch and loudness fluctuations[87,88], vocal tremor[87,88], variable rate of speech[33] and imprecise consonants[85]; whereas speech in PSP is described as hypokinetic-spastic with strained-strangled voice quality[87], varied speech rate[33,88], stuttering like behaviour and involuntary syllable or word repetition[89].

Recent work suggests that diverging speech patterns may allow for better separation of PD, MSA and PSP groups. For instance, maximum phonation time, ataxia symptoms (tremulous voice, uncontrolled pitch and loudness variations during sustained phonation) and spastic features (strained, squeezing voice, phonation breaks and voiceless ratio during the same task) can split MSA and PD[87]. Spastic speech dimensions can also differentiate people with PSP and PD[87]. When using a combination of these distinct speech patterns, PD can be accurately distinguished from MSA and PSP with an accuracy of 87–95%[33,88], even at early disease stages[34].

Atypical Parkinsonism might affect language to a greater extent compared to PD, though evidence is equivocal. When matching for age, education and global cognitive function, people with PSP exhibit severe impairments in phonological and semantic fluency, reflecting greater executive function damage, followed by those with MSA and then PwPD[90]. The PSP and MSA groups also present with more severe behavioural symptoms, including apathy and depression compared to PwPD[90]. PD and MSA groups appear to be more closely aligned on language disturbances, with the latter showing worse executive function and semantic fluency[91] but similar performance in other language testing such as repetition of words and non-words, repetition of sentences, word reading, semantic association, number of phonological errors/number of words and picture description[92]. A combined measure encompassing the full speech and language assay might enhance group differentiation.

Studies comparing PD and other neurological conditions involving movement disorders lend further support for the specificity of speech markers. PwPD and people with Huntington's disease (PwHD) can exhibit distinct phonatory and resonatory characteristics as well as language production deficits. Based upon the assessment of sustained phonation and monologue task performance, a harsh or hoarse voice was more frequently noted in PwPD compared to controls[32], whereas PwHD can present with more severe dysphonia and breathiness[32] and increased and intermittent hypernasality, likely reflecting the velopharyngeal mechanism's choreatic motions[93]. In terms of language functions, while both groups produced fewer grammatical sentences (e.g., subject-verb-objective) and verbal content that was less informative than controls, PwHD tend to produce shorter utterances with greater syntactic simplification than PwPD, despite performing similarly on cognitive and motor speech tasks[57].

PD can also be accurately separated from essential tremor (ET) even across language groups with the use of automated speech signal processing and machine learning algorithms[94]. A recent study proposed a classification model for PD and ET based on articulatory, phonatory and prosodic indices elicited via rapid syllable repetition and monologue tasks[94]. Data demonstrated that the models trained in German and Spanish achieved a classification accuracy of up to 81% for monologue and 86% for syllable repetition when applied to a Czech-speaking cohort.

While existing evidence underpins the promising diagnostic and screening values of objective speech assessment in differentiating PD from other Parkinsonian syndromes, it should be noted that most of these studies were limited by very small sample sizes with case subgroups ranging from 10 to 30 participants. Additionally, there is evidence that speaker sex, often not accounted for in these studies, influences speech outcomes in PD and similar neurodegenerative disorders, with males generally experiencing greater impairment[32,35]. During early disease stages, males with MSA can display a considerably increased *f0*, slower speech rate and longer pauses compared to those with PD, whereas MSA females but not males or those with PD can manifest voice tremor and loudness decay[35]. Similarly, although both sexes exhibit poorer voice quality in PD and HD, males with PD experience more severe breathiness in speech and those with HD show more pronounced hoarseness compared to their female counterparts[32]. This differential effect may stem from the physiological distinctions between sexes in terms of the structure of vocal folds and larynx and sexual hormonal levels[95,96], which also lead to variations in voice changes as a result of normal aging[56,96,97]. Thus, future studies with larger populations from multiple centres and proper sex stratifications are needed to validate these initial findings.

