Measurement of Tremor in the Voices of Speakers with Parkinson's Disease

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Outline

1. Introduction
2. Data – the AHN corpus
3. Acoustic measurement of vocal tremor
4. Statistical Methods
5. Results
6. Discussion
7. Conclusions
Introduction – tremor in Parkinson’s disease

**Tremor** (commonly shake, tremble) is an unintentional muscular control deficit that results in cyclic movement deviations. In **Parkinson’s disease** (PD) tremor (in rest) is one of the main symptoms – if not the most formative one. Tremor in PD is (most probably) caused by:

- reduced **motor activity**
- (as a consequence of) reduced level of the neurotransmitter **dopamine**
- (due to) destruction of the **substantia nigra**

Functionally speaking, all tremor causing phenomena can be seen as **disturbances** of or **latencies in the neuronal regulation** of a muscular process.
Introduction – vocal tremor

- vocal tremor is an *unintentional* low-frequency *modulation of the vocal fold vibration*
- unlike other tremors (the acoustic representation of) vocal tremor channels into two components:
  - frequency tremor
  - amplitude tremor
- probably *all* of the neuronal *disturbances or latencies* (caused by caffeine, aging, disease, …) of voice production *are interweaved* in both tremor types
Introduction – inconsistent literature results

But the effect of PD on vocal tremor is still not too clearly understood:

- Cnockaert et al. (2007) found:
  - vocal **tremor magnitude measures** depend rather sensitively on PD
  - tremor frequency does not relate to PD
- Nebel & Deuschl (2008) stated:
  - vocal tremor should **not** constitute an outstanding feature of PD
  - vocal tremor should be bound to **advanced stadia** of disease
  - **tremor frequencies around 9 Hz** could indicate PD
- Gillivan-Murphy (2013):
  - **amplitude tremor frequency** differs significantly between PD speakers (**below 5Hz**) and a control group (below 3 Hz)
  - PD speakers “were more likely to show greater auditory perceived [...] magnitude[s] of frequency and amplitude tremor […] , however **without statistical significance**” (sic!)


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Data – the AHN corpus

used data are a subset of the Aix Hospital Neurology (AHN) corpus: quasi-stationary parts (duration: 3s) of sustained /a/-vowels from 363 speakers

- 234 speakers (mean age = 66.66 a; SD = 9.81 a), diagnosed with Idiopathic Parkinsonism (PD), produced 416 vowels
  - 182 (of those 234) PD speakers are recorded in off and on medication (L-DOPA) condition (364 vowels)
    - female speaker (id: 37), age: 78 a, off and on medication
    - male speaker (id: 24), age: 56 a, off and on medication
- 105 speakers (mean age = 62.29 a; SD = 10.85 a) are control speakers (CG) without any pathology; 105 vowels
  - female speaker (id: 284), age: 57 a
  - male speaker (id: 64), age: 65 a
Acoustic measurement of vocal tremor with tremor.praat

tremor.praat extraction algorithm is

- based on **autocorrelation of the F₀ contour** and the **amplitude contour** and
- **corrected for the declination** that is naturally found in the F₀ contour and the amplitude contour
- **implemented in** the script language of the speech-processing program **PRAAT**
- tremor.praat (version 2.06) can be downloaded from [http://brYkl.de/tremor2.06.zip](http://brYkl.de/tremor2.06.zip)
Acoustic measurement: 6 measures

tremor.praat extracts 6 parameters of vocal tremor
- 3 measures of frequency tremor
  - frequency tremor frequency (FTrF)
  - frequency tremor intensity index (FTrI)
  - frequency tremor power index (FTrP)
- 3 measures of amplitude tremor
  - amplitude tremor frequency (ATrF)
  - amplitude tremor intensity index (ATrI)
  - amplitude tremor power index (ATrP)

tremor intensity and tremor power indices are subsumed under the term magnitude indices/measures
Acoustic measurement: tremor frequencies

tremor frequency definitions:
- FTrF is the **frequency** of the strongest low-frequency modulation of $F_0$
- ATrF is the **frequency** of the strongest low-frequency modulation of the amplitude (intensity).

computational principles (see (poster of) Brückl, 2012, for more detail):
- extract contours from sound
  - remove linear declinations (by subtraction of the linear regression estimates)
  - resample amplitude contour at constant rate (since in PRAAT’s “Amplitude Tier” amplitude values are assumed to be in the center of their period)
- autocorrelate the contours
- “strength” of low-frequency modulation is determined via the contours’ autocorrelation coefficients
Acoustic measurement: tremor intensity indices

tremor intensity definitions:
- $F_{TrI}$ is defined as the intensity of the strongest low-frequency modulation of $F_0$.
- $A_{TrI}$ is defined as the intensity of the strongest low-frequency modulation of the sound's (intensity-per-period-) amplitude ($A$).

computational principles:
- normalize the (de-declined) contours by

\[ \text{relative } F_0 = \frac{F_0 - F_0}{F_0}, \quad \text{relative } A = \frac{A - A}{A} \]

- the time marks of the contours’ extrema are found with PRAAT’s built-in function “To PointProcess (peaks)”, once the tremor frequencies are known.
- intensity indices are then determined by:

\[ (F, A)_{TrI} = \left( \frac{\sum_{i=1}^{m} \max_i}{m} + \frac{\sum_{j=1}^{n} \min_j}{n} \right) \div 2 \]
Acoustic measurement: tremor power indices

