**Early Biomarkers of Parkinson's Disease**

**Early biomarkers of Parkinson's disease based on natural connected speech**

**Introduction:**

Patients with the neurodegenerative disease Parkinson`s have numerous symptoms ranging from cognitive impairments to motor symptoms. Those symptoms may appear relatively late in the disease when the neurodegeneration has already widely spread in different areas of the brain (mainly Basal Ganglia).

Main symptoms of PD are motor dysfunctions including abnormalities in the production and sound of speech of such patients (up to 90%). These abnormalities in speech and voice are called hypokinetic dysarthria which is characterized by a decreased quality of the speech, where the voice, sound formation as well as the articulation is impaired.

As I mentioned before, often motor impairments are detected relatively late in the disease. To improve diagnostics and to detect the disease in a much earlier stage, the detection of biomarkers related to neurodegeneration could lead to a better prognosis and therapy of PD. Therefore, the investigation of prodromal speech changes could be an appropriate and suitable approach.

To investigate this approach, an automated speech monitoring system was developed, that uses a segmentation method for the precise estimation of voiced and unvoiced segments of speech, respirations and pauses. Further proposed was a set of acoustic speech features based on the segmentation algorithm applicable to connected speech, allowing the description of complex vocal disturbances due to neurodegeneration including respiratory deficits, dysphonia, imprecise articulation and dysrhythmia.

In this data analysis project, the main focus was to explore, if there are any speech patterns that support the usage of an automated speech monitoring system to detect prodromal parkinsonian neurodegeneration based on natural connected speech.

130 subjects were tested. 30 subjects with early, untreated Parkinson`s disease (PD) where the disease is already manifested. 50 subjects with REM sleep behaviour disorder (RBD), which is a disease where its relatively likely to develop PD in a later phase. As a control group, 50 healthy subjects (HD) were included.

**Data description:**

For each population (n=180) in this data set, we have the following information:

* Demographic information:
  + Age (years)
  + Gender (M for male, F for female)
* Clinical information:
  + Positive history of Parkinson`s disease in family
  + Age of disease onset (measured in years)
  + Duration of the disease from first symptoms (measured in years)
* Medication:
  + Antidepressant therapy
  + Antiparkinsonian medication
  + Antipsychotic medication
  + Benzodiazepine medication
  + Levodopa equivalent (mg/d)
  + Clonazepam (mg/d)
* Overview of motor examination: total score of two different rating scales to asse Parkinson`s disease
  + Hoehn & Yahr scale (-): total score; examination only on subjects with PD
  + UPDR III total (-): total score; examination only on subjects with PD and RBD
* UPDRS III motor scale: 14 specific items (18 to 31) regarding motor impairments on a scale from 1-4, examination only on subjects with PD and RBD

18. Speech

0 = Normal  
1 = Slight loss of expression, diction and/or volume  
2 = Monotone, slurred but understandable; moderately impaired  
3 = Marked impairment, difficult to understand  
4 = Unintelligible

19. Facial Expression

0 = Normal  
1 = Minimal hypomimia, could be normal “Poker Face”  
2 = Slight but definitely abnormal diminution of facial expression  
3 = Moderate hypomimia; lips parted some of the time  
4 = Masked or fixed facies with severe or complete loss of facial expression;

lips parted 1/4 inch or more

20. Tremor at rest (head, upper and lower extremities)

0 = Absent  
1 = Slight and infrequently present  
2 = Mild in amplitude and persistent. Or moderate in amplitude, but only intermittently present  
3 = Moderate in amplitude and present most of the time  
4 = Marked in amplitude and present most of the time

21. Action or Postural Tremor of hands

0 = Absent  
1 = Slight; present with action  
2 = Moderate in amplitude, present with action  
3 = Moderate in amplitude with posture holding as well as action  
4 = Marked in amplitude; interferes with feeding

22. Rigidity (Judged on passive movement of major joints with patient relaxed in sitting position. Cogwheeling to be ignored)

0 = Absent  
1 = Slight or detectable only when activated by mirror or other movements.  
2 = Mild to moderate  
3 = Marked, but full range of motion easily achieved  
4 = Severe, range of motion achieved with difficulty