Differential speech and language patterns among PD subtypes

It is well recognised that PD has a wide range of clinical manifestations and prognosis[98,99], indicating the presence of multiple subtypes with varying disease mechanisms. Markers of different PD phenotypes are therefore needed to better allocate patient groups and guide more appropriate and individualised clinical management. Speech, the product of highly complex motor and cognitive coordination[100], is particularly sensitive to neural structure damage and could potentially aid in classifying disease subtypes.

Multiple studies have documented the distribution of affected speech domains across PD phenotypes. In particular, an association has been observed between the severity of speech disturbances, especially temporal disruptions and dysrhythmicity, and axial motor symptoms in PD[29,37], including gait freezing[101–103], festination[104] and instability[36,105,106], implicating a shared pathomechanism between speaking and walking dysfunctions. Early evidence came from a large cohort of 800 people with early PD (mean symptom duration = 2 years) from the DATATOP clinical trial monitored for approximately 14 months[101]. Speech performance measured subjectively via clinical rating scales, among other motor traits, is a strong risk factor for the development of freezing of gait[101]. Speech and handwriting abnormalities measured within the UPDRS were also related to episodes of gait freezing, but not rigidity, bradykinesia or balance, in a Levodopa "on" state[102]. Further, the decrease in gait freezing frequency in response to Levodopa was strongly associated with an improvement in speech. Similar relationships were observed in an "off-medication" state, where changes in gait velocity, cadence (steps/min) and stride length were correlated with changes in speech initiation time, speech rate and the number of repetitions during sentence reading in patients with gait freezing[103].

The link between speech and gait is reflected in other motor assays. During diadochokinetic tasks (syllable repetition), involuntary speeding up of speech (known as oral festination) correlated strongly with festination of gait when PwPD were in the "off Levodopa" state[104]. This also plays out where prominent articulatory-prosodic abnormalities change in line with greater postural instability/gait difficulties (PIGD)[106]. Moreover, the severity

of overall speech impairment in the PIGD subtype was found to be greater compared to the tremor-dominant (TD) subtype[36,105], with distinct characteristics allowing for differentiation between the two PD phenotypes[105]. Specifically, while both TD and PIGD subtypes displayed monopitch and irregular diadochokinetic rate, consonant timing deficits, abnormal pitch breaks, articulatory decay, decreased speech rate in subsequent segments and inappropriate pauses were found only in PIGD compared to controls[36,105]. Additionally, the correlations between speech (e.g., prolonged VOT, diadochokinetic irregularity and prolonged pauses) and gait (e.g., slower gait velocity, decreased cadence and shorter stride length) features were observed in the PIGD but not TD subgroup[36]. It is also worth noting that the severity of PIGD is also associated with impaired global cognition, executive function, memory and phonemic fluency[107].

As indicated by other lines of work, discernible patterns of dysarthria are thought to be associated with the onset and form (sporadic versus monogenic) as well as cognitive involvement of the disease. PwPD with a late onset (age of onset at ≥ 70 years) seem to exhibit more pronounced speech impairment, whereas those with an early onset (age of onset at ≤ 50 years) have greater motor dysfunctions including impaired strength of inspiratory muscle[37]. When comparing subgroups of newly diagnosed PD with an early or late onset prior to treatment commencement to age- and sex-matched healthy controls ($n = 24$ for each subgroup), monopitch, monoloudness and articulatory decay were consistently related to PD regardless of age; however, weaker inspirations (the relative loudness of respiration to speech) were a distinct feature of early-onset PD, while decreased voice quality and imprecise consonant articulation were unique characteristics of late-onset PD[37].

