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A comparative study on vowel articulation in Parkinson's disease and multiple system atrophy

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Abstract

Acoustic realisation of the working vowel space has been widely studied in Parkinson's disease (PD). However, it has never been studied in atypical parkinsonian disorders (APD). The latter are neurodegenerative diseases which share similar clinical features with PD, rendering the differential diagnosis very challenging in early disease stages. This paper presents the first contribution in vowel space analysis in APD, by comparing corner vowel realisation in PD and the parkinsonian variant of Multiple System Atrophy (MSA-P). Our study has the particularity of focusing exclusively on early stage PD and MSA-P patients, as our main purpose was early differential diagnosis between these two diseases. We analysed the corner vowels, extracted from a spoken sentence, using traditional vowel space metrics. We found no statistical difference between the PD group and healthy controls (HC) while MSA-P exhibited significant differences with the PD and HC groups. We also found that some metrics conveyed complementary discriminative information. Consequently, we argue that restriction in the acoustic realisation of corner vowels cannot be a viable early marker of PD, as hypothesised by some studies, but it might be a candidate as an early hypokinetic marker of MSA-P (when the clinical target is discrimination between PD and MSA-P).

Index Terms: Vowel articulation, Acoustic vowel space, Parkinson's disease, Multiple system atrophy, Dysarthria, Vocal biomarkers.

1. Introduction

Parkinson's disease (PD) is a neurological disorder principally caused by the degeneration of midbrain dopaminergic neurons, leading to slowness of movement, muscle rigidity and resting tremor. Multiple system atrophy (MSA) belongs to the group of atypical parkinsonian disorders (APD) with a poor prognosis. MSA differs from PD by a more widespread neurodegenerative process, resulting in more rapid disease progression and poor response to dopamine replacement therapy [1, 2]. MSA has two variants, MSA-P and MSA-C, where parkinsonism and cerebellar features predominate, respectively. The majority of PD and MSA-P patients manifest similar clinical features which renders very challenging a correct differential diagnosis [2]. There exists criteria for the diagnosis of "probable" and "possible" MSA, based on clinical or/and imaging features, but the definite MSA diagnosis requires postmortem confirmation by a neuropathological examination [1]. Despite recent efforts, no validated biomarker is currently available for the differential diagnosis. There exists thus a strong need for such markers to improve diagnostic accuracy, particularly in early disease stages. An accurate early diagnosis is indeed essential not only in assessing prognosis and for treatment decisions, but also for understanding the underlying pathophysiology and for the development of new therapies [3].

Dysarthria, a class of motor speech impairments resulting from neurological disorders, is known to be an early clinical feature of PD and APD. Dysarthria is mostly caused by control or execution impairment of one or more sensorimotors. PD patients develop essentially hypokinetic dysarthria [4, 5] while MSA patients typically exhibit mixed dysarthria with various combination of hypokinetic and ataxic components [6, 5]. Whereas there exists a large amount of work on comparing PD and HC speech, there is only few studies on the comparison/discrimination between PD and APD speech or between APD subgroups [7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19].

Dysarthria can manifest in all levels of speech production [20]. In particular, the articulatory mechanism can be affected which causes deficits in range, strength, timing, stability and precision of articulators [20, 21]. This paper is a continuation of our effort towards revealing distinctive speech cues for the purpose of early differential diagnosis between PD and MSA-P. In our previous work [18], we reported on a specific impairment in voiced consonants articulation. In this work, we studied vowel articulation through an analysis of the articulatory working space of corner vowels. There have been several studies on vowel articulation in PD, however there exists no consensus on how PD affects the (corner) vowel space. Some studies have

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found statistical differences between healthy controls (HC) and PD groups [22, 23, 24, 25, 26, 27, 28, 29], whereas others have not found such differences [30, 31]. More importantly (in the context of our study), all these studies have analysed groups of PD patients with disease severity ranging from mild to severe, and with moderate to long disease duration from the onset. We found only one study dealing exclusively with early stage PD, that is, with short estimated symptom duration, as self-reported by the patients [32]. In that study, a group of 20 male PD patients were analysed, with a mean disease duration of 4.7 ± 1.6 years.

