Analysis and prediction of ALS patient disease state using machine-learning algorithms

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Abstract

Amyotrophic lateral sclerosis (ALS) is a devastating and incurable disease of motor neurons, leading to progressive paralysis and death. The disease is characterized by high heterogeneity among the patients regarding its progression and development, which makes it difficult to achieve significant results in clinical trials for developing medications and treatments.

Nowadays, clinical trials and studies focus on a disease functionality measure called ALS functional rating scale (ALSFRS) that assesses the patient's condition in performing ten daily functions (as walking, breathing, etc.). Although this measure is useful as an indicator of patient dysfunction, it is too general and not specific enough to describe patient muscle and organ deterioration patterns.

A new approach, based on data of manual muscle testing (MMT) of ALS patients to assess disease state, was found reliable and suitable. Using machine-learning tools to analyze MMT data collected in the Tel-Aviv Medical Center (TAMC) from patients' clinic visits, we uncovered different deterioration patterns of patients and found homogeneous groups in the heterogeneous patient population. We explored these groups separately to find common as well as distinguishing characteristics, with the hope of simplifying the study of the disease and its causes.

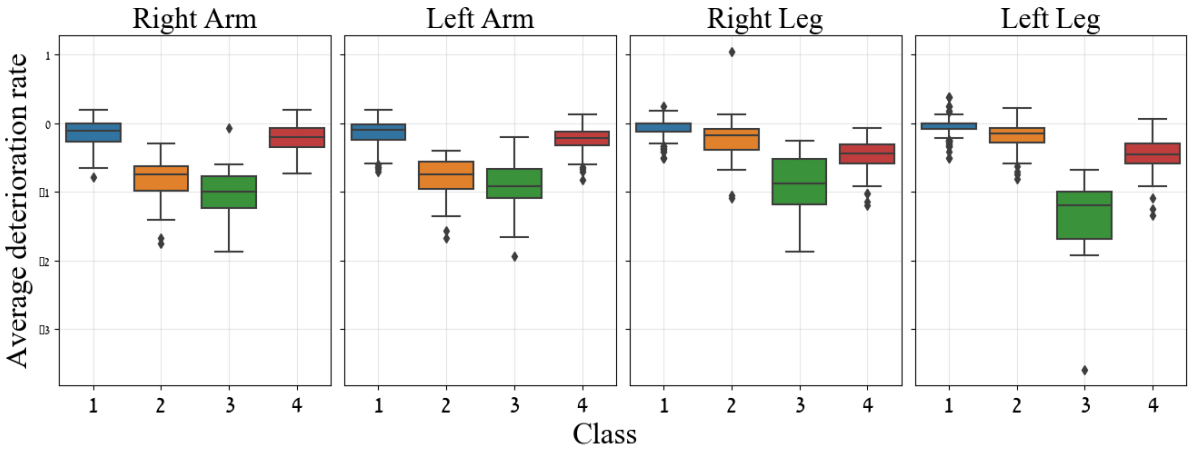

Figure 1: MMT limb deterioration rate by cluster (4 clusters)

Figure 1 demonstrates the results of patient stratification. Cluster 1 is characterized by high overall rate of deterioration. Cluster 2 is characterized by a high deterioration rate in the arm muscles and low deterioration rate in the leg muscles. Cluster 3, in contrast to cluster 1, is characterized by a high rate of overall deterioration, and cluster 4, in contrast to cluster 2, is characterized by a high deterioration rate in the leg muscles and a low deterioration rate in the arm muscles.

For prediction, we compared non-temporal ensemble models (random forest and XGBoost) with a temporal neural network, called long-short term memory (LSTM), by comparing the ALSFRS predicted values with the real ones (representing the real disease state) for each clinic visit.

Method	RMSE	MAE	PCC	CI
LSTM	4.79 (0.44)	3.74 (0.36)	0.81 (0.05)	0.78 (0.03)
RF	3.70 (0.28)	2.87 (0.22)	0.91 (0.02)	0.85 (0.02)
XGBoost	**2.99 (0.25)**	**2.32 (0.20)**	**0.93 (0.02)**	**0.86 (0.02)**

Table 1 Model comparison results.

In Table 1, we demonstrate that the ensemble methods achieve higher accuracies than the LSTM using the TAMC clinical database, and especially the XGBoost with the best prediction performance according to all the evaluation measures.

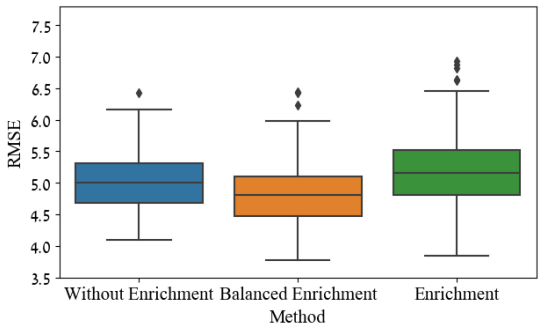

Figure 32 RMSE reduction using balanced enrichment methodology

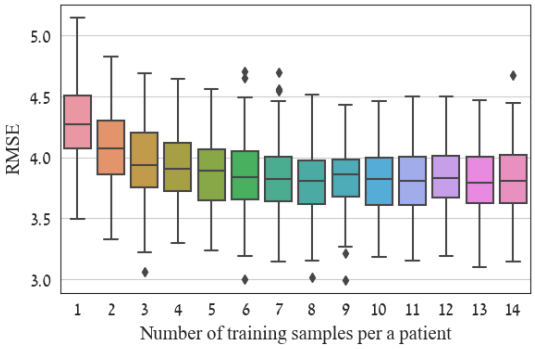

Figure 23 RMSE reduction using enrichemnt methodology

In addition, we demonstrate accuracy improvement when using a data enrichment methodology, we developed and applied during training. Data enrichment enables the models to learn from more data extracted from the available longitudinal data. The results show that for both the LSTM (Figure 2) and random forest model (Figure 3), enrichment improves the accuracy.

Keywords: machine learning, clustering, ALS, longitudinal data, prediction, MMT