23. Finger Taps (Patient taps thumb with index finger in rapid succession)

0 = Normal  
1 = Mild slowing and/or reduction in amplitude  
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement  
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement  
4 = Can barely perform the task

24. Hand Movements (Patient opens and closes hands in rapid succesion)

0 = Normal  
1 = Mild slowing and/or reduction in amplitude  
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement  
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement  
4 = Can barely perform the task

25. Rapid Alternating Movements of Hands (Pronation-supination movements of hands, vertically and horizontally, with as large an amplitude as possible, both hands simultaneously)

0 = Normal  
1 = Mild slowing and/or reduction in amplitude  
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement  
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement  
4 = Can barely perform the task

26. Leg Agility (Patient taps heel on the ground in rapid succession picking up entire leg. Amplitude should be at least 3 inches)

0 = Normal  
1 = Mild slowing and/or reduction in amplitude  
2 = Moderately impaired. Definite and early fatiguing. May have occasional arrests in movement  
3 = Severely impaired. Frequent hesitation in initiating movements or arrests in ongoing movement  
4 = Can barely perform the task

27. Arising from Chair (Patient attempts to rise from a straightbacked chair, with arms folded across chest)

0 = Normal  
1 = Slow; or may need more than one attempt  
2 = Pushes self up from arms of seat  
3 = Tends to fall back and may have to try more than one time, but can get up without help  
4 = Unable to arise without help

28. Posture

0 = Normal erect  
1 = Not quite erect, slightly stooped posture; could be normal for older person  
2 = Moderately stooped posture, definitely abnormal; can be slightly leaning to one side  
3 = Severely stooped posture with kyphosis; can be moderately leaning to one side  
4 = Marked flexion with extreme abnormality of posture

29. Gait

0 = Normal  
1 = Walks slowly, may shuffle with short steps, but no festination (hastening steps) or propulsion  
2 = Walks with difficulty, but requires little or no assistance; may have some festination, short steps, or propulsion  
3 = Severe disturbance of gait, requiring assistance  
4 = Cannot walk at all, even with assistanc

30. Postural Stability (Response to sudden, strong posterior displacement produced by pull on shoulders while patient erect with eyes open and feet slightly apart. Patient is prepared)

0 = Normal  
1 = Retropulsion, but recovers unaided  
2 = Absence of postural response; would fall if not caught by examiner  
3 = Very unstable, tends to lose balance spontaneously  
4 = Unable to stand without assistance

31. Body Bradykinesia and Hypokinesia (Combining slowness, hesitancy, decreased armswing, small amplitude, and poverty of movement in general)

0 = None  
1 = Minimal slowness, giving movement a deliberate character; could be normal for some persons. Possibly reduced amplitude  
2 = Mild degree of slowness and poverty of movement which is definitely abnormal. Alternatively, some reduced amplitud  
3 = Moderate slowness, poverty or small amplitude of movement  
4 = Marked slowness, poverty or small amplitude of movement

* Speech examination - speaking task of reading passage: speakers read a standardized, phonetically-balanced text of 80 words twice
  + Entropy of speech timing (-)
  + Rate of speech timing (-/min)
  + Acceleration of speech timing (-/min2)
  + Duration of pause intervals (ms)
  + Gaping in between voiced intervals (-/min)
  + Duration of unvoiced stops (ms)
  + Decay of unvoiced fricatives (‰/min)
  + Relative loudness of respiration (dB)
  + Pause intervals per respiration (-)
  + Rate of speech respiration (-/min)
  + Latency of respiratory exchange (ms)
* Speech examination - speaking task of monologue: participants were instructed to provide monologue about their interests, job, family or current activities for approximately 90 seconds.
  + Duration of pause intervals (ms)
  + Duration of voiced intervals (ms)
  + Gasping in-between voiced intervals(-/min)
  + Duration of unvoiced stops (ms)
  + Decay of unvoiced fricatives (‰/min)
  + Relative loudness of respiration (dB)
  + Pause intervals per respiration (-)
  + Rate of speech respiration (-/min)
  + Latency of respiratory exchange (ms)