Towards disease-specific speech markers for differential diagnosis in Parkinsonism

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Introduction

Parkinsonism is primarily a group of neurodegenerative disease.

- **Disease groups:**
  - **Parkinson’s Disease (PD):** The clinical diagnosis requires the presence of bradykinesia, rigidity, resting tremor and postural instability.
  - **Atypical Parkinsonian Disorder (APS):**
    - **Progressive Supranuclear Palsy (PSP):** Spasticity is a major symptom for PSP patients. Symptom of parkinsonism is also prevalent for PSP.
    - **Multiple System Atrophy (MSA):** It is characterized by a variable combination of parkinsonism, cerebellar impairment, autonomic failure and pyramidal tract signs.
  - The majority of PSP and MSA patients develop clinical features that overlap those of PD.
  - The correct diagnosis can be very challenging in early stages of the disease.
Dysarthria is frequently an early and prominent clinical feature of PD as well as APS.

Specific kind of dysarthria can provide insight of neurophysiological bases and localization of neurologic disease.

This study is a continuation of our previous work on discrimination between PSP and MSA [J. Rusz et al. 2015; G. Li et al. 2018]
Objective

- Propose disease specific speech markers for differential diagnosis for PSP and MSA.
- Propose method for accurate and objective discrimination between PSP and MSA.
Speech recording

- Recording task
  - Sustained vowel /A/
  - Fast syllable repetition task /Pa-Ta-Ka/
  - Monologue

- Recording setup:
  - Head mounted microphone (Bayerdynamic Opus 55, Heilbornn, Germany).
  - Speech signal is sampled at 48kHz with 16 bit resolution.
Speech database

- **Subjects**
  - 13 MSA (10 MSA-P, 3 MSA-C); 6 men, 7 women
  - 12 PSP (9 PSP-RS, 2 PSP-P, 1 PAGF); 10 men, 2 women

<table>
<thead>
<tr>
<th></th>
<th>PSP</th>
<th>MSA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean/SD (range)</td>
<td>Mean/SD (range)</td>
</tr>
<tr>
<td><strong>General</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age of disease onset (years)</td>
<td>62.1/5.5 (50-68)</td>
<td>57.2/5.4 (50-70)</td>
</tr>
<tr>
<td>Symptom Duration</td>
<td>3.8/1.4 (1-6)</td>
<td>3.6/1.3 (2-6)</td>
</tr>
<tr>
<td>L-dopa equivalent (mg)</td>
<td>800/373 (500-1500)</td>
<td>899/394 (260-1480)</td>
</tr>
<tr>
<td>Amantadine (mg)</td>
<td>200/107 (100-400)</td>
<td>300/89 (200-400)</td>
</tr>
<tr>
<td>NNIIPPS</td>
<td>66.3/28.7 (19-116)</td>
<td>78.5/19.9 (46-123)</td>
</tr>
<tr>
<td>UPDRS III speech 18 item</td>
<td>2.0/1.0 (0-3)</td>
<td>2.0/0.7 (1-3)</td>
</tr>
<tr>
<td><strong>Subscore</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tremor</td>
<td>2.5/2.6 (0-6)</td>
<td>1.7/2.6 (0-9)</td>
</tr>
<tr>
<td>Rigidity</td>
<td>3.0/2.7 (0-7)</td>
<td>4.7/3.2 (0-11)</td>
</tr>
<tr>
<td>Bradykinesia</td>
<td>20.6/11.3 (4-40)</td>
<td>27.1/7.4 (16-39)</td>
</tr>
<tr>
<td>Bulbar/pseudobilbar</td>
<td>9.1/4.1 (3-17)</td>
<td>7.9/2.3 (4-12)</td>
</tr>
<tr>
<td>Pyramidal</td>
<td>0.3/0.5 (0-1)</td>
<td>0.8/1.2 (0-3)</td>
</tr>
<tr>
<td>Cerebellar</td>
<td>0.1/0.30 (0-1)</td>
<td>5.6/7.1 (0-22)</td>
</tr>
</tbody>
</table>