There has been also some studies on other neurodegenerative diseases [30, 22, 33, 23] but, surprisingly and to the best our knowledge, there exists none on APD. This work is thus the first contribution in this area. Moreover, we focused on studying exclusively early disease stage patients because our main target is the early differential diagnosis between PD and MSA-P. As compared to [32], we included both male and female patients with shorter symptom duration, not only for PD but also for MSA-P. We analysed the acoustic vowel space realisation (AVSR) of the 3 corners vowels /a/, /i/ and /u/ using the traditional measures: Vowel Space Area (VSA) [33], Formant Ratio (FR)[34], Vowel Articulation Index (VAI)[27] and its inverse the Formant Centralisation Ratio (FCR)[26]. We started by assessing the gender (in)sensitivity of these measures. We then carried out a statistical analysis to compare their distribution across the PD, MSA-P and HC groups. We found no statistical group difference between PD and HC but a significant one between MSA-P and PD as well as HC. We also carried out correlation analysis and found that FR and VAI conveyed complementary discriminative information. These findings led us to argue that AVSR[1] impairment should/can not be considered as an early marker of PD, as stated in some studies, but could rather be an early hypokinetic marker of MSA-P.

The paper is organised as follows. The speech database and the analysis tools are described in the next section. Results are presented in Section 3. Discussion and conclusion are given in the last section.

2. Method

2.1. Data

From 2018 to the time of writing this paper, a total of 59 French speakers were recruited in the framework of a research project involving the neurology and ENT departments of 2 French university hospitals (recruitment is continuing). Twenty six patients (10 females and 16 males) were diagnosed with idiopathic PD (mean age of 62.2 ± 7.2 and mean symptom duration of 3.1 ± 1.6 years). Thirteen subjects (8 females and 5 males) were diagnosed with MSA-P (mean age of 63.5 ± 7.3 and mean symptom duration of 3.3 ± 0.9 years). Twenty healthy controls (HC) with a mean age of 59.1 ± 8.6 (10 females and 10 males) without any history of neurological or communication disorders were recruited. ENTs carried out all the recording sessions for all participants. Each participant performed several speech tasks including sustained phonation, isolated pseudo-words, syllables repetition, a reading task and a monologue (other non-speech biosignals were also recorded, such as electroglottography and laryngostroboscopy). In this study, we used only one sentence extracted from the reading task dataset. The speech signals were recorded with 48kHz sampling frequency and 16 bit resolution by a headmount condenser microphone (t.bone HC 444 TWS) placed at a distance of approximately 5cm from the speaker's mouth. Ethics approval was obtained prior to recruitment and all participants gave written informed consent.

[1] We emphasise that the term AVSR we use in this paper refers to the specific vowel analysis we performed in our evaluation, that is, using the 3 corner vowels extracted from a sentence and the traditional measures we considered. Vowel articulation can be indeed analysed by the mean of other vowels, measures and speech tasks.

2.2. Computation of the vowel space measures

We used the French sentence *"Il les perdait toutes de la même façon"* from a reading passage of [35]. Three corner vowels /i/, /u/, and /a/ were extracted from the words "**I**l", "t**ou**tes", and "f**a**çon" respectively. Sentence utterance is commonly used in AVSR analysis and has been reported in [32] to be a suitable task to reveal alteration in PD (as opposed to sustained phonation, for instance). We manually segmented the 3 vowels of each sentence by visual examination of the waveform and the wide-band spectrogram using Praat [36]. We followed the criteria of [37] to set the vowel boundaries, we refer to [37] for details. We then computed the F1 and F2 formants on the resulting vowel segments using two methods, an automatic one, using Praat, and a manual annotation in order to ensure that the results are not biased by the potential estimation inaccuracies of the automatic algorithm (which may occur particularly for unhealthy speech). In the Praat method, with used the default setting parameters of the wide-band spectrogram, the highest formant frequency was set to 5500 Hz for female and 5000 Hz for male, the maximum number of formants was set to 5. In the manual method, we computed F1 and F2 manually using Praat's wide-band spectrograms, F1 and F2 values were averaged over a 50% time interval around the temporal midpoint of each vowel. Then the measures were computed using both the raw formants in Hz and the their semitone conversion because the latter has been reported to reduce gender sensitivity [27, 31]:

$$VSA = \frac{1}{2}|F1_i(F2_a - F2_u) + F1_a(F2_u - F2_i) + F1_u(F2_i - F2_a)|$$

$$FR = \frac{F2_i}{F2_u}$$

$$VAI = \frac{F2_i + F1_a}{F1_i + F1_u + F2_u + F2_a}$$

$$FCR = \frac{1}{VAI}$$

where $F1_a$, $F2_a$, $F1_i$, $F2_i$, $F1_u$ and $F2_u$ are the first and second formant frequencies of vowel /a/, /i/ and /u/, respectively.

