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Dysprosody differentiate between Parkinson's disease, progressive supranuclear palsy, and multiple system atrophy

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Abstract

Parkinson's disease (PD), progressive supranuclear palsy (PSP), and multiple system atrophy (MSA) are distinctive neurodegenerative disorders, which manifest similar motor features. Their differentiation is crucial but difficult. Dysfunctional speech, especially dysprosody, is a common symptom accompanying PD, PSP, and MSA from early stages. We hypothesized that automated analysis of monologue could provide speech patterns distinguishing PD, PSP, and MSA. We analyzed speech recordings of 16 patients with PSP, 20 patients with MSA, and 23 patients with PD. Our findings revealed that deviant pause production differentiated between PSP, MSA, and PD. In addition, PSP showed greater deficits in speech respiration when compared to MSA and PD. Automated analysis of connected speech is easy to administer and could provide valuable information about underlying pathology for differentiation between PSP, MSA, and PD.

Index Terms: automated acoustic analysis, speech disorder, dysprosody, atypical parkinsonian syndromes, Parkinson's disease, progressive supranuclear palsy, multiple system atrophy

1. Introduction

Parkinson's disease (PD) is an idiopathic neurodegenerative disorder characterized by progressive loss of dopaminergic neurons in substantia nigra. Bradykinesia, rigidity, tremor, and postural instability represent the clinical symptoms of PD. Atypical parkinsonian syndromes (APS) such as progressive supranuclear palsy (PSP) and multiple system atrophy (MSA) are distinctive neurodegenerative disorders that involve various neuronal systems in addition to substantia nigra and progress more rapidly than PD. APS manifest characteristic clinical signs together with shared parkinsonian features. Because of this overlap in symptoms, patients with PSP, MSA, and PD are frequently misdiagnosed [1]. The accurate diagnosis plays an important role in deciding upon drug therapy, monitoring response to therapy and determining prognosis of the disease.

Previous studies have shown that motor speech impairment, called hypokinetic dysarthria, is a common symptom for approximately 70%-90% of PD patients [2, 3]. Hypokinetic dysarthria is a multidimensional impairment affecting all aspects of speech including respiration, phonation, articulation, and prosody [4]. Speech in PD is mainly characterized by imprecise articulation of consonants and vowels, monopitch, monoloudness, reduced vocal loudness, harsh voice, breathy voice quality, dysrhythmia, inappropriate

silences and rushes of speech [4]. PSP and MSA typically manifested mixed dysarthria including various combinations of hypokinetic, spastic, and ataxic components [5, 6] due to different involvement of the basal ganglia, corticobulbar pathways, and the cerebellum. Excess pitch, reduced speech rate, reduced maximum phonation time, reduced intonation variability and substantial prolongation of pauses is typical for speech impairment in PSP [7-9]. Slow, effortful speech and strained-strangled vocal quality characterize speech in MSA [10].

Various speech tasks have been used to examine hypokinetic dysarthria. These speech tasks including prolonged phonation of isolated vowel, articulatory pattern of rapid syllables repetition, and rhythmic pattern of syllable repetition in steady pace endeavour to isolate specific aspect of dysarthria. Prosody comprehensively includes all dimensions of speech and is commonly quantified upon text reading or spontaneous speech such as monologue that require coordination of all subsystems of speech. These tasks offer the most natural way to seek characteristics of speech. Especially, the spontaneous speech seems to represent the purest condition of speech, as it is conducted by speaker itself nor by his disposition to read. The previous study considered spontaneous speech as the most sensitive marker of true deficits in PD speech [11].

Prosody describes utterance of speech in suprasegmental terms of factors such as intonation, tone, stress, rhythm, and spectrum. Prosody, in general, may reflect the emotional state of the speaker; however, dysprosody in PD is related to a combination of respiratory, phonatory, articulatory, and rhythmic disturbances associated with hypokinetic dysarthria [4, 12, 13]. Dysprosody of hypokinetic dysarthria may exhibit monopitch and monoloudness but particularly speech-timing disturbances.

Rhythm characteristics of speech in PD are constrained by the timing pattern of spoken language, hypokinetic movements of speech apparatus, and self-pacing. Impaired self-pace rhythm with a tendency to accelerate is frequent in hypokinetic dysarthria [12, 14]. Consequently, rhythm can either be abnormally accelerated or slowed as PD progresses. An accelerated rhythm is considered to be a salient feature of hypokinetic dysarthria [13].

