Predicting Disease Progression Trajectories in Individuals with Amyotrophic Lateral Sclerosis using Multimodal Digital Biomarkers

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Methodological Issue Being Addressed Disease progression in ALS is heterogeneous due to the varying presentation of clinical symptoms. This heterogeneity makes it difficult to accurately quantify longitudinal disease severity in people with ALS (pALS), thereby making it difficult to determine the efficacy of therapeutic interventions. Most of the work done to model disease progression in ALS assumes that the clinical gold standard to measure disease state, the ALSFRS-R, declines in a linear manner. However, there is evidence that ALS progression can be non-linear and that progression may vary longitudinally.

Introduction In this work, we explore a non-linear model that can help predict individual trajectories in pALS with sparse data.

Methods We used data from 143 pALS who interacted with a cloud-based multimodal assessment platform comprising standard speaking exercises. Analytical modules were used to extract multimodal metrics in real time from data collected during these exercises. We trained a nonlinear Bayesian logistic mixed effects model to predict individual trajectories of 21 features - 17 speech/orofacial video/linguistic metrics, a perceptual rating of speech impairment (PSI; derived using a visual analogue scale and multiple raters), the total ALSFRS-R score, ALSFRS-R bulbar subscore and the ALSFRS-R speech score. We used a leave-one-out cross validation approach to test the performance of the model in predicting the values of these 21 features for all participants. Model performance was evaluated using normalized mean absolute error (nMAE) which accounts for the difference in ranges across features.

Results We found that nMAE was < 0.2 for all automatically-extracted multimodal metrics, PSI and for the ALSFRS-R total score and ALSFRS-R bulbar subscore. Speech biomarkers performed better than orofacial video biomarkers. We observed the best performance for the mean fundamental frequency while reading a passage (nMAE = 0.06). Model performance was the worst in predicting the ALSFRS-R speech score (nMAE = 0.26).

Conclusion This suggests that non-linear models using multimodal digital biomarkers offer more promise and precision than the current clinical standard for predicting individual disease progression trajectories in ALS.

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Keywords

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