Background & Aims

Background: Modality.AI and EverythingALS created an open data collection platform initiative in 2020 to investigate the potential of speech and facial biomarkers to serve as endpoints in clinical trials and in assessment of ALS disease progression [1, 2]. The interactive platform, powered by Modality’s virtual agent Tina, records speech, facial video and survey instrument data from participants, emulating the role of a neurologist or speech pathologist walking them through speaking exercises [1].

Aim: To summarize our progress and lessons learned from a 1.5-year long data collection of speech and video recordings of people with ALS and healthy controls via the platform. The research community can use this data to accelerate the development of biomarkers, diagnostics, therapies, and fundamental scientific understanding of ALS.

Findings: Multimodal dialog based remote patient monitoring allows us to:
(i) measure changes in speech markers frequently and cost-effectively, while
(ii) capturing differences between slow and fast progressors.

Key Stats

<table>
<thead>
<tr>
<th></th>
<th>#subjects (F: female)</th>
<th>total #sessions</th>
<th>Mean age (years)</th>
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</thead>
<tbody>
<tr>
<td>pALS</td>
<td>112 (54 F)</td>
<td>2,188</td>
<td>60.2 ± 10.2</td>
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<tr>
<td>Controls</td>
<td>202 (137 F)</td>
<td>3,459</td>
<td>53.7 ± 13.7</td>
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<tr>
<td>Total</td>
<td>314 (191 F)</td>
<td>5,647</td>
<td>56.0 ± 13.0</td>
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Table 1. Participants stats as of 2022-02-22

Mean time since onset (months) = 50.2 ± 45.9

Analyses

- Each session consists of structured and spontaneous speech tasks (Table 2), followed by self-reported ALSFRS-R questionnaire.
- We earlier shy away from these remotely extracted speech and facial biomarkers show promise for assisting early diagnosis (classifying healthy vs bulbar presymptomatic) and progress monitoring (bulbar presymptomatic vs bulbar symptomatic) of ALS. See [3] for more details.
- To investigate how well metrics capture rate of progression (calculated on first and last ALSFRS-R score; pALS were stratified into slow- and fast-to-progressors based on a threshold of 0.47 points/month. Statistical tests were conducted to identify acoustic & visual metrics where rates of change were significantly different between the two cohorts [4].

Speech task

<table>
<thead>
<tr>
<th>Acoustic measures</th>
<th>Visual measures</th>
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<tbody>
<tr>
<td>Held vowel phonation</td>
<td>mean F0, HNR, jitter, shimmer, CPP, duration</td>
</tr>
<tr>
<td>velocity, acceleration, and jerk of lower lip and jaw center, eye opening, vertical eyebrow displacement, eye blinks, area of the mouth, symmetry ratio of the mouth area</td>
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Table 2. Stimuli and corresponding extracted acoustic & visual speech measures. DDK: AMR: diadochokinesis; SIT: speech intelligibility test; HNR: harmonics-to-noise ratio; CPP: cepstral peak prominence; cTV: cycle-to-cycle temporal variation; PPT: percent pause time.

Opportunities:
- Frequent measurements aid progress monitoring
- Remote setup enables scalable and inexpensive collection of large dataset

77% average monthly retention rate (as of Mar 5, 2022)
70% average completion rate (as of Mar 5, 2022)

Challenges:
- Noisy data:
  - Missing observations (participant fatigue, boredom, forgetfulness, etc.)
  - Heterogeneous w.r.t. time since onset, number of sessions per user, time between sessions, total duration from first to last session
- Self-reported ALSFRS-R and ROADS: subjective and not always reliable (mistakes happen)
- Technical challenges due to device and browser settings (e.g., attenuation of loudness, which can affect feature extraction)

Conclusions:
- Frequent and continuous monitoring of acoustic and visual speech markers can capture objective physiological changes that may not be captured by subjective scales like the ALSFRS-R instrument, the current clinical standard to track progression in ALS.
- Changes in these audiovisual metrics could serve as potential digital biomarkers, which could contribute towards patient stratification and tracking of outcomes following pharmaceutical interventions.