Comparative Study of Cognitive Impairment Modeling for Alzheimer's Disease – Longitudinal *vs*. Cross-Sectional

Mahdi Moghaddami
Department of Computer Science and Engineering
Oakland University
Rochester, MI, USA
moghaddami@oakland.edu

Mohammad-Reza Siadat
Department of Computer Science and Engineering
Oakland University
Rochester, MI, USA
siadat@oakland.edu

Abbas Babajani Feremi
Department of Neurology
University of Florida
Gainesville, FL, USA
babajani.a@ufl.edu

for the Alzheimer's Disease Neuroimaging Initiative

***Abstract*— This study compares two modeling categories, longitudinal and cross-sectional, for predicting the clinical diagnosis of cognitive impairment in Alzheimer's disease. Various machine learning algorithms from each class are applied to neuroimaging and cognitive assessment features of subjects in the TADPOLE dataset. Statistical tests are utilized to compare the performances of algorithms within and between the two categories. Surprisingly, the study found that, on average, cross-sectional algorithms outperformed longitudinal ones. This contrasts with the expectation that longitudinal algorithms would perform better. The results suggest the need for further development of longitudinal algorithms for cognitive impairment modeling or, more importantly, exploring additional features that more precisely represent the development and progression of cognitive impairment toward Alzheimer's disease.**

I. INTRODUCTION

Early detection and accurate diagnosis of cognitive impairment (CI) are crucial for effectively managing and potentially treating Alzheimer's disease (AD) [1]. Numerous studies have been conducted to model CI and predict the onset of AD. Two distinct approaches have been used in these studies: 1) cross-sectional [2] and 2) longitudinal [3]. Longitudinal algorithms, leveraging the progression of CI over time, are expected to outperform cross-sectional algorithms [4]. However, no comparative statistical study has investigated this expectation.

This study aims to compare the performance of algorithms within and between the two categories for predicting the clinical diagnosis of CI and its progression.

II. METHODS

The study uses subjects from the Alzheimer's Disease Prediction Of Longitudinal Evolution (TADPOLE) [5] challenge dataset. We examine linear state space (LSS), minimal recurrent neural network (mRNN), and long short-term memory (LSTM) for the longitudinal category, and Logistic Regression (LR), Naïve Bayes (NB), and Random Forest (RF) for the cross-sectional category.

The features considered in this study include neuropsychological evaluation scores, PET measures, and previous diagnosis. Because cross-sectional algorithms do not perform missing value treatment, they can only use visits with no missing clinical diagnosis and features. On the other hand, longitudinal algorithms impute missing values as they arrive at each visit, allowing them to utilize all visits and features in the dataset. We adopt the same metrics as those used in the TADPOLE challenge: multiclass area under the operating curve (mAUC) and balanced class accuracy (BCA).

III. RESULTS

We compare the performance of longitudinal and cross-sectional algorithms predicting the test set's clinical status within and between the two categories using statistical tests. Table I reports the average performance of algorithms in the two categories.

TABLE I. PERFORMANCE OF ALGORITHMS IN EACH CATEGORY

	BCA	***mAUC***
Longitudinal	0.869 ± 0.062	0.907 ± 0.080
Cross-Sectional	0.878 ± 0.070	0.926 ± 0.066

The two-sample *t*-test indicates that the average performance of the cross-sectional algorithms is significantly better than that of the longitudinal category, which is an unexpected result.

IV. DISCUSSION & CONCLUSION

One important factor to consider is that the number of visits used to train the longitudinal algorithms was about five times larger than that of the longitudinal algorithms. Additionally, the cross-sectional algorithms lacked five features that were available to the longitudinal algorithms.

While longitudinal algorithms are expected to outperform cross-sectional ones when applied to datasets with longitudinal characteristics, our study of modeling CI progression and predicting the onset of AD did not support this expectation. This suggests the need for further development of longitudinal algorithms for cognitive impairment modeling. More importantly, the results highlight the importance of discovering new features that more accurately represent the development of cognitive impairment and its progression towards Alzheimer's disease.

REFERENCES

[1] W. Jagust, "Vulnerable neural systems and the borderland of brain aging and neurodegeneration," Neuron, vol. 77, Issue 2, pp. 219–234, 2013. (https://doi.org/10.1016/j.neuron.2013.01.002)

[2] K. Silva, H. Kunz, "Prediction of Alzheimer's disease from magnetic resonance imaging using a convolutional neural network," Intelligence-Based Medicine, vol. 7, pp. 1-7, 2023.

[3] M. Nguyen, T. He, L. An, et al., "Predicting Alzheimer's disease progression using deep recurrent neural networks," NeuroImage, vol. 222, 2020.

[4] S. Tang, P. Cao, M. Huang, X. Liu, O. Zaiane, "Dual feature correlation guided multi-task learning for Alzheimer's disease prediction," Computers in Biology and Medicine, vol. 140, pp. 1-22, 2022.

[5] R. V. Marinescu, N. P. Oxtoby, A. L. Young, et al., "TADPOLE Challenge: prediction of longitudinal evolution in Alzheimer's disease," CoRR abs/1805.03909, 2018.