The tempo of speech is defined as a number of speech units per time. Most authors express the tempo of speech as the articulation rate, i.e., the number of words or syllables per time typically measured for a standardized speech sentence. Because the flow of a syllable stream is phrased by pauses, the number and duration of pauses have a considerable impact on the perceived tempo of speech. In general, tempo is strictly related

to pause characteristics. For healthy speech, it has been suggested that the number of pauses increases as overall speaking tempo decreases, whereas articulatory speech tempo remains relatively stable [15, 16]. As pauses tend to vary more freely than phonemes, overall changes in tempo are mostly dependent on changes in pauses [17].

In hypokinetic dysarthria, the suggested mechanism of tempo execution may be affected by articulatory “undershoots” and slurring of stop consonants [12, 18]. Indeed, PD speakers compensate for hypokinetic movement of articulators by reducing the amplitude of movement to achieve a higher articulatory rate [14]. Reduced amplitude of articulators’ movement causes imprecise articulation of phonemes. In particular, stop consonants tend to have a fricative character with insufficient oral closure [19, 20].

Correctly articulated speech also requires well-timed voicing. PD causes disturbances in the coordination of laryngeal and supralaryngeal musculature, rigid laryngeal musculature, increased the stiffness of vocal folds and reduction in vocal fold opening [21-23]. As a result of voicing deficits in PD, voice onset time may be prolonged or shortened, initial consonants may be omitted, and voicing may interfere with voiceless consonants or may be continuous within utterance containing voiceless consonants [21-24].

Respiration abnormalities are quintessentially responsible for common loudness impairments and dysprosody in PD. Rigidity, hypokinesia, and difficulty initiating movements of muscles of respiratory apparatus lead to faster breathing rates, greater minute ventilation, a smaller relative contribution of the rib cage to changes in lung volume, lower effort of expiration, and irregularities in breathing patterns [25, 26].

The analysis of parkinsonian speech has been a subject of research over the last half-century. The reliability of speech assessment makes this research field attractive. Assessment of speech in PD is an inexpensive, non-invasive, sensitive, and effective tool for monitoring disease progression [27, 28], monitoring treatment efficacy [29], and providing objective feedback in speech therapy [30]. The benefits of speech analyses include improved healthcare, reduced cost of physical visits, and encouraging effects of objective feedback on speech therapy.

Prosody assessment using rate and pause characteristics has already been the subject of previous research based on a large sample of PD patients [12]. Liss et al. [31] suggested using cross-linguistic metrics to quantify rhythm abnormalities across various dysarthrias using standardized sentences. Lowit [32] also investigated the applicability of cross-linguistic rhythm metrics for dysarthria assessment. Unfortunately, no significant differences were reported in a small group of 3 PD patients. Lowit [32] concluded that there is a need for the complex measurement of rhythmic performance in a clinical context. Prosody assessment in the abovementioned studies [12, 31, 32] was based on intervals obtained using hand-labelling, which is the most common technique used to obtain sensitive segmentation. However, hand-labelling is considerably time-consuming. Moreover, hand labels are non-deterministic as their recognition varies from person to person.

Automated assessment of spontaneous speech for dysarthric speakers is currently very limited. Rosen [33] proposed an automated analysis of pause distributions of connected speech. Speech rate measurement for dysarthria was also automated [34, 35]. Bandini et al. [36] developed a method

for the automated measurement of basic temporal and phonatory characteristics of the short standardized sentence. The automatic evaluation of rhythm and respiratory characteristics based on continuous speech has not been available until now [37]. Thus, a complex investigation of dysprosodic patterns in PSP and MSA through continuous speech with respect to all subsystems of speech has never been performed. The aim of the present study was to explore dysprosody in PSP, MSA and PD using fully automated analysis.

