Investigating the Utility of Multimodal Conversational Technology and Audiovisual Analytic Measures for the Assessment and Monitoring of Amyotrophic Lateral Sclerosis at Scale

Michael Neumann‡, Oliver Roesler‡, Jackson Liscombe‡, Hardik Kothare††, David Suenndermann-Oefti, David Pautler‡, Indu Navar‡, Aria Anvar‡, Jochen Kumm‡, Raquel Norel‡, Ernest Fraenkel‡, Alexander V. Sherman‡, James D. Berry‡, Gary L. Pattee§, Jun Wang§, Jordan R. Green‡ and Vikram Ramanarayanan††

vikram.ramanarayanan@modality.ai

Abstract

We propose a cloud-based multimodal dialog platform for the remote assessment and monitoring of Amyotrophic Lateral Sclerosis (ALS) at scale. This paper presents our vision, technology setup, and an initial investigation of the efficacy of the various acoustic and visual speech metrics automatically extracted by the platform. 82 healthy controls and 54 people with ALS (pALS) were instructed to interact with the platform and completed a battery of speaking tasks designed to probe the acoustic, articulatory, phonatory, and respiratory aspects of their speech. We find that multiple acoustic (rate, duration, voicing) and visual (higher order statistics of the jaw and lip) speech metrics show statistically significant differences between controls, bulbar symptomatic and bulbar pre-symptomatic patients. We report on the sensitivity and specificity of these metrics using five-fold cross-validation. We further conducted a LASSO-LARS regression analysis to uncover the relative contributions of various acoustic and visual features in predicting the severity of patients’ ALS (as measured by their self-reported ALSFRS-R scores). Our results provide encouraging evidence of the utility of automatically extracted audiovisual analytics for scalable remote patient assessment and monitoring in ALS.

Index Terms: conversational agent, amyotrophic lateral sclerosis, computer vision, dialog systems.

1. Multimodal Conversational Agents for Health Monitoring

The development of technologies that rapidly diagnose medical conditions, recognize pathological behaviors, continuously monitor patient status, and deliver just-in-time interventions using the user’s native technology environment remains a critical need today [1]. The COVID-19 pandemic has further highlighted the need to make telemedicine and remote monitoring more readily available to patients with chronic neurological disorders. [2]. However, early detection or progress monitoring of neurological or mental health conditions, such as clinical depression, ALS, Alzheimer’s disease, dementia, etc., is often challenging for patients due to various reasons, including, but not limited to: (i) no access to neurologists or psychiatrists; (ii) lack of awareness of a given condition and the need to see a specialist; (iii) lack of an effective standardized diagnostic or endpoint; (iv) substantial cost and transportation involved in conventional or traditional solutions; and in some cases (v) lack of medical specialists in these fields [3].

The NEurological and Mental Health Screening Instrument (NEMSI) [4], has been developed to bridge this gap. NEMSI is a cloud-based multimodal dialog system that can be used to elicit evidence required for detection or progress monitoring of neurological or mental health conditions through automated screening interviews conducted over the phone or via web browser. While intelligent virtual agents have been proposed in previous work for such diagnosis and monitoring purposes [5,6], NEMSI offers three significant innovations: First, NEMSI uses readily available devices (web browser or mobile app), in contrast to dedicated, locally administered hardware, like cameras, servers, audio devices, etc. Second, NEMSI’s backend is deployed in an automatically scalable cloud environment allowing it to serve an arbitrary number of end-users at a small cost per interaction. Thirdly, the NEMSI system is natively equipped with real-time analytics modules that extract a variety of speech and video features of direct relevance to clinicians in the neurological space, such as speech and pause duration for the assessment of ALS, or geometric features derived from facial landmarks for the automated detection of orofacial impairment in stroke.

This paper investigates the utility of audio and video metrics collected via NEMSI for early diagnosis and monitoring of ALS. We specifically investigate two research questions. First, which metrics demonstrate statistically significant differences between (a) healthy controls and bulbar pre-symptomatic people with ALS or pALS (thereby assisting in early diagnosis), as well as (b) bulbar-presymptomatic patients and bulbar symptomatic patients (thereby assisting in progress monitoring)? Second, for pALS cohorts, which metrics are most predictive of their self-reported ALS Functional Rating Scale-Revised (ALSFRS-R) score? Before addressing these questions, however, we briefly summarize the current state of ALS research, and describe our data collection and metrics extraction process.

