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Electroglottography for the assessment of dysphonia in Parkinson's disease and multiple system atrophy

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Abstract

Electroglottography (EGG) is a noninvasive technique which allows accurate measurements of vocal folds dynamics and perturbations during speech. It has been widely used in medical diagnosis and monitoring of several laryngeal pathologies, but its use in neurological disorders has been very limited. This paper presents the first study on EGG in early stages of Parkinson's disease (PD) and an atypical parkinsonian disorder, multiple system atrophy (MSA). Our first objective was to investigate whether EGG can reveal distinctive dysphonia features that could help in the challenging early differential diagnosis between PD and MSA-P, the parkinsonian variant of MSA. The second objective was to verify some hypothesis on early markers of PD drawn from speech-alone acoustic analysis. For MSA-P patients, our analysis revealed a reduced open quotient and confirmed excessive pitch variation. The analysis also mitigated some hypothesis on dysphonia in early stages of PD.
Index Terms: Electroglottography, Parkinson's disease, Multiple system atrophy, Dysphonia, Differential diagnosis

1. Introduction

Idiopathic Parkinson's disease (PD) is a neurodegenerative disease essentially caused by the degeneration of midbrain dopaminergic neurons. The cardinal clinical features of PD are bradykinesia, postural instability, muscle rigidity and resting tremor. Atypical parkinsonian disorders (APD) are rare neurodegenerative diseases which share similar symptoms and features with PD, but with generally a poor response to drug treatment with levodopa. Multiple system atrophy (MSA) belongs to APD with a poor prognosis and differs from PD by a more widespread neurodegenerative process [1, 2]. MSA has two subtypes, MSA-C where cerebellar features predominate and MSA-P where parkinsonism predominates. An accurate differential diagnosis between PD and MSA-P patients can be very challenging because most patients manifest similar clinical features [2]. Currently, there exists no validated biomarker for the differential diagnosis, though progress has been achieved in clinical and imaging techniques [3]. The development of such a biomarker, especially in early disease stages, would be thus a significant contribution towards the improvement of diagnosis accuracy.

The assessment of speech disorders is known to be an appealing approach towards the development of a speech-based biomarker, as these disorders are early and prominent clinical features of PD and MSA-P (and APD in general). There is a consensus that PD speech is essentially characterized by hypokinetic dysarthria while MSA speech is characterized by a mixed hypokinetic and ataxic dysarthria [4, 5]. Consequently, PD speech has been extensively studied during the last decades (see [6, 7] for recent reviews), whilst the objective analysis of APD speech has gained interest more recently [8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22].

A large amount of research on PD speech have reported on dysphonia, the impairment of voice production caused by alterations in the vocal folds dynamics, essentially by analyzing the realization of sustained phonations (of the vowel /a/ most commonly) [23]. The vast majority of these studies have reported altered voice quality [24, 25], most commonly by computing classical dysphonia features such as jitter, shimmer, HNR and pitch perturbation. However, all have analyzed data from PD patients with mild to severe disease severity or/and moderate to long disease duration. In this work, our main objective was to provide an accurate evaluation of some dysphonia dimensions in (relatively) early PD and MSA-P speech. To do so, we used one of the most performing techniques to assess dysphonia, the electroglottography.

The electroglottograph (EGG) is a noninvasive measurement device of the electrical flow in the larynx [26]. It uses two electrodes which are placed close to the larynx, as shown in Figure 1. Because the vocal folds are good conductors of electricity, the glottis opening and closing phases produce a variation of impedance which is sensed by the EGG and output as a waveform signal. EGG signals are more accurate than speech signals in tracking vocal folds vibrations because the effect of the supra-glottal vocal tract is negligible as compared to the acoustic sensing beyond the lips. When correctly captured, the EGG signal can thus provide, in particular, ground truth measurements of the glottal opening and closing instants as well as the open/closed quotient (also referred to as contact quotient) which is a measure of glottal competence [27]. These allow then accurate analysis of important dynamics of the vocal folds vibrations and (potential) perturbations.