Sporadic and genetic PD can result in mixed acoustic profiles. Consistent with previous research indicating heterogeneous neuropathology between the two forms of PD[108,109], preliminary data suggest that PD associated with mutations in the leucine-rich repeat kinase 2 (*LRRK2*) gene may exert a distinct impact on speech compared to idiopathic PD[110]. In one case, voice characteristics based on sustained phonation, such as entropy (calculated following sound wavelet decomposition and quantifies the degree of randomness in a voice signal), skewness of the amplitude distribution, glottis to noise excitation ratio (signal strength relative to noise) and vocal fold excitation ratio (signal strength versus noise) combined with other acoustic parameters differentiated the two subtypes with a mean sensitivity of 95% and specificity of 90%[110]. Differences were also observed among asymptomatic *LRRK2*-mutation carriers, asymptomatic relatives without *LRRK2*-mutations and unrelated healthy controls, although to a lesser degree (sensitivity 75–76% and specificity 78–82%). Nonetheless, the generalisability of this evidence is constrained by the limited sample size with only 7–20 individuals in each PD subgroup. Further validation in larger cohorts is necessary to confirm these initial findings.

Linguistic and speech features may indicate declined cognition in PD, even in the early stages and mild forms. Greater linguistic impairment associated with MCI can be seen through reduced content density[23], a smaller lexicon and more frequent dysfluencies in both PD and the RBD prodromal phase[79]. Pausing patterns also appear to be a useful marker of MCI in PD[4,111,112]. The location (e.g., pauses before and between utterances irrespective of verb class) and duration of pauses within utterances during a picture description task were found to be associated with cognitive function in PD evaluated by the Montreal Cognitive Assessment (MoCA)[111,112]. PwPD with MCI present with longer pauses between and within utterances as well as before action utterances and more frequent pauses before and within utterances than those with unremarkable cognition[111]. The association between pauses before action but not non-action utterances and cognitive dysfunction persists even after controlling for age, sex and UPDRS motor scores. Similarly, motor speech function can also reflect cognitive impairment, with lower *f0* variation, CPP[113] and VAI[114], as well as more pronounced temporal coordination deficits[112]. Notably, tasks with a higher cognitive load, such as story retelling compared to reading, may more effectively capture alterations in cognition[112,115].

We are reaching a point where distinct patterns of speech and linguistic features across PD phenotypes can be identified, supporting their potential as valuable tools for detecting and differentiating patient subgroups, even early in the disease process, to facilitate timely and personalised interventions. However, it is important to note that nearly all current studies focused on only one aspect of the disease spectrum, and the utility of speech markers in simultaneously identifying disease subtypes needs attention.

Speech and language markers of PD stages and progression

Speech and language functioning declines as PD progresses. Several lines of research have provided initial evidence on the value of acoustic markers across different speech subsystems as well as linguistic features in estimating the progression and severity of the disease. Early investigations assessing PwPD at early (disease duration ≤ 5 years without motor fluctuations) and late stages (disease duration ≥ 6 years) as compared to controls implicate a cooccurrence between changes in the characteristics of speech and voice dysfunctions and disease severity and duration[51]. Based on sustained vowels, scaling/gliding singing and monologue, people at late PD stages manifest a perceptually softer and more prominent breathy voice compared to those at early stages, with vocal tremor being a unique feature of advanced PD. The extent of vocal loudness reduction, limited variability in pitch and loudness, restricted maximum phonation frequency range, jitter and breathiness deteriorates as PD progresses. Among these, monopitch and monoloudness may differentiate the three groups. Sex-specific voice changes were also observed, with higher mean and minimum *f0* in advanced stages for males and a more pronounced reduction in *f0* variability and maximum *f0* in females. However, this pattern can occur as a part of normal aging[96], and whether it signals more widespread disease pathology is unclear.

