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Early Identification of Speech Changes Due to Amyotrophic Lateral Sclerosis Using Machine Classification

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Abstract

We used a machine learning (ML) approach to detect bulbar amyotrophic lateral sclerosis (ALS) prior to the onset of overt speech symptoms. The dataset included speech samples from 123 participants who were stratified by sex and into three groups: healthy controls, ALS symptomatic, and ALS presymptomatic. We compared models trained on three group pairs (symptomatic-control, presymptomatic-control, and all ALS-control participants). Using acoustic features obtained with the OpenSMILE ComParE13 configuration, we tested several feature filtering techniques. ML classification was achieved using an SVM model and leave-one-out cross-validation. The most successful model, which was trained on symptomatic-control data, yielded an AUC=0.99 for females and AUC=0.91 for males. Models trained on all ALS-control participants had high diagnostic accuracy for classifying symptomatic and presymptomatic ALS participants (females: AUC=0.85; males: AUC=0.91). Additionally, probabilities from these models correlated with speaking rate (females: Spearman coefficient=-0.60, $p<0.001$; males: Spearman coefficient=-0.43, $p<0.001$) and intelligible speaking rate (females: Spearman coefficient=-0.65, $p<0.001$; males: Spearman coefficient=-0.40, $p<0.01$), indicating their possible use as a severity index of bulbar motor involvement in ALS. These results highlight the importance of stratifying patients by speech severity when testing diagnostic models and demonstrate the potential of ML classification in early detection and progress monitoring of ALS.

Index Terms: amyotrophic lateral sclerosis, machine classification, acoustic analysis

1. Introduction

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disease characterized by the progressive loss of upper and lower motor neurons. The motor neuron degeneration in ALS can lead to dysphagia, dysarthria, and impaired limb and respiratory function [1]. Although ALS has no cure, two drugs have been FDA approved for increasing life expectancy [1]-[3]. Minimizing the time between onset of the disease and its diagnosis can enable earlier treatment and better prepare patients and caregivers for life with ALS [4].

The site of onset and progression pattern and rate of ALS are variable across patients [2], [5]. ALS symptoms can first manifest in limb (i.e., spinal onset) or head and neck (i.e., bulbar onset) muscles. The heterogeneity of ALS expression across individuals has presented an ongoing challenge for developing accurate early detection and progress monitoring systems. Currently, there is no single accepted biomarker used to diagnosis ALS. Instead, a diagnosis is made by expert clinicians who identify the presence of motor symptoms that are consistent with both upper and lower motoneuron involvement [6]-[7].

Approximately one third of cases have a bulbar onset [8], and within bulbar onset ALS, dysarthria is a more common initial symptom than dysphagia [9]-[10]. Patients with ALS have a median life expectancy of 20-48 months from onset, with a worse prognosis for patients with a bulbar onset [2]. While not all patients present with dysarthria as an initial symptom, at least 80% of patients with ALS experience dysarthria, regardless of onset location [8]-[9].

Because speech production engages a vast cortical and subcortical network [11], it may be particularly sensitive to motor neuron degeneration. Using speech for early ALS detection, therefore, has the potential to identify people with bulbar onset ALS or people with spinal onset ALS who have less-pronounced, though still present, bulbar symptoms [12]-[15]. Earlier detection of speech symptoms could confirm a diagnosis of ALS and lead to early treatment [1].

Current measures of ALS speech signs and symptoms include one item on the patient-reported ALSFRS-R [16], speaking rate, speech intelligibility [5], pausing, and articulatory kinematics [8], [13], [17]. While there are several well-identified acoustic characteristics of ALS dysarthria, including changes to vocal quality, loudness, and speaking rate, these symptoms vary among patients [13]. Machine learning (ML) approaches that are based on a large number of acoustic speech features might be particularly well suited to detect speech changes despite the large heterogeneity in speech symptoms across patients. The studies in [18]-[23] have demonstrated that ML can detect ALS and monitor its progression based on individual speech samples. Like [18]-[23], our approach used large-space acoustic features extracted using OpenSMILE [24].

In this study, we tested an ML approach (support vector machine) to detect ALS before overt speech symptoms develop. We also evaluated the use of an ML classifier as a progress monitor for speech severity in ALS. To address these aims, we sought to answer the following questions: What is the best speech acoustic feature set for an early diagnostic classifier? Should an early diagnostic model include only bulbar presymptomatic ALS participants, or should it

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comprise the full range of ALS speech severity? How well do these classifiers respond to speech severity change?

2. Methods

2.1. Speech corpus

The dataset included a total of 123 participants with one speech sample produced by each participant. Participant demographics are displayed in Table 1. As in [25]-[26], the speech samples were of the first sentence of the Bamboo passage, "Bamboo walls are getting to be very popular." The samples were recorded to a wav file with a sample rate of 44.1k or higher (16 bit) using a professional headset microphone that was positioned approximately 5 cm from the mouth. Incomplete or poor-quality recordings were excluded from analyses and the participant count.