Consequently, EGG has been widely used to study various types of laryngeal pathologies, such as vocal fold paralysis [28, 29], vocal folds nodules and polyps [30], spasmodic dysphonia [31], nonorganic dysphonia [32], muscle tension dysphonia [33]. It has been also used in other clinical settings such as chronic cough [34, 35], reflux [36] and multiple sclerosis [37]. A comprehensive recent review on the use of EGG in medical diagnosis can be found in [38]. As for PD, the investigation of EGG data has been very limited. Early preliminary work suggested that EGG may provide detailed information about the vibratory perturbation patterns of the vocal folds among patients with PD [39]. In [40], PD was used as a sub-group of a larger group of patients identified with neuromuscular lesions affecting the vocal folds. They reported that EGG and speech signals could not distinguish between dysphonia caused by neuromuscular disorders and the one caused by mass lesions of the vocal folds, but could distinguish between normal and pathological

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Figure 1: *EGG and placement of the electrodes*

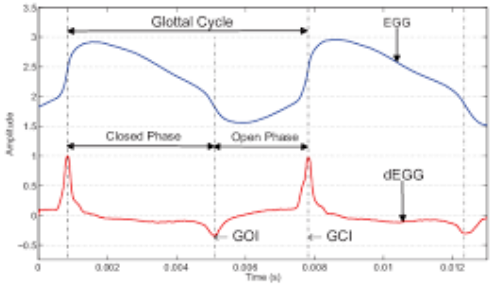

Figure 2: *Example of an EGG signal frame and its derivative (dEGG)*

voices. In [41], parameters computed from EGG spectrograms were reported to distinguish between men and women' dysphonia. In a case study [42], the authors analyzed voice change of a patient with PD as he increased vocal intensity. More recently, [43] studied the correlation between EGG, speech and perceptual data. The authors reported that use of these three tools revealed distinctive features between PD and healthy speech.

To the best of our knowledge, there exist no study on EGG data collected from early PD patients nor from APD patients. This work is thus the first contribution in this framework, investigating the potential of EGG measurements in revealing discriminative dysphonia features between PD and MSA-P, as well as in verifying some hypothesis on dysphonia in early PD. Most of EGG studies have focused on the analysis of sustained phonation of the vowel /a/. In our study, we additionally analyzed EGG signals associated with a normal phonation of the vowel /a/ produced in a DDK task (rapid repetition of the syllable sequence /pataka/). The choice of that task was motivated by its suitability to reveal articulatory impairments and, thus, to assess the potential impact of such impairments on short-time vibrations of the vocal folds.

The paper is organized as follows. The dataset and the computational methodology are presented in the next section. The results are presented in Section 3. A discussion and a conclusion are provided in the last section.

2. Method

2.1. Data

The EGG data used in study were collected from 43 French subjects. A larger amount of subjects were recruited but EGG was not recorded from some and the signal quality was not good enough for others, the latter were excluded from the analysis. Fourteen patients (3 females and 11 males) were diagnosed with idiopathic PD (mean age of 61 $\pm$ 7.3 and mean symptom duration of 3.7 $\pm$ 2.5 years). Twelve patients (6 females and 6 males) were diagnosed with "possible" or "probable" MSA-P (mean age of 62.2 $\pm$ 8.4 and mean symptom duration of 3.9 $\pm$ 0.6 years). At the time of the examination, patients were in a stable "on" state with dopaminergic medication. Ethics approval was obtained prior to recruitment and all subjects wrote informed consent. Seventeen healthy controls (HC) with a mean age of 59.7 $\pm$ 9.5 (8 females and 9 males) with no history of neurological or communication disorders were included. All the recording sessions were performed by otorhinolaryngologists for all the subjects. Each subject produced several speech tasks including sustained phonation, syllables repetition, read speech and a monologue. In parallel to speech recordings, EGG signals were synchronously sensed using the two-channel EGG, model EG2-PCX, manufactured by Glottal Enterprises (www.glottal.com). The EGG signals were recorded with 48kHz sampling frequency and 16 bit resolution. In this study, we analyzed data from sustained phonation of the vowel /a/ and rapid repetition of the syllable sequence /pataka/.