Evidence from a larger PD cohort ($n = 200$) utilising a 2 min conservational speech task documents a gradual deterioration of speech accompanied by corresponding changes in different speech domains[17]. Dysphonia, including harsh voice quality, decreased volume and impaired intonation are common and predominantly impact the speaker in the initial PD stages. As the disease and overall speech impairment become more pronounced, the prevalence and degree of articulatory (e.g., imprecise articulation due to articulatory movement undershoot) and fluency impairments (e.g., difficulties in motor initiation, inappropriate pauses, syllable repetition and rushes in speech) increase, with articulation deficits being the most prevalent and significant feature in advanced stages.

Efforts to apply automated speech processing and novel machine learning methods to predict disease status and severity utilising speech samples as simple as sustained phonation[116–120] or combined with other tasks[76,121] provide corroborating evidence. Analysis of acoustic indices extracted from sustained vowels over 2 years revealed increased perturbations in sound frequency and intensity in PwPD, which predicted PD progression measured by UPDRS part III with an error rate of ~26% and part IV with an error rate of ~11%[116]. Higher accuracies were obtained by employing more sophisticated feature selection and classification algorithms[117,118,120,121], or incorporating simple motor tasks[76]. For instance, the UPDRS total and motor scores over an interval of ~6 months can be precisely estimated by random forest classifiers based on phonatory acoustic measures, with a discrepancy of < 2 points from the clinician's ratings[117,118]. The integration of extra motor information such as posture, gait and finger tapping alongside speech features also achieves accurate predictions for both the presence and status of the disease[76]. Notably, the extension to smartphone applications marks a pivotal juncture in remote symptom monitoring on a more regular basis[76,117,118], facilitating more effective disease management and improved patient care.

While multiple studies provide compelling evidence on the potential of speech markers in tracking disease progression, important methodological limitations are noted; most of them either adopted a cross-sectional approach[51], relied solely on case observations[116–118] or both[17,119–121]. Small sample sizes (< 100) used in model training and lack of validation in independent populations also raise concerns about the potential overfitting.

Longitudinal comparisons with control groups generally provide more power in assuring that changes in speech are the result of disease progression rather than natural aging or individual variability in symptomatology. Evidence from this study design can also provide insights into the cooccurrence of progressive voice and speech impairment with the overall disease course. An instable pace and pace acceleration during syllable during syllable repetitions may present in PD with further deterioration over the disease course, as observed over a period of 34 months on average (range = 12–88 months)[28]. These features evaluated by diadochokinetic tasks differentiated PwPD from healthy individuals at baseline, though data is not available for controls at follow-up examinations[28]. In this cohort, alterations in speech functions are independent of the UPDRS motor scores, suggesting that impaired syllable repetition could potentially be used as a marker of non-dopaminergic disease progression in PD. However, PD can manifest as varying speaking rates, and evidence regarding the characteristics and temporal changes of over time in the disease course is often mixed. Some data suggests that PwPD speak at faster rates than those without the condition as evaluated by different speech tasks (standard passage reading[122] or narration of a self-chosen topic[123]) with subsequent increases in speech rate and impairments over time, whereas others indicate a slower speech rate[31] or a gradual decline towards normal patterns[124].

Sex may play an important role. Data from a German-speaking cohort revealed that although the total speech rate of males with PD was significantly faster than age-matched male controls at baseline, this difference diminished after a mean interval of 25 months (range = 7–79 months) and was comparable to that of controls at follow-up[124]. In PD females, while there is a progressive decline in prosodic abilities indicated by notably reduced lower range and standard deviation of *f0* compared to female controls at both time points, fluctuations in speech rate are not observed[124]. Altered cognition in PD can also have an impact. Slowed speech rate, which further declined over time, was observed in PD complicated by dementia compared to non-demented PD[31], possibly related to the consequent difficulties in planning, initiating and maintaining speech output.