2. Current State of ALS Diagnosis and Monitoring

ALS is a neurodegenerative disease that affects roughly 4 to 6 people per 100,000 of the general population [8,9]. Early
were extracted and all ALSFRS-R questions were answered. For this cross-sectional study we included one dialog session per subject. However, recent studies show that objective measures allow for earlier detection of ALS symptoms [13, 14, 15, 16, 17, 18, 19], stratification and classification of patients [20] and can provide markers for disease onset, progression and severity [21, 22, 23, 24, 25]. These objective measures can be automatically extracted, thereby allowing for more frequent monitoring, potentially improving treatment. The success of the Beive Research Platform [26] to track ALS disease progression demonstrates the viability of such remote monitoring solutions.

### 3. Methods

#### 3.1. Collection Setup

NEMSI end users are provided with a website link to the secure screening portal and login credentials by their caregiver or study liaison (physician, clinic, a referring website or patient portal). After completing microphone and camera checks, subjects participate in a conversation with “Nina”, a virtual dialog agent. Nina’s virtual image appears in a web window, and subjects are able to see their own video. During the conversation, Nina engages subjects in a mixture of structured speaking tasks and open-ended questions to elicit speech and facial behaviors relevant for the type of condition being screened for.

Analytics modules automatically extract speech (e.g., speaking rate, duration measures, fundamental frequency (F0)) and video features (e.g., range and speed of movement of various facial landmarks) in real time and store them in a database, along with meta-data about the interaction, such as call duration and completion status. All this information can be accessed by the study liaison through an easy-to-use dashboard, which provides a summary of the interaction (including access to a video recording and the analytic measures computed), as well as a detailed breakdown of the metrics by individual interaction turns.

#### 3.2. Data

Data from 136 participants (see Table 1) were collected between September 2020 and March 2021 in cooperation with EverythingsALS and the Peter Cohen Foundation. For this cross-sectional study we included one dialog session per subject.

The conversational protocol elicits five different types of speech samples from participants, inspired by prior work [27, 28, 29, 30]: (a) sustained vowel phonation, (b) read speech, (c) measure of diadochokinetic rate (rapidly repeating the syllables /patu/), and (d) free speech (picture description task). For (b) read speech, the dialog contains six speech intelligibility test (SIT) sentences of increasing length (5 to 15 words), and one passage reading task (Bamboo Passage; 99 words). After dialog completion, participants filled out the ALS Functional Rating Scale-revised (ALSFRS-R), a standard instrument for monitoring the progression of ALS [7]. The questionnaire consists of 12 questions about physical functions in activities of daily living. Each question provides five answer options, ranging from normal function (score 4) to severe disability (score 0). The total ALSFRS-R score is the sum of all sub-scores (therefore ranging from 0 to 48). The ALSFRS-R comprises four scales for different domains affected by the disease: bulbar system, fine and gross motor skills, and respiratory function.

We stratified subjects into three groups for statistical analysis: (a) Healthy controls (CON); (b) pALS with a bulbar sub-score < 12 (first three ALSFRS-R questions) were labeled bulbar symptomatic (BUL); and (c) pALS with a bulbar sub-score of 12 were labeled bulbar pre-symptomatic (PRE). Similar to [14] we aim at identifying acoustic and visual speech measures that show significant differences between these groups.

### 4. Signal Processing and Metrics Extraction

#### 4.1. Acoustic Metrics

We use measures commonly established for clinical speech analysis with regard to ALS [14], including timing measures, frequency domain measures, and measures specific to the diadochokinesia task (DDK), such as syllable rate and cycle-to-cycle temporal variation [31]. Table 2 shows the metrics and speech task types from which they are extracted. Additionally, speech intensity (mean energy in dB SPL excluding pauses) was extracted for all utterances. The picture description task (free speech) was not used for this analysis.

All acoustic measures were automatically extracted with the speech analysis software Praat [32]. Speaking and articulation rates are computed based on expected number of words because forced alignment is error-prone for dysarthric speech [33]. For that reason, these measures can be noisy, if for example a patient did not finish the reading passage. Hence, we automatically remove outliers based on thresholds for the Bamboo task: speaking rates > 250 words/min, articulation rates > 350 words/min, and PPT > 80% are excluded.