2.3. Statistical analysis

All analyses were performed in Python. The one-sample Kolmogorov–Smirnov test was used to evaluate the normality of 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 correlations were applied to test for significant pairwise linear correlation between the measures, in each group. Statistical significance was set at a p-value $p < 0.05$.

The classification performance (sensitivity, specificity and accuracy) of differentiating between groups was calculated using binary logistic regression with leave-one-speaker-out (LOSO) cross-validation. In PD vs. MSA-P classification, the MSA-P group was considered as the positive label.

3. Results

We first analysed the gender sensitivity of the different measures by comparing their distributions across HC male and female groups. Only VSA computed in Hertz yielded a statistically significant group difference ($p = 0.04$ and $p = 0.02$ for the manual and Praat method, respectively), confirming the gender sensitivity of that measure [26, 25]. VAI , FCR and FR did not yield statistical differences, which confirms that ratio-based measures are less sensitive to gender difference [38, 26]. Using the semitone conversion, none of the measures yielded a statistical difference between the male and female groups. This indicates that the logarithmic conversion can indeed reduce inter-speaker variability, as reported in [26]. We thus opted for semitones in our evaluation.

We then compared the distribution of the measures across the 3 groups. For the sake of simplicity, we do not report the results of FCR because they (naturally) yielded very similar (analogous) outcomes as VAI. The p-values of group differences are presented in Table 1, for the automatic (Praat) and manual formant estimation. Both methods agreed on group differences. The PD group showed no statistical difference with the HC group, for none of the measures. Hence, we consider that the PD group of our study does not (statistically) manifest impairment in AVSR, which is in accordance with the studies [32, 29] on the sub-group of perceptually non-dysarthric PD. In early stage PD, the speech disorders are generally mild and barely perceptible [39]. This result tends thus to suggest that, most likely, early stage PD patients with no perceptible dysarthria would not manifest impairment in AVSR.

On the other hand, with all the measures, the MSA-P group showed significant statistical differences with the PD and HC groups. Thus, we can consider that the MSA-P group of our study does manifest impairment in AVSR.

	Manual formant estimation			PRAAT formant estimation		
Measure	HC vs PD	HC vs MSA	PD vs MSA	HC vs PD	HC vs MSA	PD vs MSA
VAI	0.37	**0.02**	**0.0011**	0.49	**0.017**	**0.0005**
VSA	0.92	**0.007**	**0.002**	0.39	**0.017**	**0.001**
FR	0.77	**0.0006**	**0.001**	0.77	**0.032**	**0.008**

Table 1: *p-values of statistical group differences between HC, PD and MSA-P, for the 3 measures. Bold values indicate significant difference.*

The boxplots of the distributions of the 3 measures for all groups are displayed in Figure 1, for both the manual and Praat's method. Globally, the 3 measures yielded lower values for MSA-P than PD and HC. This is consistent with previous findings which observed the same behaviour in the presence of hypokinetic dysarthria, that is, a tendency to articulatory undershooting and formant centralisation [26, 33, 30]. Classification with individual features yielded either (relatively) low sensitivity or low specificity. VAI was the most discriminant in term of accuracy, as compared to FR and VSA.