Changes in speech loudness and output length also vary based on the specific cohort sampled in a study. Over an average timeframe of 3.7 years, vocal loudness assessed within a reading task increased in one PD cohort compared to controls[122] but remained stable in the other cohort using a narration task[123]. Similarly, utterance length decreased from the first to second time points in one PD cohort to a greater extent than in controls[123], whereas no significant changes were observed either between groups or between time points in another cohort[122]. Discrepancies between studies might be attributed to 1) small sample sizes, ranging from only eight to fifty individuals with and without PD, respectively, which could substantially impede the reliability and generalisability of the findings; 2) bias introduced by the heterogeneity among PwPD in terms of disease duration upon enrolment, treatment or medication regimes and possibly disease subtypes; 3) variable time intervals between data collection points among PwPD and between PD and control groups, although speech performance was found to be independent of the intervals between examinations[124] or 4) intrinsic variability in each person's pathological processes and disease course.

Imprecise vowel articulation could serve as a marker for disease status as its deterioration likely parallels the progression of the disease and especially axial motor symptoms[29]. Using the triangular VSA (tVSA) and VAI of vowels /a/, /i/ and /u/ extracted from a standardised passage reading task, PwPD exhibit progressively impaired vowel articulation over an interval of ~33 months, with VAI appearing to be more sensitive to altered vowels and further decline in performance over time[29]. Of interest, although being independent of overall motor impairment evaluated by UPDRS part III or disease duration, a decline in both tVSA and VAI correlated with axial gait dysfunctions as measured by the UPDRS gait subscores.

Alterations in other speech modalities may also reflect disease progress. Assessment on a broader scale, encompassing both perceptually and acoustically measured phonation, articulation, prosody and fluency along with perceptual intelligibility, in a larger sample (80 PwPD and 60 age- and sex-matched controls) revealed that impaired voice and speech functions may be present even in the mild form of the disease and continue to decline in the disease course[27]. Based on the performance in reading and sustained vowel tasks, PwPD showed a decline in all perceptually evaluated speech modalities and acoustic parameters including shimmer, noise-to-harmonics ratio, net speech rate, VAI and stop consonant articulation over 12 to 88 months[27]. Notably, perceptual speech decline correlated with the baseline Hoehn-Yahr scale disease stages and UPDRS motor scores, while pause ratio and percentage of pauses within polysyllabic words from acoustic analysis correlated with disease stages at baseline and follow-up.

Longitudinal research, though relatively limited, suggests that the decline in higher-level language functioning and speech-related breathing also occurs in tandem with the progression of PD. Compensatory speech respiratory adaptations (e.g., increase in lung volume excursion and vital capacity per syllable to maintain subglottal pressure for speech production) that are typically seen in normal aging may be compromised in PD, which can instead induce opposite alterations in these mechanisms such as lowered lung volume at initiation and termination of speech[122] and decreased lung volume excursion[123]. PwPD, in comparison to healthy individuals, also experience reduced oral fluency and inappropriate pauses that worsen over disease progression[54]. Less frequent breath pauses at major syntactic boundaries and periods and more breath pauses at non-punctuational locations were also noted as PD progressed. In particular, breath pauses at non-syntactic boundaries and linguistic errors including repetitions of multiple words, additions during passage reading and other deviations from the given content were identified as the main attributing factors to overall speech impairment[54].

Language production capabilities may also progressively decline over time, especially in the presence of altered cognitive capacity. When evaluated on a picture narration task, the verbal output is shorter and less informative in PwPD with dementia and people with DLB compared to healthy individuals and PwPD without dementia[31]. PwPD with dementia also experienced a significant decline in all language measures (e.g., fluency, grammar and content density) during a mean period of 38 months, while PwPD without dementia remained stable. Speech and language impairments, according to the structural MRI scans, were related to grey matter atrophy in regions important for language performance but not motor brain regions. However, this evidence is still tentative considering the constrained sample size.

Taken together, initial explorations in small cohorts have shed light on voice, speech and language changes occurring over the course of PD that are independent of normal aging. Acoustic and language features appear sensitive for monitoring disease status as they alter progressively over time even though motor symptoms remain widely stable.