2.2. Computation of dysphonia features

An illustration of a portion of an EGG signal and its derivative (dEGG) is given in Figure 2. Each glottal cycle is composed of an open and a closed phase. During the latter, the air pressure builds up below the vocal folds. During the former, the air blow up through the vocal folds, initiating the sound wave. The time instant when the glottis opens (resp. closes) is called the glottal opening (resp. closing) instant, or GOI (resp. GCI). The GOI (resp. GCI) is characterized by a low (resp. high) positive peak of the dEGG. The most common features extracted from the EGG are the open quotient (OQ), the open quotient perturbation (POQ), jitter and the pitch standard deviation (stdF0). Precisely, given an EGG signal with N glottal cycles $\{G_i, i = 1, ..., N\}$, the instantaneous glottal period T_i is defined as the duration (in seconds) of the cycle G_i, the instantaneous fundamental frequency as $F_i = \frac{1}{T_i}$ and the fundamental frequency F_0 is the mean of the F_i. The instantaneous open quotient OQ_i is defined as the ration between the duration of the open phase and T_i. Then:

1. $\text{OQ} = \frac{1}{N} \sum_{i=1}^{N} OQ_i$
2. $\text{POQ} = \frac{\frac{1}{N-1} \sum_{i=2}^{N} |OQ_i - OQ_{i-1}|}{\text{OQ}} \times 100$
3. $\text{jitter} = \frac{\frac{1}{N-1} \sum_{i=2}^{N} |T_i - T_{i-1}|}{\frac{1}{N} \sum_{i=1}^{N} T_i} \times 100$
4. $\text{stdF0} = \sqrt{\frac{1}{N} \sum_{i=1}^{N} |F_i - F_0|^2}$

To compute these features we used an established algorithm available in the Covarep [44] repository (covarep.github.io/covarep/) and developed by N. Henrich based on the work in [45]. The signals was framed by a 30ms window with a 10ms window-shift. The algorithm integrated a thresholding so that the unvoiced frames of DDK speech were discarded in the computation, thus only the vowel was analyzed.

2.3. Statistical analysis

All analyses were performed in Matlab. The one-sample Kolmogorov–Smirnov test was used to evaluate the normality of

	HC	PD	MSA	HC vs PD	HC vs MSA-P	PD vs MSA-P
Feature	mean(std)	mean(std)	mean(std)	p-value	p-value	p-value
OQ	0.50(0.12)	0.48(0.14)	0.36(0.08)	0.66	***	*
POQ(%)	5.02(7.22)	4.46(7.71)	6.57(6.34)	0.83	0.54	0.45
jitter(%)	0.42(0.16)	0.57(0.28)	0.91(0.43)	0.09	**	*
stdF0(Hz)	3.17(1.61)	3.08(1.79)	6.98(5.01)	0.88	*	*

Table 1: *Statistical difference between groups on sustained /a/:* $*p < 0.05$, $**p < 0.01$, $***p < 0.001$

distributions. Group differences were calculated using analysis of variance for normally distributed data and the pairwise Kruskal–Wallis test for non-normally distributed data. Pearson correlation (r) was used to test linear correlation between the measures. Statistical significance was set at a p-value $p < 0.05$. The classification performance (specificity and sensitivity) between PD and MSA-P groups was performed using a decision tree with a leave one speaker out (LOSO) cross-validation. The MSA-P group was considered as the positive label.