#### 4.2. Visual Metrics

Facial metrics were calculated for each utterance in three steps: (i) face detection using the Dlib face detector, which uses

---

Table 1: Participant characteristics for the three groups – controls (CON), bulbar symptomatic (BUL), and bulbar pre-symptomatic (PRE). Age and ALSFRS-R scores are presented as: median; mean (standard deviation).

| Group      | Female | Male | Age (years) | ALSFRS-R Total | ALSFRS-R Bulbar |
|------------|--------|------|-------------|----------------|-----------------|
| CON        | 68     | 14   | 43; 41.62 (19.00) | 48; 47.89 (0.94) | 12; 11.94 (0.36) |
| BUL        | 17     | 15   | 63; 59.56 (10.29) | 36; 33.09 (7.46) | 9; 8.75 (1.57)  |
| PRE        | 12     | 10   | 61; 57.18 (11.31) | 40; 36.45 (8.58) | 12; 12.00 (0.00) |

1https://www.beive.org/
2https://www.everythingsals.org/research
3If a subject participated in multiple dialog sessions, we took the first successful one, i.e., the first complete call for which valid metrics were extracted and all ALSFRS-R questions were answered.
4The outlier thresholds and the tasks for which they are applied were determined by manual inspection of the data.
5http://dlib.net/
five histograms of oriented gradients to determine the (x, y)-coordinates of one or more faces for every input frame [34]. (ii) facial landmark extraction using the Dlib facial landmark detector, which uses an ensemble of regression trees proposed in [35] to extract 68 facial landmarks according to Multi-PRE [36], and (iii) facial metrics calculation, which uses 20 facial landmarks to compute the metrics shown in Table 3 (cf. [37] for details). Finally, all facial metrics in pixels were normalized within every subject by dividing the values by the interlachrymal distance in pixels (measured as distance between the right corner of the left eye and the left corner of the right eye) for each subject.

### 5. Analyses and Observations

To normalize for sex-specific differences in metrics (such as F0), we z-scored all metrics by sex group. Additionally, all metrics reported below (except speaking and articulation duration) were averaged across speech task type. An important caveat to all the analyses presented here is the imbalance of sample size between the cohorts; also, future extensions to this work will need a larger sample size of the BUL and PRE cohorts to make robust and generalizable statistical claims.

We conducted a non-parametric Kruskal-Wallis test for every acoustic and facial metric to identify the metrics that showed a statistically significant difference between the cohorts. For all metrics with $p < 0.05$ a post-hoc analysis was done (again Kruskal-Wallis) between every combination of two cohorts to find out which groups can be distinguished. Figure 1 shows effect size, measured as Glass’ $\Delta$ [38], for all metrics that show statistically significant difference ($p < 0.05$) between different subject groups.

In addition to the statistical tests, we conducted 5-fold cross-validation with logistic regression to investigate binary classification performances, and in turn sensitivities and specificities, of our aforementioned metrics in distinguishing the symptomatic and bulbar symptomatic pALS cohorts.

We looked at acoustic features, we found that timing measures (speaking and articulation duration and rate; PPT; syllable rate, cTV) exhibit strong differences between groups and that the effect sizes of these metrics are highest between the BUL group and the CON group. Mean F0 also showed a significant difference with small effect sizes. For visual metrics, the

![Figure 1: Effect sizes of acoustic and visual metrics that show statistically significant differences at $p < 0.05$. Effect sizes are shown with a 95% confidence interval and are ranked by the BUL–CON group pair.](image)
Figure 2: ROC curves displaying the performance of binary classification with 5-fold crossvalidation for all group pairs.

Figure 3: Acoustic and visual features from the LASSO LARS regression path.

results indicate that velocity, acceleration and jerk measures are generally the best indicators for ALS. Additionally, while the jaw center (JC) seems to be more important than the lower lip (LL) for detecting ALS, further investigations are necessary to ensure that the difference between the JC and LL metrics is not just due to a difference in facial landmark detection accuracy.

5.2. RQ2: Which metrics contribute the most toward predicting the ALSFRS-R score?

In a regression analysis, we investigated the predictive power of the extracted metrics with regard to both BUL and PRE pALS cohorts. To investigate this, we employed a LASSO (least absolute shrinkage and selection operator) regression with the objective to predict the total ALSFRS-R score (implemented using least-angle regression (LARS) algorithm [39]). The algorithm is similar to forward stepwise regression, but instead of including features at each step, the estimated coefficients are increased in a direction equiangular to each one’s correlations with the residual.