**Table:** Clinical information of patients
Feature set

Figure: List of the 13 features, grouped by dysarthria type
Methodology 1: univariate analysis

**Selected features:**
- **Hypokinetic (H)** = \{jitter, shimmer, HNR, intra-word pause, rapid AMR, no. of pauses, PPT\}
- **Ataxic (A)** = \{F0 SD, irregular AMR, vocal tremor\}
- **Spastic (S)** = \{DUV, slow AMR\}

**Figure:** Feature-wise distance between PSP and MSA
Methodology 2

- Feature dimension reduction:
  - In our experiment, we are in a small dataset machine learning scenario.
  - Typically, only a 1-dimensional feature space may provide acceptable statistics.
  - We have used Fisher Discriminative Analysis (FDA) for feature dimensionality reduction.

- Classification:
  - For classification, we use a simple 1d linear Support Vector Machine (SVM) with $C = 1$ as classifiers.
  - Considering small amount of data, a Leave-One-Speaker-Out (LOSO) training approach is adopted in all the experiments.
Results

- FDA on each dysarthric group (H, A, S) followed by classification:

<table>
<thead>
<tr>
<th></th>
<th>H</th>
<th>A</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy (%)</td>
<td>68</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

*Table: Classification accuracy for individual dysarthric groups*

- Individual dysarthria groups did not provide disease specificity.
Results...

- We now proceed to evaluate the combination of dysarthric groups.

<table>
<thead>
<tr>
<th></th>
<th>H+S+A</th>
<th>H+S</th>
<th>S+A</th>
<th>H+A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accuracy (%)</td>
<td>72</td>
<td>60</td>
<td>24</td>
<td>84</td>
</tr>
</tbody>
</table>

**Table:** Classification accuracy for combined dysarthric groups

- "Mutual amount" of hypokinetic and ataxic dysarthria can allow discrimination between MSA and PSP.
- Simple linear combination provide the discrimination.

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Results...

- We analyzed linear weights to understand feature’s contribution.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hypokinetin Weight</th>
<th>Ataxic Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jitter</td>
<td>1.03</td>
<td>2.14</td>
</tr>
<tr>
<td>Shimmer</td>
<td>3.02</td>
<td>-0.49</td>
</tr>
<tr>
<td>HNR</td>
<td>4.77</td>
<td>0.37</td>
</tr>
<tr>
<td>Intra-word pause</td>
<td>-0.10</td>
<td>0.80</td>
</tr>
<tr>
<td>No. of pauses</td>
<td>-0.02</td>
<td>2.14</td>
</tr>
<tr>
<td>PPT</td>
<td>-1.11</td>
<td>-0.49</td>
</tr>
<tr>
<td>Rapid AMR</td>
<td>0.80</td>
<td>0.37</td>
</tr>
<tr>
<td>F0 SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irregular AMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vocal tremor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table: Feature weights obtained by FDA

- Intra-word pause and no. of pauses have lower weights compared to the other feature.
- After discarding two features, selected H+A feature yields a classification score of 88%.
- We mention however that these classification scores should be considered with precaution because of the LOSO bias (different weights at each iteration).
Figure: Values of the new speech feature for each patient
Conclusion and Discussion

- We addressed the difficult problem of defining disease-specific speech features which is crucial in the perspective of early differential diagnosis in Parkinsonism.
- We focused on MSA and PSP and investigated this problem under the constraint of small dataset machine learning.
- Using FDA, we ended up defining a new scalar variable which measure degree of hypokinetic and ataxic “impairment”.
- This new variable can be considered as disease specific.
- We achieved 88% accuracy using hypokinetic and ataxic features is encouraging for future study.
- Above finding need to be confirmed by additional data and studies.
Thank you