Exploring Predictive Models of Alzheimer's Disease Severity based on Resting State EEG and MRI Features

Belmir Jesus Jr.[1], Raymundo Cassani[1], Marco Cecchi [2], K.C. Fadem [2], William J. McGeown [3] and Tiago H. Falk [1]

[1] Institut National de la Recherche Scientifique, University of Quebec, QC, Canada.

[2] Cognision, Louisville, KY, USA.

[3] School of Psychological Sciences and Health, University of Strathclyde, Glasgow, UK.

Abstract

Objectives: With the objective to characterize the progression of the cognitive impairment associated with Alzheimer's disease, this project investigates the relationship between features derived from electroencephalography (EEG) and from magnetic resonance imaging (MRI) scans, with mean-mental state examination (MMSE) scores in participants in different stages of AD. Furthermore, selected groups of these features were utilized to develop a regression model to predict MMSE scores.

Features Description: The data analyzed in this study was derived from two different datasets: Dataset 1 (D1) was comprised by EEG and MRI recordings, and dataset 2 (D2) by EEG recordings only. Dataset D1 corresponds to data collected from 89 subjects diagnosed with mild AD, and have MMSE scores in the 21 to 26 range. EEG signals were collected from 7 electrodes with sampling frequency of 125 Hz during a 3-min resting-awake eyes-open period. T1-weighted structural MRI scans from the same subjects were also captured and the available scans presented no movement or subsequent segmentation artifacts. In dataset D2, in turn, EEG signals were collected from a different group comprised by 32 subjects diagnosed with mild-to-severe AD with MMSE scores between 4 and 26. EEG signals were collected with a sampling frequency of 200 Hz during a 8-min resting-awake eyes-closed period from 20 electrodes which later were decimated channel-wise to have the same electrode layout as in dataset D1, thus allowing for comparison between the results. For both datasets, four different types of features were computed from the acquired EEG signals: spectral power, magnitude squared coherence, amplitude modulation rate-of-change, and modulation domain features. Moreover, these four types of features were computed from raw EEG signals and wavelet independent component analysis (wICA) pre-processed EEG signals. Additionally, the summary statistics (mean, standard deviation, coefficient of variation, median, skewness, and kurtosis) were calculated for the four types of EEG features [1]. Lastly, MRI features were computed for dataset D1 using Freesurfer with the default recon-all pipeline. Subcortical volumes, region-of-interest (ROI) cortical thickness (CT) were extracted.

Feature Selection: Since the number of computed features was high relative to the number of available data samples, feature selection was performed. In an attempt to select the most significant features, an evaluation by their Spearman correlation coefficient with the MMSE scores of the subjects was performed. The computed EEG and MRI features were further organized into five categories, namely features derived from: raw EEG from dataset D1, wICA-processed EEG from dataset D1, raw EEG from dataset D2, wICA-processed EEG from dataset D2, and MRI data from dataset D1. In this regard, the correlation coefficients for each of the groups were ranked and the correlations that presented a p-value smaller than 0.05 were taken into consideration.

Once the feature rankings were computed, the top-10 features of each of the five feature categories were used to assemble five groups of features as follows: the first group corresponded to the top-10 features of the first category of features; the second group to the top-10 features of the second category of features; a third group of features was formed by the top-10 features of the fifth category

of features (MRI features). These three feature groups were formed from dataset D1 to allow the comparison between MRI and EEG features. Additionally, two more feature groups were formed with the purpose of evaluating features that appeared in the top-10 rankings of both datasets. Thus, the fourth group of features was formed from the top-10 common EEG features between the first and third categories. Lastly the fifth group of features comprised the top-10 common EEG features from the second and fourth categories. To explore the complementary nature of MRI and EEG features in the determination of severity of AD, four additional feature groups were created by combining pairs of EEG and MRI features. Thus, the sixth group was the combination of the first and third feature groups; group seven comprised the second and third feature groups; group eigh was formed from the concatenation of groups four and three; and, the ninth group consisted in the combination of the third and fifth feature groups. Feature groups from 1 to 5 are considered unimodal as they are associated with features from only one modality (either EEG or MRI). On the other hand, groups 6 to 9 are considered multimodal since they are associated with the two modalities.

Regression Analysis: Four different regression models were explored: multiple linear regression (LR) [2], support vector machine regression with linear (SVM-linear) and Gaussian (SVM-RBF) kernels [3], and random forest regression (RF) [4]. All the models were developed using each of the selected groups of features and the models were implemented with the open-source scikit-learn library for python [5]. The min-max normalization was applied to all sets of selected features before training of the models. In order to evaluate each of the models the root mean squared error (RMSE) was selected as an evaluation metric. Ten-fold cross-validation (CV) was used and grid search was implemented in order to identify the best parameters to be used in each model.

Results/Discussion: Overall, the average RMSE values obtained from the predictions stayed below 10% of the average MMSE scores (i.e., 2.333). The best result was achieved with the sixth feature group (features from group 1 and 3) using the SVM-linear algorithm; an RMSE = 1.54 was obtained. Models that used LR seemed to perform worse for most feature groups. Analyzing the unimodal feature groups (1 to 5), the features derived from raw EEG signal (without a pre-processing stage) resulted in better performances when compared to features from wICA-processed EEG. In addition, the SVM-linear algorithm presented similar performance to the SVM-RBF for these groups of features. The models that were trained with the features derived from MRI features (group 3), with exception of the LR algorithm, presented similar performance among them. Additionally, the models using the MRI features resulted in lower RMSE scores relative to the models trained with only EEG features. Finally, SVM-linear algorithm for the multimodal group of features 6, and RF algorithm for multimodal groups of features 7, 8 and 9 presented the lowest RMSE overall, thus emphasizing the complementarity of the EEG and MRI modalities for Alzheimer's disease severity prediction.

***Keywords*—** Alzheimer's Disease, severity, rsEEG, MRI, multimodal models.

References

[1] R. Cassani, T. H. Falk, F. J. Fraga, M. Cecchi, D. K. Moore, and R. Anghinah, "Towards automated electroencephalography-based alzheimers disease diagnosis using portable low-density devices," *Biomedical Signal Processing and Control*, vol. 33, pp. 261–271, 2017.

[2] R. H. Myers and R. H. Myers, *Classical and modern regression with applications.* Duxbury press Belmont, CA, 1990, vol. 2.

[3] A. J. Smola and B. Schölkopf, "A tutorial on support vector regression," *Statistics and computing*, vol. 14, no. 3, pp. 199–222, 2004.

[4] M. R. Segal, "Machine learning benchmarks and random forest regression," 2004.

[5] F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, M. Blondel, P. Prettenhofer, R. Weiss, V. Dubourg *et al.*, "Scikit-learn: Machine learning in python," *Journal of machine learning research*, vol. 12, no. Oct, pp. 2825–2830, 2011.