Figure 3a shows the final 17 features, in the order they were selected by the LASSO-LARS regression, on data from 19 PRE samples along with the cumulative model $R^2$ at each step. We observe that both facial metrics (mouth opening and symmetry ratio, higher order statistics of jaw and lips) and acoustic metrics (particularly voice quality metrics such as jitter, shimmer and mean F0) added useful predictive power to the model, suggesting that these might be useful in modeling severity in bulbar pre-symptomatic pALS.

On the other hand, for the BUL cohort, Figure 3b shows a slightly different set of 20 features obtained using LASSO-LARS (based on 26 participants). We observe that facial metrics (eye blinks and brow positions, in addition to higher order statistics of jaw and lips) add more predictive power to the model than acoustic metrics (such as cTV, CPP and mean F0), suggesting that these might find utility in modeling severity in bulbar symptomatic pALS.

6. Conclusions

Our findings demonstrate the utility of multimodal dialog technology for assisting early diagnosis and monitoring of pALS. Multiple automatically extracted acoustic (rate, duration, voicing) and visual (higher order statistics of the jaw and lip) speech metrics show significant promise in assisting with both early diagnosis of bulbar pre-symptomatic ALS vs healthy controls, as well as for progress monitoring in pALS. Moreover, using LASSO-LARS to model the relative contribution of these features in predicting the ALSFRS-R score highlights the utility of incorporating different speech and facial metrics for modeling severity in bulbar pre-symptomatic and bulbar symptomatic pALS. While higher order statistics of the jaw and lower lip facial features and timing, pausing and rate-based speech features were useful across the board for both cases, voice quality and mouth opening and area metrics seem to be more useful for the bulbar pre-symptomatic group, while spectral and eye-related metrics are relevant for the bulbar symptomatic group. Future work will expand these analyses to more speakers to ensure the statistical robustness and generalizability of these trends.
7. References

[1] S. Kumar, W. Nilsen et al., “Mobile health: Revolutionizing healthcare through transdisciplinary research,” Computer, vol. 46, no. 1, pp. 28–35, 2012.

[2] A. Bombaci, G. Abbadesa et al., “Telemedicine for management of patients with amyotrophic lateral sclerosis through covid-19 tail,” Neurological Sciences, pp. 1–5, 2020.

[3] R. Steven and M. Steinhube, “Can mobile health technologies transform health care,” JAMA, vol. 92037, no. 1, p. 1–2, 2013.

[4] D. Suendermann-Oeft, A. Robinson et al., “Nems: A multimodal dialog system for screening of neurological or mental conditions,” in Proceedings of the 19th ACM International Conference on Intelligent Virtual Agents, 2019, pp. 245–247.

[5] D. DeVanter, R. Al, et al., “Simson Kiosk: A virtual human interviewer for healthcare decision support,” in Proceedings of the International Conference on Autonomous Agents and Multi-Agent Systems (AAMAS), Paris, France, 2014 May.

[6] C. Lisetti, R. Amini, and U. Yasavu, “Now all together: Overview of virtual health assistants emulating face-to-face health interview experience,” Künstliche Intelligenz, vol. 29, pp. 161–172, March 2015.

[7] J. M. Cedarbaum, N. Stambler et al., “The alsrfrs-t: a revised als functional rating scale that incorporates assessments of respiratory function,” Journal of the neurological sciences, vol. 169, no. 1-2, pp. 13–21, 1999.

[8] D. Majoor-Krakauer, P. Willems, and A. Hofman, “Genetic epidemiology of amyotrophic lateral sclerosis,” Clinical genetics, vol. 63, no. 2, pp. 83–101, 2003.

[9] A. Al-Chalabi and O. Hardiman, “The epidemiology of als: a conspiracy of genes, environment and time,” Nature Reviews Neurology, vol. 9, no. 11, p. 617, 2013.

[10] S. Pagannoni, E. A. Macklin et al., “Diagnostic timelines and delays in diagnosing amyotrophic lateral sclerosis (als): Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, vol. 15, no. 5-6, pp. 453–456, 2014.