Finally, we performed an analysis of the correlation between the measures. We report only the outcome of the Praat method, as they were quite similar to the manual one. VSA and VAI were highly correlated for all groups ($r \sim 0.8$ in each group, where r is the correlation coefficient). FR and VSA were highly correlated for HC and PD ($r = 0.8$ and $r > 0.7$, respectively) but were uncorrelated for MSA-P ($r = 0.3$). Interestingly, FR and VAI were moderately correlated for HC and PD ($r = 0.6$ and $r = 0.5$, respectively) but uncorrelated for MSA-P ($r = 0.3$). This suggests that FR and VAI captured different and potentially complementary aspects of vowel realisation, particularly in MSA-P. This can be explained by the fact that the vowel /a/ is not considered in FR. In order to reveal their potential complementarity, in term of discrimination, we performed a bivariate statistical analysis of these two measures. Figure 2 displays the biplot of the projection of PD and MSA-P patients over the FR and VAI dimensions. The latter led indeed to an improvement in discrimination between PD and MSA-P as compared to individual features: sensitivity $= 77\%$; specificity $= 75\%$ and accuracy $= 76\%$. We emphasise that the point here is not to argue that ASVR measures *alone* could discriminate between PD and MSA-P, but only to illustrate that FR and VAI convey complementary discriminative information.

4. Discussion and conclusion

There is a consensus that PD patients develop essentially hypokinetic dysarthria while MSA patients develop mixed hypokinetic and ataxic dysarthria. From this perspective, detecting ataxic speech impairments in early MSA-P, such as in [18, 14, 5], is very appealing for the purpose of early differential diagnosis. Still, determining whether specific hypokinetic impairments are shared or not by early PD and MSA-P (or any APD) is also important. Indeed, this can indicate whether the associated descriptive features can be discarded or retained as potential early markers of both diseases. Additionally, it can bring insights on how hypokinetic dysarthria manifests and evolves in parkinsonism, which can be very informative in understanding how different parkinsonian disorders affect the speech production mechanism.

Impairment in AVSR can be associated with a reduction in the articulatory range of motion. The latter is a characteristic of hypokinetic dysarthria which is known to manifest in both PD and MSA (and APD in general). The analysis of our data revealed that the MSA-P group manifested impairment in AVSR while the PD group did not present differences with HC. The latter observation (on PD) is in accordance with many studies which did not find AVSR impairment, even in later PD stages. This suggests that this specific hypokinetic impairment might not be shared by PD and MSA-P in early stages. We believe, however, that more studies focusing on early stage PD are necessary to confirm or reject such an hypothesis. Consequently, at this point, we may reasonably state the following two hypothesis:

1. AVSR impairment is not a viable early marker of PD, since we found that it can manifest in early MSA-P patients with matched age and symptom duration.
2. AVSR impairment is a candidate as an early marker of MSA-P, if PD is proven to not manifest such an impairment in early stages. That is, suspicion of MSA-P should be raised in its presence, especially when a strong impairment is observed. We underline that this hypothesis is restricted to the setting where the clinical purpose is to assist in distinguishing between PD and MSA-P. There exists indeed no study on AVSR in the early disease stage of other APD subgroups.

There are some limitations to our study. The most significant is obviously the relatively small size of the dataset due to the difficulty of recruiting patients, particularly with a rare disease such as MSA-P. We are continuing the effort of recruitment to confront these findings (and others) to additional data. Another limitation is that we used only one vowel instance per speaker, we do not thus know how the results stand to intra-speaker pronunciation variability. However, while more

