Motor speech phenotype of Huntington’s disease:

A clinical biomarker in the premanifest phase

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Speech vs Language

**SPEECH**
- Dysarthria = motor execution deficit
- Apraxia = motor planning deficit

**LANGUAGE**
- Aphasia = content, rules (semantics, syntax, grammar)

How we say it

What we say
What are the best features / sets to explore?

**Summative**

**Intelligibility** (how well we are understood)

**Naturalness** (difference between disease & healthy speakers)

Or

**Individual / combination**

Features describing individual or combined *speech subsystems*
Speech subsystems

Respiration – breath support
Phonation – voice
Articulation – lips & tongue
Resonance – nasality
Prosody – intonation & timing
Speech behaviors themselves tell us a lot about the speaker

Speech tasks can be:
- cognitively demanding
- motorically complex
- both

Vogel et al. Neurology 2017; Vogel et al. Speech Comm 2014
Quantification of speech subsystems

**Quality**: noise / turbulence / energy
- Noise (perturbation)
- Frequency & power distribution

**Control**: variance or precision
- Variability of pitch or loudness
- Vowel articulation
- Consonant production

**Timing**: rate / stability / duration
- Speech rate
- Syllable stability
- Duration of pauses
Speech and its stakeholders

Altered speech leads to meaningful change in QoL

Intelligibility/naturalness/SRQoL

Changes in speech reflect effect of compound on CNS

Speaker

Clinician

Regulators

U.S. FOOD & DRUG ADMINISTRATION

THE UNIVERSITY OF MELBOURNE
517 pts from 12 studies

Speech in PreHD characterized by impaired speech agility, phonatory dysfunction and slower speech rate

Some disagreement re nature & magnitude of speech deficits (Skodda et al. Neurology 2016; Vogel & Stout, Neurology 2017)

Relationship with cognition & pathophysiology not clear
Listening for pathology – blinded expert raters

Figure. Group comparisons on the occurrence of dysarthric speech features in PreHD, EarlyHD and controls

* = Significant difference between PreHD and control groups | ** = Significant difference between EarlyHD and control groups

*p <0.05, **p < 0.01, ***p < 0.001
# Prodromal vs Presymptomatic vs Early stage HD

<table>
<thead>
<tr>
<th></th>
<th>PresymHD (n=14)</th>
<th>ProdromHD (n=18)</th>
<th>EarlyHD (n=14)</th>
<th>MidHD (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean+/−SD)</strong></td>
<td>39.2 (11.8)</td>
<td>45.1 (12.1)</td>
<td>56.6 (10.7)</td>
<td>48.7 (13.7)</td>
</tr>
<tr>
<td><strong>Burden disease scores</strong></td>
<td>186 (41.4)</td>
<td>340.6 (61.8)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>UHDRS total motor score</strong></td>
<td>1.2 (2.3)</td>
<td>3.1 (5.4)</td>
<td>18.1 (7.7)</td>
<td>32.7 (11.2)</td>
</tr>
<tr>
<td><strong>Total Functional Capacity</strong></td>
<td>12.8 (0.8)</td>
<td>12.9 (0.2)</td>
<td>10.0 (2.4)</td>
<td>6.6 (1.5)</td>
</tr>
<tr>
<td><strong>CAG repeats</strong></td>
<td>40.5 (1.3)</td>
<td>43.4 (2.2)</td>
<td>43.2 (4.1)</td>
<td>44.8 (5.3)</td>
</tr>
</tbody>
</table>

**Premanifest HD**: Disease burden scores (DBS) [DBS = age * (CAG-35.5)]. Langbehn et al. (2004).

**Presymptomatic HD** = DBS <250 | **Prodromal HD** = DBS ≥250.

**Manifest HD**: TFS (0 = complete loss of function and 13 = normal function; EarlyHD TFS = 7-13 | MidHD TFS = 4-6).

Age and sex matched controls.
Voice quality – sustained vowel
Timing – syllable repetition [papa]

Mean syllable duration

Perturbation
Timing – syllable repetition [pata]

Mean syllable rate

Perturbation
Timing – reading

Reading - Pause (mean)

Reading - Speech rate

Group comparison

PresymHD vs Control-A
ProdromalHD vs Control-B
EarlyHD vs Control-C
MidHD vs Control-D

HD
Control

**

***
Timing – unprepared monologue

Monologue - Pause (mean)

Monologue - Percentage of silence
Stability [pataka]

![Graph showing stability over time](image)

**Perturbation**

- **HD**
- **Control**

The graph compares stability over time for different groups, indicating changes in perturbation levels from baseline to 6 months.
Inter-relatedness of speech & disease features

DDK Rate vs Total Motor Score in Paired Syllable Repetition

$r = -0.66$

$p < 0.01$
Moving ahead

Composite measures of HD speech

Stability work across time frames similar to trials

Larger natural history cohort – longitudinal data

Dysarthria Impact Scale – ~6 items across 3 domains validated in HD
Clinical assessment of dysphagia in neurodegeneration (CADN): development, validity and reliability of a bedside tool for dysphagia assessment

Authors

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11 items (7 mins): 2 parts - case history & consumption – validated against videofluoroscopy
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