Gaps and future directions

Currently available evidence seems to confirm that speech features hold promise for early disease detection, prediction as well as disease progress tracking. Validated speech and language analysis tools can become a viable component of healthcare practice during health check-ups and screening for at-risk individuals, such as older adults and people with a family history of PD or early motor symptoms.

However, findings are somewhat conflicting especially regarding the longitudinal changes of speech and language functioning, likely due to heterogeneity among the underlying study populations. Replication in larger cohorts across ancestral and language groups (e.g., non-European populations) and studies following people newly diagnosed with PD before the commencement of treatment are necessary to substantiate existing findings and to elucidate the natural progression of speech-related symptoms.

Notably, existing research has primarily anchored on motor speech features, particularly phonation, articulation and prosody, while largely overlooking cognitive-linguistic abnormalities. To gain a comprehensive understanding of how PD impacts speech, it is essential to explore a broader spectrum of related impairments. This includes voice quality, respiration and resonance, as well as linguistic and language aspects such as lexicon,

grammar, syntax, verbal output content and fluency. Integrating both motor and cognitive-linguistic metrics will help delineate a complete picture of speech and language changes in PD and identify the best combination of markers for effective disease detection and prediction.

In a similar vein, while distinct speech patterns have been linked to different disease phenotypes, studies often concentrate on isolated subtypes. However, evaluation of speech features across multiple PD subtypes can reveal overlapping and unique patterns that might not be apparent when studied in isolation, which can improve diagnostic accuracy and patient group allocation. Thus, further research on clinical phenotyping through a holistic lens is needed to determine the utility of speech indicators for concurrent recognition of various PD subtypes.

Future studies exploring functional communication outside of structured, clinical settings are also necessary to assess how effectively speech-related markers perform in practical, everyday situations. This insight is crucial for developing tools that enable frequent and remote monitoring, thereby facilitating ongoing management and treatment of PD.

Integration of additional factors alongside speech and language features has not yet been thoroughly investigated but could potentially enhance the prediction, diagnosis and monitoring of PD. For instance, incorporating extra information on early motor and non-motor symptoms, as well as demographics, lifestyle and environmental risk factors, many of which are often readily available or easily measured, could further refine the diagnostic process. Combining these diverse elements can help achieve a more accurate assessment of PD, leading to better-informed diagnostic and management strategies.

Finally, future research is required to uncover the pathogenesis of speech and language deficits and their associated risk profiles. While some aspects of the pathophysiological mechanisms underlying these symptoms in PD have been explored, a comprehensive understanding remains elusive. The enhanced knowledge could provide valuable insights into a more nuanced understanding of the overall disease onset and progression, facilitate the identification of disease-modifying targets and improve early intervention strategies.

In summary, PD is a complex neurodegenerative disorder that poses a significant global health burden. Diagnosis currently hinges solely on the presence of its key motor symptoms, which reflects considerable neuronal damage and restricts the effectiveness of neuroprotective treatments. Early detection of PD could be improved with the integration of speech-related features, which often appear early and progress with the disease, allowing for timely intervention. Specific patterns of speech and language impairment across different PD phenotypes could also aid in better patient classification and inform personalised clinical management strategies. Moreover, the simplicity and low cost of speech analysis, combined with automated processing on digital platforms, enable remote and frequent evaluations accessible to a wider population. However, further research with larger samples and a holistic approach is required to validate these preliminary findings before clinical application.

Data availability

This narrative review does not involve original data collection. All data supporting the conclusions of this review are available in the reference list and can be accessed through the respective journals.

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Author contributions

F.C.: Contributed to the conceptualisation of the study, conducted the literature review and led the drafting of the manuscript. A.P.V. and M.E.R. supervised the study and reviewed and edited the manuscript. P.G. advised and reviewed the manuscript. All authors have read and approved the final version of the manuscript.

Competing interests

The authors declare no competing interests.

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