2.2. Participant stratification

Participants were stratified into one of three groups: Control, Symptomatic, and Presymptomatic. Participants in the Symptomatic were operationally defined as having ALS as well as speech intelligibility below 96% and/or speaking rate below 150 words per minute (WPM), both measured using the Sentence Intelligibility Task (SIT) [27]. Participants in the Presymptomatic group had ALS but did not meet the above criteria for bulbar symptoms. Control participants were age-matched, neurologically normal, and had normal intelligibility and speaking rate.

Speaking rate and intelligibility were chosen as stratification criteria. Prior work has linked speaking rate to early bulbar symptoms in ALS [5]-[8], [13], [17], [28]. Speech intelligibility, how well a listener can understand a speaker, is a common metric used to assess speech function [29], [8]. Participants who met either Symptomatic criterion were stratified into the Symptomatic group. Sexes were evaluated separately since sex differences are known to affect F0, harmonic spacing, and resonatory characteristics [30].

Table 1: *Participant stratification.*

Group	Total	Male	Female
Control	36	15	21
Symptomatic ALS	51	36	15
Presymptomatic ALS	36	23	13

2.3. Acoustic analysis

Acoustic analysis was conducted using the OpenSMILE [24] large-space acoustic feature extractor on audio that was down-sampled to 16kHz. OpenSMILE extracts low-level acoustic descriptors from the audio sample (e.g., MFCC 1-14, F0) and then applies a set of functions (e.g., arithmetic mean, skewness) to those descriptors [24]. We used the ComPare13 configuration to extract our feature set [31], with additional measures of formant frequencies, bandwidth, and loudness. This acoustic analysis yielded 6861 features.

2.4. Classification

Off-the-shelf support vector machine (SVM) classifiers [32] were trained on feature sets using leave-one-out cross-validation with within-fold univariate feature selection and z-score standardization. We compared SVM classifiers with a non-linear radial basis function (RBF) and a linear kernel.

2.4.1. Feature selection and model sample

To determine the optimal feature set for ALS classification, we compared feature selection, which evaluates feature subsets, and feature filtering, which selects individual features.

We tested feature selection methods of recursive feature elimination and random forest classification [32]. However, an SVM approach with univariate feature selection (KBest) was favored because it proved less computationally demanding and equally successful. We then categorized the features into seven broad categories: mel-frequency cepstral coefficients (e.g., MFCC 1-14), formant (e.g., F1), energy (e.g., RMS energy), F0 (e.g., F0), spectral (e.g., spectral flux), temporal (e.g., MCR), and voice quality (e.g., shimmer).

To determine the best of three possible diagnostic models, we compared the accuracy of models trained on samples from Symptomatic vs. Control, Presymptomatic vs. Control, and all ALS vs. Control participants. The all ALS group included both Symptomatic and Presymptomatic ALS participants.

2.4.2. Classifier evaluation

Classifiers were evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC), an accuracy approximation that was used to derive specificity and sensitivity. The classifiers assigned each participant a bulbar ALS probability. We compared the distribution of bulbar ALS probability among Control, Presymptomatic, and Symptomatic groups to determine whether the classifier-assigned probability of having ALS could distinguish the three groups. If so, then the classifier could potentially serve as an index of speech severity or as a progress monitoring tool. The validity of the bulbar ALS probability scores was assessed by determining the strength of association between the scores and three measures of speech severity: speaking rate, speech intelligibility, and intelligible speaking rate [19], [33]. Intelligible speaking rate (speaking rate x speech intelligibility) measures communication efficiency [20].

3. Results

3.1. Feature set optimization

Because the linear and RBF kernels performed comparably, we only report the results obtained using the linear kernel.

Overall, classifiers trained on filtered feature sets had higher AUC than those trained on the complete set of features. Classifiers trained on MFCC features performed better than classifiers trained on other categories of features. Table 2 presents the AUC for female Symptomatic-Control classifier models trained on an illustrative selection of feature sets. Models trained on both genders performed more inconsistently than gender-specific models, though occasionally reaching comparable results.

Table 2: *Performance of female Symptomatic-Control classifier models with various feature sets.*

Feature Set	AUC
Complete feature set	0.83 ± 0.35
64-best features	0.99 ± 0.00
All MFCC features	0.90 ± 0.27
All voice quality features	0.80 ± 0.36

3.2. Model set optimization

The model with the highest accuracy for females was the Symptomatic-Control model trained on the 64-best features (AUC=0.99). The top-performing female all ALS-Control model was trained on the 4-best features (AUC=0.85). The female Presymptomatic-Control model with the highest AUC was trained on the complete feature set (AUC=0.69). See Figure 1 and Table 3.