3. Results

3.1. Results on sustained /a/

Table 1 presents the results of the statistical test of difference between group pairs. None of the features reveled significant difference between PD and HC groups. In particular, the OQ values of PD patients was within the range of healthy voices values, with an equilibrated open and closed phases [46]. The jitter was also within the range of healthy voices values (normative value in Praat of jitter $< 1.06\%$). On the other hand all the features but POQ revealed significant difference between MSA-P and HC groups as well as between MSA-P and PD groups. MSA-P patients manifested a significantly lower OQ, around 0.36, indicating a deficit in vocal folds tension. The pitch variation of MSA-P patients was excessive, in average about 2.5 times the stdF0 of PD and HC, indicating a deficit in stabilizing the vibration of the vocal fold during the sustained phonation. This result confirmed previous findings, based on acoustic analysis, on excess pitch variation in MSA sustained phonations [11, 15, 14, 21]. Most MSA-P patients also manifested irregular short-time fundamental frequency fluctuations, as measured by jitter, but some patients had a jitter within the range of normative values. Interestingly, the cycle-to-cycle fluctuations of the open quotient of MSA-P patients were statistically similar to those of PD and HC, indicating a steadiness of the reduced open phase.

3.2. Results on normal /a/

The results of the statistical test of difference between group pairs revealed that there was no impairment in POQ, jitter and pitch variation for MSA-P as well as for PD. This suggested, in particular, that the effort required to maintain the vocal folds vibrating for a long period had a significant contribution in the excess pitch variation observed in MSA-P sustained phonations. On the other hand, MSA-P manifested the same reduced OQ observed in sustained /a/, with almost the same values over patients, as reported in Table 2. This indicated that a reduced open quotient was a prominent and persistent feature of MSA-P phonation regardless of the speech task. Consequently, we hypothesized that the open quotient should be considered as a valuable discriminative feature between PD and MSA-P.

	HC	PD	MSA	HC vs PD	HC vs MSA	PD vs MSA
Feature	mean(std)	mean(std)	mean(std)	p-value	p-value	p-value
OQ	0.50(0.13)	0.47(0.11)	0.36(0.11)	0.44	**	*

Table 2: *Statistical difference between groups on normal /a/ in the DDK task:* $*p < 0.05$, $**p < 0.01$

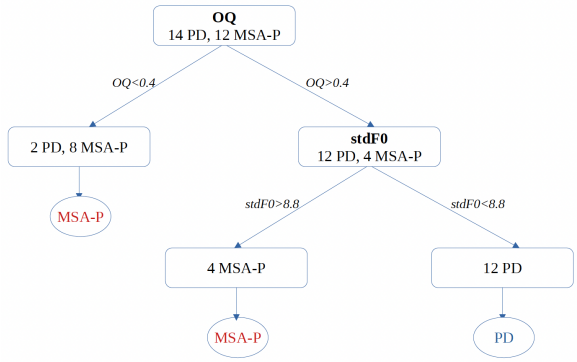

Figure 3: *Decision tree classifier between PD and MSA-P using the OQ and stdF0 variables computed on sustained /a/*

3.3. Bivariate analysis

For sustained /a/, correlation analysis revealed that OQ and stdF0 were highly correlated for the MSA-P group ($r = 0.84$), whilst they were highly uncorrelated for HC and PD groups ($|r| < 0.15$). In particular, the MSA-P patients with OQ close to low OQ values of HC were the very ones who had very high stdF0 ($> 8Hz$), as compared to the other MSA-P patients. This indicated that even when an MSA-P patient tried to achieve a normal opening phase, the cost was an even stronger loss in pitch control.

The high correlation between OQ and stdF0 could naturally and easily be exploited by classifiers such as decision trees to combine the mutual information they conveyed in order to achieve a good classification performance. Indeed, a LOSO learning yielded the decision tree model shown in Figure 3. This model yielded a high specificity of 85.7% and a perfect sensitivity, indicating that an MSA-P patient would be most probably correctly classified. However, given the data size, these high scores should be read with caution. We do not argue indeed that OQ or/and stdF0 could be sufficient to distinguish PD and MSA-P, the only purpose of this experiment was to illustrate the discriminative power of these two features on our data.