2. Materials and methods

2.1. Subjects

The majority of patients for this study was originally recruited for the previous study [38]. Data were obtained from a total of 79 subjects, 16 of which were diagnosed with PSP (10 men, 6 women; 14 Richardson’s syndrome, 2 PSP-parkinsonism), and 20 with MSA (9 men, 11 women; 17 parkinsonian type, 3 cerebellar type). Additionally, 23 PD (12 men, 11 women) were recruited to match the PSP and MSA groups in terms of age and disease duration estimated from the self-reported occurrence of first symptoms. The group of 20 healthy controls (HC) with no history of neurological or communication disorder consisted of 10 men and 10 women with mean age of 63.6 years \pm 6.4 standard deviation in the range from 50 to 70 years. The diagnosis of PSP was established by the NINDS-PSP clinical diagnosis criteria [39], MSA by the consensus diagnostic criteria for MSA [40], and PD by the UK Parkinson’s Disease Society Bank Criteria [41]. Disease severity of APS patients was rated by the natural history and neuroprotection in Parkinson plus syndromes–Parkinson plus scale (NNIPPS, ranging from 0 to 332, where higher scores indicate more severe disability) [42]. Disease severity of PD patients was scored according to the Unified Parkinson’s Disease Rating Scale motor subscore (UPDRS III, ranging from 0 to 108, where higher scores indicate more severe disability) [43]. Speech severity of all patients was described perceptually by the item 18 of the UPDRS III (ranging from 0 to 4, where 0 represents normal speech and 4 unintelligible speech). A well-trained professional neurologist conducted diagnosis and motor evaluation. APS subjects were medicated by various doses of levodopa alone or in combination with different dopamine agonists and/or amantadine. PD subjects were medicated for at least 4 weeks by levodopa and different dopamine agonists. None of the patients received antipsychotic therapy. Each participant provided written, informed consent. The Ethics Committee of the General University Hospital in Prague, Czech Republic approved the study. Table 1 summarizes patient characteristics.

Table 1: *Clinical characteristics of patients described as mean / standard deviation (range).*

	PSP	MSA	PD
Age (years)	66.9 / 6.4 (45-71)	60.8 / 6.4 (45-71)	62.5 / 9.5 (41-80)
Disease duration (years)	3.9 / 1.4 (2-7)	3.9 / 1.4 (2-7)	4.8 / 1.3 (1-7)
Disease severity	70.6 / 26.6 (19-116)	71.4 / 23.2 (35-123)	17.5 / 9.2 (6-38)
Speech severity	1.9 / 0.7 (1-3)	1.7 / 0.7 (1-3)	0.8 / 0.5 (0-2)

2.2. Speech recordings

All patients were recorded in a quiet room with a low ambient noise using a head mounted condenser microphone (Beyerdynamic Opus 55, Heilbronn, Germany) positioned approximately 5 cm from the mouth. Recordings were sampled at 48 kHz with 16-bits resolution. The speech specialist instructed each patient to provide monologue about his or her interests, job, family, or current activities for approximately 90 seconds (mean duration 138 seconds \pm 26 standard deviation).

2.3. Speech analyses

The speech analyses were based on the recently published method for assessment of parkinsonian speech deficits in natural connected speech [37]. The method recognizes four basic physiological sources of speech signal including voiced, unvoiced, pause, and respiratory intervals and then applies the set of 12 descriptive speech features to carry out specific aspects of parkinsonian speech.

2.3.1. Segmentation

The segmentation consisted of class-by-class recognition of voiced speech, unvoiced speech, pause, and respiration. Parameters of power (PWR), variance of autocorrelation function (ACR), zero-crossings-rate (ZCR), and linear-frequency cepstral coefficients (LFCC) were computed inside sliding window of 15ms, in steps of 5ms. Recognition was executed by cluster analysis of the parametric space. Voiced intervals were recognized using parameters PWR, ACR, and ZCR. Subsequently, unvoiced intervals were classified using first five LFCC of 24 LFCC total. Pauses were determined as the remaining intervals (i.e. not voiced and not unvoiced intervals) including respirations. Respirations were recognized in pauses using first five LFCC. Decision smoothing consisted only of duration-based conditions such as minimal duration.

2.3.2. Speech features

The set of 12 descriptive features computed upon segmentation intervals was applied to assess timing, articulatory, phonatory, and respiratory aspects of speech (see Figure 1).

Timing aspects summarize rhythmic organization of speech. Speech rate was evaluated as rate of speech timing (RST) determined from voiced, unvoiced, and pause intervals. These intervals were accounted during the speech and then approximated by regression line. The gradient of regression line robustly estimates RST. The tendency to accelerate speech rate was determined using acceleration of speech timing (AST) computed as the difference of RST between two overlapping halftimes divided by total time. The ability to intermit and initiate speech was characterized by duration of pause intervals (DPI). The heterogeneity of speech was described as entropy of speech timing (EST), which is a Shannon entropy computed from the occurrence of voiced, unvoiced, pause, and respiratory intervals.