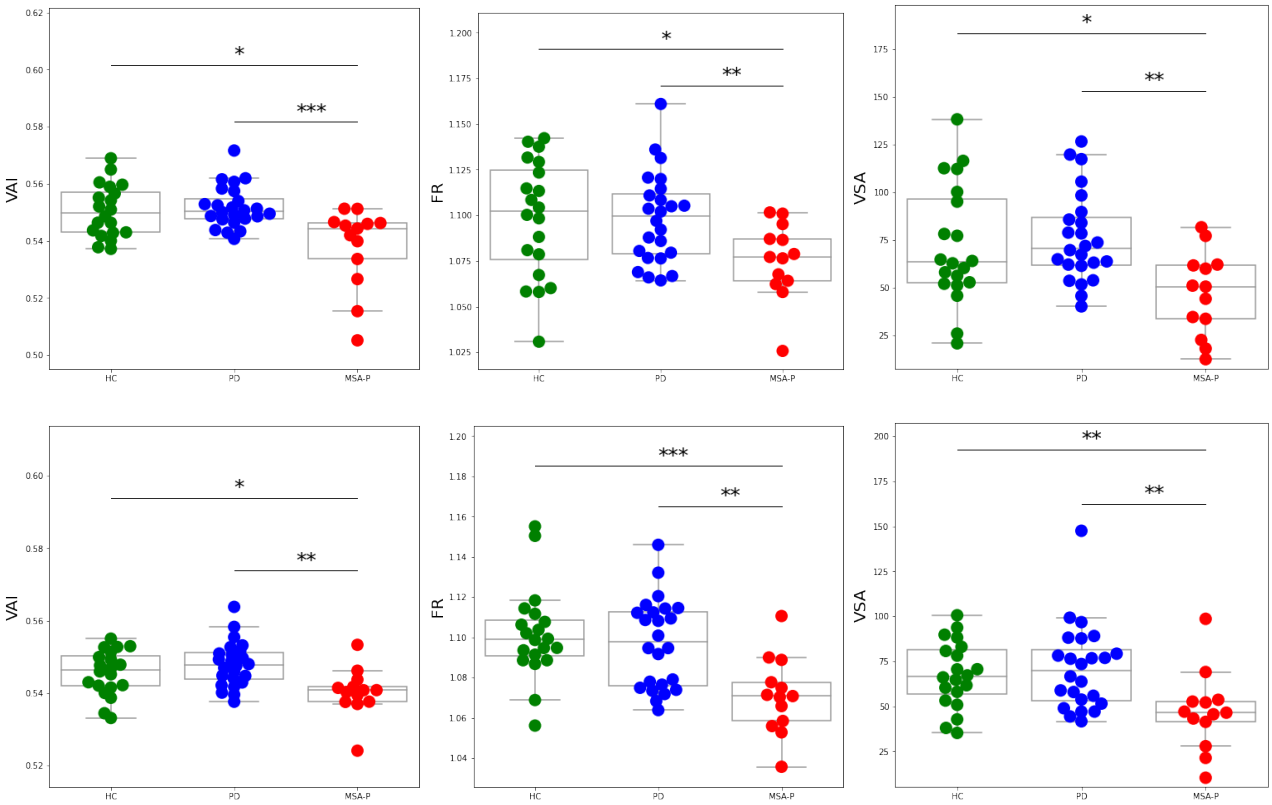

Figure 1: *Boxpolts of the distribution of the measures across groups, using Praat's (top) and manual (bottom) formant estimation. Statistically significant differences between groups:* $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

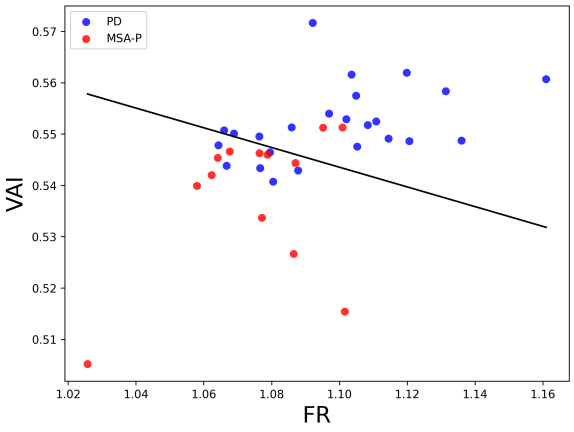

Figure 2: *Two-dimensional projection of all subjects over* FR *and* VAI*. The black line is the logistic regression boundary for the classification between PD and MSA-P using all data.*

instances would definitely improve our understanding on AVSR in parkinsonism, it should not call into question our two hypothesis. From this perspective, this work should be considered as a promising preliminary (first) study on AVSR in parkinsonism as well as an illustration of the necessity to consider APD in any hypothesis relative to early PD (speech) markers. The confirmation/rejection of those hypothesis can be achieved, for instance, by *longitudinal* data collected from the very beginning of parkinsonian symptoms (the latter approach belongs also to our future work perspectives).

Author contribution:
1) Research project: A. Conception, B. Organisation, C. Execution
2) Acoustic Analysis: A. Design, B. Execution, C. Review & Critique
3) Manuscript: A. Writing of the first draft, B. Review & Critique
KD: 1A-C, 2A+B, 3A. **BD**: 2A+B, 3B. **APL, AFS, OR**: 1A, 3B. **MF**: 1B, 3B. **SM, VW**: 1A+C, 3B. **WM**: 1A-C, 3B.

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