4. Discussion and conclusion

We conducted the first study on dysphonia assessment using EGG measurements of phonations produced by (relatively) early stage PD and MSA-P patients. We analyzed the pronunciation of the vowel /a/ in a sustained and a DDK task. We performed univariate and bivariate statistical analysis of the most common EGG-based features, the open quotient and fundamental frequency variations, computed using a state-of-the-art algorithm. We underline that dysphonia can be caused by several laryngeal impairments, but it is beyond the scope of this paper to analyze all possible laryngeal perturbations that could be captured by an EGG. The first finding was that none of the analyzed features yielded a significant statistical difference between PD and HC group, neither on sustained nor on normal /a/. Given that these features were ground truth measurements of

an important component of vocal folds dynamics, these results suggested that the dysphonia dimension characterized by these features is not a viable early marker of PD. This was confirmed by the deviance of these features for early MSA-P patients with matched age and symptom duration. Still, it is worth noting that a large number of studies have reported deviance of these (and other) dysphonia features when estimated from PD speech signals and there is a consensus that PD patients manifest dysphonia [5, 47]. Since none of these studies analyzed exclusively early PD speech, our findings supported the hypothesis that dysphonia would rather be associated with disease *severity*.

The second finding was that OQ was significantly reduced for MSA-P, as compared to PD and HC, on both sustained and normal /a/. This reflected an inherent deficit in tensing the vocal folds which was not due to the effort required to perform the sustained phonation task. This evidenced a prominent deficit of phonatory control which might be due to a loss of peripheral sensory function of MSA-P patients. From this perspective, a reduced OQ could be considered as an ataxic distinctive feature of MSA-P. The next step is to confront this finding with the open quotient (or equivalent) measures estimated from speech signals, for instance using glottal source inverse filtering [48]. The latter is an extensively studied field and allows estimation of the glottal flow, the airflow excitation signal generated by the vocal folds. Several features related to glottal dynamics can be then estimated, such as the (quasi-)open quotient. This is the purpose of our ongoing research.

Finally, MSA-P patients manifested a significant excess in pitch fluctuation (stdF0) in sustained /a/. This behavior has already been reported in several studies which analyzed MSA-P speech signals [21, 19, 15, 11]. Our study confirmed it by using EGG ground truth data, thus emphasizing the discriminative nature of this feature. Moreover, OQ was highly correlated with stdF0, the excess pitch variation being know to be an ataxic feature of MSA [49, 15], this supported the hypothesis on the ataxic nature of a reduced open quotient. Interestingly, in DDK speech, MSA-P patients were able to keep steady the vibration of their vocal folds in short-time phonations. This suggested that the (expected) articulatory impairment in DDK realizations of MSA patients [21, 15, 11] did no affect this phonatory component.

Our study is obviously limited by the relatively small amount of subjects considered, particularly because of the difficulty to recruit MSA-P patients and because not all the recorded EGG signals were exploitable, especially for females. It is indeed well-know that good quality EGG data are more difficult to obtain from women than men [50]. We continue however our effort in recruitment and in collecting the best possible EGG data. From this perspective, our findings/hypothesis must thus be considered with caution, they need indeed to be confirmed (or rejected) by additional data and processing. Still, despite the preliminary nature of our study, it definitely showed that EGG data was valuable in revealing unknown discriminative dysphonia features and in assessing the (in)validity of some hypothesis on dysphonia drawn for acoustic analysis. Electroglottography is clearly not prone to large scale use but, when possible, EGG should be applied to (at least) assess acoustic findings with the associated EGG measurements, not only in sustained phonation or DDK tasks but also in continuous speech (such as read and spontaneous) [51]. Studying the latter can indeed reveal valuable prosodic or/and timing cues for differential diagnosis. We plan to explore this dimension in the close future.

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2) Acoustic/statistical analysis: A. Design, B. Execution
3) Text: A. Writing of the 1st draft, B. Review & Critique
KD: 1A-C, 2A+B, 3A. **SMSV, VW**: 1A+C, 3B. **APL, AFS, OR**: 1A, 3B. **MF**: 1B, 3B. **WM**: 1A-C, 3B.

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