For males, the highest performing model was the all ALS-Control mode trained on the full set of 1416 MFCC features (AUC=0.91). The top-performing male Symptomatic-Control model (AUC=0.90) and the top Presymptomatic-Control model (AUC=0.70) were also trained on the full set of MFCC features. See Figure 2 and Table 4.

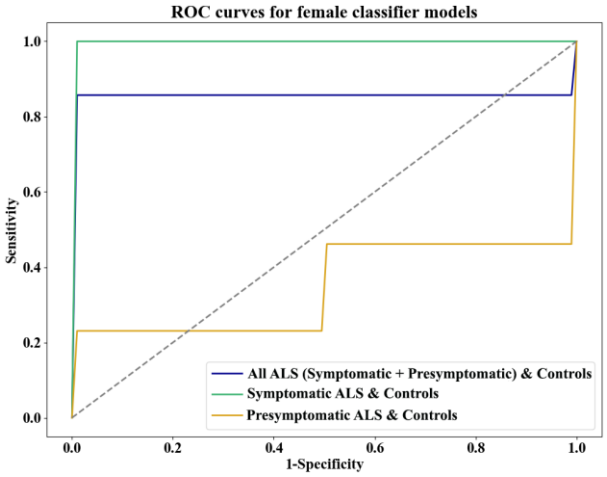

Figure 1: *ROC curves for female classifier models.*

Table 3: *Top-performing female classifiers for each model.*

Female Classifier Model	Feature Set	AUC
all ALS-Control	4-best features	0.85 ± 0.35
Symptomatic-Control	64-best features	0.99 ± 0.00
Presymptomatic-Control	All features	0.69 ± 0.42

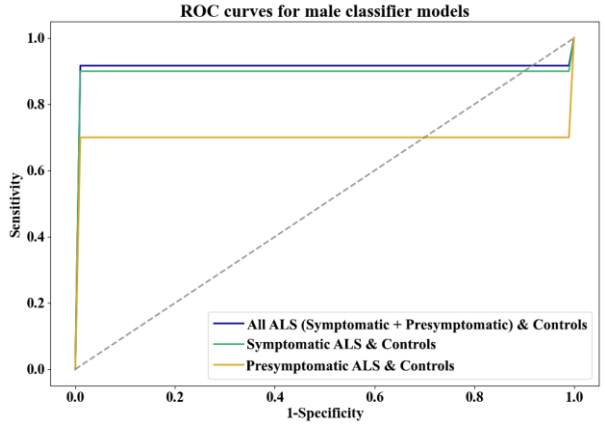

Figure 2: *ROC curves for male classifier models.*

Table 4: *Top-performing male classifiers for each model.*

Male Classifier Model	Feature Set	AUC
all ALS-Control	MFCC features	0.91 ± 0.15
Symptomatic-Control	MFCC features	0.90 ± 0.27
Presymptomatic-Control	MFCC features	0.70 ± 0.44

3.2.1. Distribution of classification probability

Figure 3 and Figure 4 contain boxplots of the bulbar ALS probability distribution for each group using the models trained on the all ALS-Control sample. We performed an ANOVA with Tukey's HSD post-hoc test to compare the bulbar ALS probability distribution between the groups.

For females, the bulbar ALS probability differed significantly among all groups ($p<0.001$), between Presymptomatic and Control ($p<0.001$), and between Symptomatic and Control ($p<0.001$); it did not differ significantly between Symptomatic and Presymptomatic ($p=0.196$). The bulbar ALS probability for males was significantly different among all groups ($p<0.001$), between Presymptomatic and Control ($p<0.001$), Symptomatic and Control ($p<0.001$), and Symptomatic and Presymptomatic ($p<0.05$).

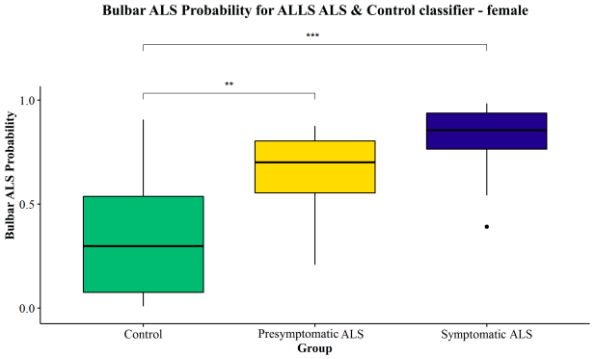

Figure 3: Group differences in the distribution of classification probability using the best all ALS-Control model for female participants. ***: $p<0.001$, **: $p<0.01$, *: $p<0.05$