Articulatory aspects were quantified for unvoiced fricatives and stop consonants independently, as the friction tells about the stability of supra-laryngeal movements and explosion about its preciseness. These two types of consonants differ in duration and can be easily recognized using Bayes discriminant applied to bimodal distribution estimated using Expectation Maximization algorithm (EM-algorithm). The noisy prolongation of poorly articulated stops was described by duration of stop consonants (DUS) computed as median

duration of unvoiced stops. The temporal weakening of friction was evaluated by decay of unvoiced fricatives (DUF) determined as difference of the second MFCC computed upon unvoiced fricatives of two overlapping halftimes.

Phonatory aspects provide information about disabilities to control opening and closing of vocal folds. The deteriorated ability to stop voicing properly results in decreased pause rate during vocalisation. The rate of pauses in-between voiced intervals was measured as gaping in-between voiced intervals (GIV). Clear pauses (i.e. pauses in-between voiced speech) were modelled as a bimodal distribution of formal pauses and gaps using EM-algorithm. GIV was computed as the rate of clear gaps recognized by Bayes discriminant. Incomplete or unperformed closure of vocal folds is measured by duration of voiced intervals (DVI). Mean duration of voiced intervals determines DVI.

Respiratory aspects were measured on inspirations represented by respiratory intervals and expirations represented by speech intervals (i.e. both voiced and unvoiced intervals). Rate of speech respiration (RSR) was estimated as median duration between respirations. Breath groups were evaluated by pause intervals per respiration (PIR) determined as mean number of pauses between respirations. Hypokinesia and decreased range of rib cage motion were measured using relative loudness of respiration (RLR) computed as difference between median loudness of respiration and median loudness of speech. Increased latency of exchange between expiration and inspiration associated with rigidity and bradykinesia of respiratory muscles were determined by latency of respiratory exchange (LRE) calculated as mean duration between end of speech and start of consequent respiration.

A fully automated algorithm written in MATLAB[®] executed the segmentation and computation of speech features on all speech signals.

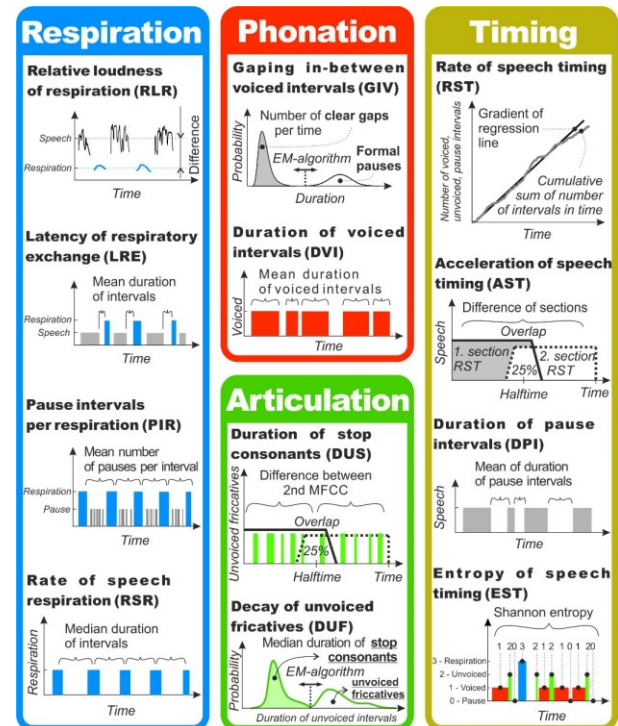


Figure 1: Illustrated principles of speech features organized to their respective speech aspects. MFCC = Mel-frequency cepstral coefficients.

2.4. Statistics

We excluded the HC group from the statistical analysis, as the main goal of this study was to show the contribution of automated speech assessment for differentiating PSP, MSA and PD. Speech features in HC were analysed only to provide a reference point for interpretation of speech features regarding severity. Group differences between all three groups of patients (PSP, MSA, PD) were analysed by One-way ANOVA with post hoc Tukey's honest significance test. Correlations between speech features and clinical scales were tested using Pearson's correlation coefficient. The level of significance was set at $p < 0.05$.