[11] A. Chiò, A. Gauthier et al., “A cross sectional study on demendants of quality of life in als,” Journal of Neurology, Neurosurgery & Psychiatry, vol. 75, no. 11, pp. 1597–1601, 2004.

[12] K. Joubert, J. Bornman, and E. Alant, “Speech intelligibility and articulatory samples,” in Proceedings of the International Conference on Autonomous Agents and Multi-Agent Systems (AAMAS), Paris, France, 2014 May.

[13] C. Barnett, J. R. Green et al., “Reliability and validity of speech & pause measures during passage reading in als,” Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, vol. 21, no. 1-2, pp. 42–50, 2020.

[14] J. D. Berry, S. Pagannoni et al., “Design and results of a smartphone-based digital phenotyping study to quantify als progression,” Annals of Clinical and Translational Neurology, vol. 6, no. 5, pp. 873–881, February 2019.

[15] A. K. Silbergleit, A. F. Johnson, and B. H. Jacobson, “Acoustic analysis of voice in individuals with amyotrophic lateral sclerosis and perceptually normal vocal quality,” Journal of Voice, vol. 11, no. 2, pp. 222–231, 1997.

[16] B. Tomik and R. J. Guilloff, “Dysarthria in amyotrophic lateral sclerosis: A review,” Amyotrophic Lateral Sclerosis, vol. 11, no. 1-2, pp. 4–15, 2010.

[17] M. Novotny, J. Melechovsky et al., “Comparison of automated acoustic methods for oral diadochokinesis assessment,” in Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, vol. 15, no. 3-4, pp. 112–122, 2014.

[18] A. Blandini, J. R. Green et al., “Kinematic features of jaw and lips distinguish symptomatic from presymptomatic stages of bulbar decline in amyotrophic lateral sclerosis,” Journal of Speech, Language, and Hearing Research, vol. 63, no. 10, pp. 341–347, 2020.

[19] R. Noel, M. Pietrowicz et al., “Detection of amyotrophic lateral sclerosis (als) via acoustic analysis,” Journal of Speech-Language Pathology, vol. 21, no. 1-2, pp. 34–41, 2011.

[20] Y. Yunusova, J. R. Green et al., “Speech in als: longitudinal changes in lips and jaw movements and vowel acoustics,” Journal of medical speech-language pathology, vol. 21, no. 1, p. 1, 2013.

[21] K. M. Allison, Y. Yunusova et al., “The diagnostic utility of patient-report and speech-language pathologists’ ratings for detecting the early onset of bulbar symptoms due to ALS.” Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, vol. 18, no. 5-6, pp. 358–366, August 2017.

[22] P. Gomez, D. Palacios et al., “Articulation acoustic kinematics in als speech,” in 2017 International Conference and Workshop on Bioinspired Intelligence (IWOBI). IEEE, 2017, pp. 1–6.

[23] R. Noel, M. Pietrowicz et al., “Comparison of automated acoustic methods for oral diadochokinesis assessment,” in Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, vol. 21, no. 6, pp. 1309–1316, 2015.

[24] A. Bandini, J. R. Green et al., “Kinematic features of jaw and lips distinguish symptomatic from presymptomatic stages of bulbar decline in amyotrophic lateral sclerosis,” Journal of Speech, Language, and Hearing Research, vol. 61, no. 1, pp. 1118–1129, 2018.

[25] B. J. Perry, R. Martino et al., “Lingual and jaw kinematic abnormalities precede speech and swallowing impairments in als,” Dysphagia, vol. 33, no. 6, pp. 840–847, 2018.

[26] S. Kumar, W. Nilsen et al., “Mobile health: Revolutionizing healthcare through transdisciplinary research,” Computer, vol. 46, no. 1, pp. 28–35, 2012.

[27] A. Wisler, K. Tepiansky et al., “The effects of symptom onset location on automatic amyotrophic lateral sclerosis detection using the correlation structure of articulatory movements,” Journal of Speech, Language, and Hearing Research, 2021. [Online]. Available: https://pubs.asha.org/doi/abs/10.1044/2020_JSLHR-20-00288

[28] P. Rong, Y. Yunusova et al., “A speech measure for early stratification of fast and slow progressors of bulbar amyotrophic lateral sclerosis: lip movement jitter,” Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, vol. 21, no. 1-2, pp. 34–41, 2020.