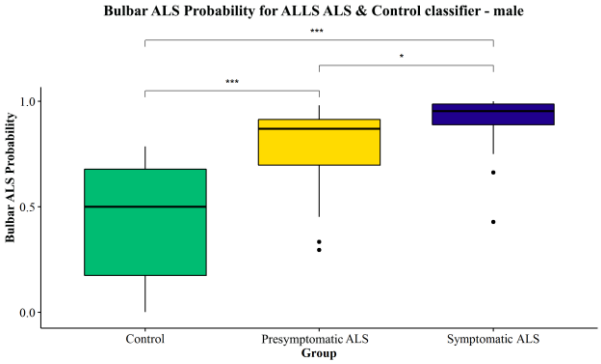

Figure 4: Group differences in the distribution of classification probability using the best all ALS-Control model for male participants. ***: $p<0.001$, **: $p<0.01$, *: $p<0.05$

3.3. Correlation with speech severity measures

For these top-performing all ALS-Control classifiers, we compared bulbar ALS probability to measures of ALS speech severity (Table 5). For the female model, bulbar ALS probability was negatively correlated with speaking rate and intelligible speaking rate but not with speech intelligibility. For the male model, bulbar ALS probability was negatively correlated with speaking rate, intelligible speaking rate, and weakly with intelligibility.

Table 5: *Correlation between bulbar ALS Probability and three measures of speech severity: speaking rate, intelligible speaking rate, and intelligibility. Probabilities were obtained from top-performing male and female all ALS-Control classifiers. ***: p<0.001, **: p<0.01, *: p<0.05*

All ALS-Control model	**Speech severity measure**	**Spearman coefficient**	**p**	**df**
Female Trained on the 4-best features	Speaking rate	-0.60	***	26
	Intelligible speaking rate	-0.65	***	
	Intelligibility	-0.34	NS	
Male Trained on MFCC features	Speaking rate	-0.43	***	57
	Intelligible speaking rate	-0.40	**	
	Intelligibility	-0.35	**	

4. Discussion

To test an early bulbar ALS diagnostic tool, we trained ML models for each sex on several filtered feature sets. We found that models trained on reduced feature sets tended to outperform models trained on the complete set of OpenSMILE extracted features. Of note, classifiers trained on MFCC features had a higher accuracy than those trained on other feature categories. While MFCC features lack a clear anatomic interpretation, these features have been used extensively in prior research to identify speakers and their affective states [34]. Thus, these models may also be detecting changes from comorbid affective states, such as depression [1]-[2]. Future studies should explore the potential link between comorbid conditions in ALS and their effects on speech.

The ML model performed exceptionally well when trained on Symptomatic and Control participants data, yielding an AUC=0.99 for female participants and AUC=0.91 for male. These results affirm the ability of an ML model to classify symptomatic ALS speech. The relatively small sample size may have influenced the high success of the female Symptomatic-Control model. However, because all the classifiers were tested using the same set of participants, sample size did not account for differences in classifier performance.

Although our diagnostic goal was to identify presymptomatic patients, we found that models trained on Presymptomatic-Control data performed around chance, probably due to our small sample size. [21] obtained an above-chance classification performance for participants with early ALS (71.6% sensitivity and 80.9% specificity), possibly due to their larger gender-mixed dataset and more complicated ML algorithm (convolutional neural network).

Our gender-specific models trained on all ALS-Control data performed with high accuracy (AUC=0.85 for female; AUC=0.91 for male) and had a probability distribution that differentiated Presymptomatic and Control participants ($p<0.001$ for each sex). Perhaps all ALS-Control models achieved higher accuracy than models trained on ALS subsets because the dataset provided a fuller range of speech severity with which to contrast the groups. Indeed, our results indicate that these models classified Control, Presymptomatic, and Symptomatic groups along a gradient: Symptomatic had the highest ALS probability, followed by Presymptomatic, and finally Control. Furthermore, these classifiers seem capable of detecting subtle differences in ALS speech that are separate from speaking rate and speech intelligibility. Such performance supports the use of a machine learning classifier as a diagnostic tool to identify people with early signs of bulbar ALS.

Because our study used cross-sectional data, we were unable to confirm whether the Presymptomatic group later developed more pronounced speech signs of ALS. A future study could use longitudinal data to directly track disease progression in participants or create a predictive model.

To asses ML classifiers for indexing speech severity, we compared the ALS probability with currently used clinical measures of speech severity. We found that the ALS probability correlated with SIT speaking rate and with SIT intelligible speaking rate for both sexes, and it correlated weakly with SIT intelligibility for males. These results align with previous findings that speaking rate is more sensitive to early speech changes in ALS than speech intelligibility [13] and support ML classifiers as disease progression monitors of ALS.

5. Conclusion

We developed machine learning classifiers trained on filtered sets of acoustic features to accurately identify male and female participants with symptomatic and presymptomatic bulbar ALS. With further development, the approach may be useful for monitoring the clinical progression of speech symptoms.

6. Acknowledgements

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