3. Results

Figure 2 illustrates numerical data and statistical analysis of all 12 speech features across PSP, MSA, and PD groups. Generally, APS showed more severe speech than PD. Moreover, speech impairment was evidently more pronounced in PSP than MSA. Statistical analysis showed significant differences between PSP and PD as well as between MSA and PD for speech features RST, DPI, and DUS. Specifically, PSP was more severe than PD for DVI, LRE, PIR and RSR. Comparison between PSP and MSA revealed significant differences in DPI and PIR. Generally, RST, DPI, DUS, and PIR provide useful information for differentiation of PD, MSA, and PSP. No significant correlations between speech features and clinical scales were found.

4. Discussion

In the presented study, we explored speech motor abnormalities in patients with PSP, MSA, and PD across all aspects of connected speech including timing, articulation, phonation, and respiration. Evidently, deviant pause production reflects different pathophysiology of PSP and MSA. The most prominent feature differentiating APS from PD was slow rate of speech intervals, which indicates that dysprosody in APS is strongly altered by decreased range of motion of the speech apparatus.

Respiratory aspects seem to be impaired predominantly in PSP. Rigid chest wall muscles and diaphragm of speaking PSP patient cannot expand fully, which causes increased respiratory rate. Additionally, PSP patients have difficulties in initiating inspiration and expiration, likely due to bradykinesia and rigidity of respiratory muscles. As a result, pauses were produced less frequently during breath groups and were more prolonged in PSP. According to our findings, deviant pause production in PSP also relates to disabilities to stop voicing properly. We observed decreased range of articulatory motion in the performance of unvoiced stop consonants, which PSP patient may spirantize or omit from the speech production. In general, these disabilities result in a significantly decreased rate of speech timing in PSP. These findings are limited by a small number of women in PSP group, as it is difficult to recruit new patients of this rare disease.

We observed a trend of more severe disability for PSP compared to MSA and PD, which is in accordance with previous perceptual findings [44]. Patients with MSA manifested prolonged unvoiced stops and pauses in comparison with PD patients. Considering that no differences between MSA and PD were found for respiratory aspects, we hypothesize that production of pauses during breath groups in

MSA is conditioned mainly by interaction with other subsystems of speech.

In summary, while MSA showed particularly timing and articulatory disabilities, PSP demonstrated speech abnormalities in all speech dimensions of timing, articulation, phonation, and mainly respiration. In particular, respiratory abnormalities in PSP contribute to the considerable deterioration of all speech subsystems, indicating more severe dysprosody in PSP compared to MSA and PD.

5. Conclusions

Results presented in this study suggest that the assessment of dysprosody has high potential as objective indicator differentiating PD, PSP, and MSA. Notably, the analysis of dysprosodic patterns can be executed by a fully automated algorithm.

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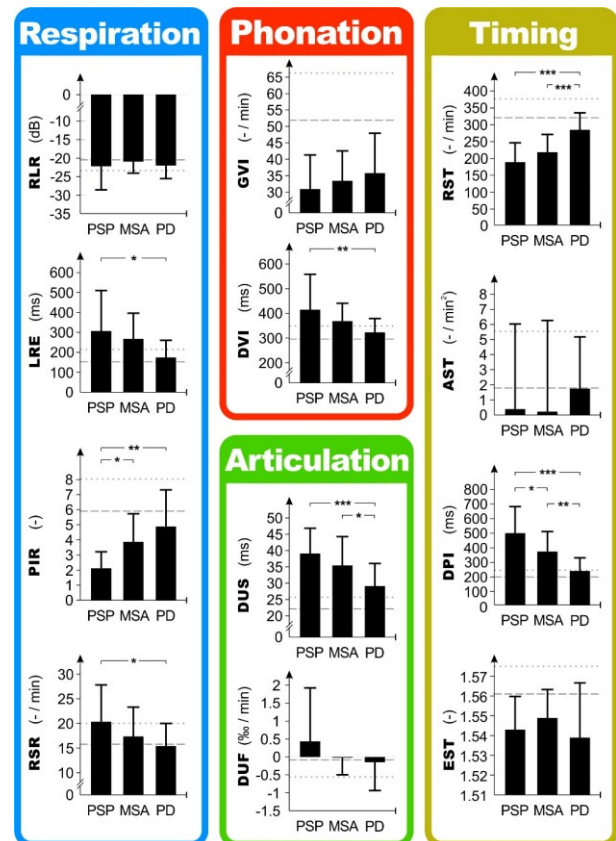


Figure 2: Results of acoustic speech analysis. Bars represent mean values, and error bars standard deviations. HC group is plotted as mean value (dashed grey line) and standard deviation (dotted grey line) for proper interpretation of severity. Group differences are denoted by asterisks: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

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