- FTrP and ATrP result from **weighting the intensity indices with** factors that are depending on **tremor frequencies**
- these factors are defined smaller for lower frequencies and therefore a lower power index would emerge if the **same tremor intensity** was found at a **lower tremor frequency**

\[
FTrP = FTrI \cdot \frac{FTrF}{FTrF + 1} \quad ATrP = ATrI \cdot \frac{ATrF}{ATrF + 1}
\]

- power indices are thought to be **biologically and psychologically more significant for the concept “tremor magnitude”** than the known intensity indices, since the (perceived) effect of tremor events of the same intensity should be bigger, if they occur more often per time unit
Acoustic measurement: examples
demonstration of the PRAAT script tremor.praat

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<th>id</th>
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<th>gender</th>
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<th>FTrI</th>
<th>FTrP</th>
<th>ATrF</th>
<th>ATrI</th>
<th>ATrP</th>
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Statistical methods

Problem: we aim to test the influence of PD on vocal tremor

1. main objective is to compare (means of) tremor measures between the group of PD speakers and the CG.

2. second aim is to test tremor measures within PD speakers in relation to the presence or absence of dopamine medication

Tests of the hypotheses:

H₀: There is no difference in tremor magnitude between PD speakers and the control group respectively between the off and the on medication condition or even lowered tremor values are found in the PD group respectively in off medication condition.

H₁: Raised tremor magnitude values are found in PD speakers respectively in the off medication condition.

(hypotheses for tremor frequencies are non-directional)
Statistical methods

18 Analyses of co-variance (ANCOVAs):

- 6 (“independent samples”) analyses comparing PD speakers off medication (PDoff) to the control group (CG)
  - DV: (6) tremor measure(s)
  - (grouping) factors: pathology (observed and fixed), gender (observed and fixed)
  - covariate: speaker age

- 6 (“independent samples”) analyses comparing PD speakers on medication (PDon) to the CG
  - DV: (6) tremor measure(s)
  - (grouping) factors: pathology (observed and fixed), gender (observed and fixed)
  - covariate: speaker age

- 6 (“paired samples”) analyses comparing within PD speakers PDoff to PDon
  - DV: (6) tremor measure(s)
  - (grouping) factor: gender (observed and fixed)
  - (within subjects) factor: medication (manipulated and fixed),
  - covariate: speaker age
Statistical methods

- unbalanced designs: type 3 square sums
- only saturated models are used
- since all tremor measures are positively skewed (distributed): logarithm (ln) of measures is used in statistical (parametric) analyses
Results

- **tremor frequencies** (FTrF and ATrF) are not influenced by any factor in all 18 analyses.
- In the 6 comparison(s) of PD on with the CG only **speaker age varies** significantly with the tremor magnitude measures (no differences due to pathology).
- An **influence of gender** on the tremor (magnitude) measures may be seen as a trend (greater differences in female speakers) but does not reach significance level.
Results – PDoff vs. CG

<table>
<thead>
<tr>
<th>EMMS &amp; CIs, PD, Gender</th>
<th>FTrI</th>
<th>FTrP</th>
<th>ATrI</th>
<th>ATrP</th>
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</thead>
<tbody>
<tr>
<td>yes / M yes / F no / M no / F</td>
<td>yes / M yes / F no / M no / F</td>
<td>yes / M yes / F no / M no / F</td>
<td>yes / M yes / F no / M no / F</td>
<td></td>
</tr>
</tbody>
</table>

- **PD**
  - p = 0.05%
  - $\eta^2_P = 4.04\%$, $\eta^2_G = 3.73\%$

- **Age**
  - p < 0.05%
  - $\eta^2_P = 7.34\%$, $\eta^2_G = 7.04\%$

$\rightarrow$ tremor magnitude measures are significantly raised in PDoff

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Results – PDoff vs. PDon

<table>
<thead>
<tr>
<th></th>
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<th>FTrP</th>
<th>ATrI</th>
<th>ATrP</th>
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<td>2,20</td>
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<tr>
<td>CI</td>
<td>2,00</td>
<td>1,80</td>
<td>1,60</td>
<td>1,40</td>
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<tr>
<td>EMMs G</td>
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<td>11,0</td>
<td>10,0</td>
</tr>
<tr>
<td>CI</td>
<td>9,0</td>
<td>8,0</td>
<td>7,0</td>
<td>6,0</td>
</tr>
</tbody>
</table>

- Frequency tremor magnitude measures are significantly raised in PDoff.

→ Frequency tremor magnitude measures are significantly raised in PDoff.

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Discussion

based on our findings we have to
- **reject** the statements of Nebel & Deuschl (2008) as well as the results from Gillivan-Murphy (2013)
- **confirm** the findings of Cnockaert et al. (2007) as well as Gillivan-Murphy's speculations based on (insignificant results on) auditory perceived scales:

→ the **tremor magnitude measures** indeed are **observable features of PD** and

→ may serve to diagnose the disease even better and also in early stadia
  - if they are combined with other dysphonia measures (see Tsanas et al., 2012)
  - if the speaker age is controlled
  - and if they are measured properly

A. Tsanas et al. (2012): “Novel speech signal processing algorithms for high-accuracy classification of Parkinson's disease”, in *IEEE Transactions on Biomedical Engineering*
Conclusions

− amplitude and frequency tremor magnitudes (intensity and power indices) are increased in sustained vowels that are produced by people that are diagnosed with PD and off medication.
− frequency tremor magnitudes also differ between the on and off medication conditions.

− Hence, tremor magnitude measures probably can be used -- together with other (vocal) measures and as long as the speakers' age is controlled -- to diagnose PD, maybe even in early stadia.
Questions?