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POSTER PRESENTATION

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TA-RNN: an Attention-based Time-aware Recurrent Neural Network Architecture to Predict Progression of Alzheimer's Disease

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Abstract

Background: Alzheimer's Disease (AD) is a widespread neurodegenerative disease with Mild Cognitive Impairment (MCI) acting as an interim phase between normal cognitive state and AD. The irreversible nature of AD and the difficulty in early prediction present significant challenges for patients, caregivers, and the healthcare sector. Deep learning (DL) methods such as Recurrent Neural Networks **(RNN)** have been utilized to analyze Electronic Health Records (EHR) to model disease progression and predict diagnosis. However, these models do not address some inherent irregularities in EHR data such as irregular time intervals between clinical visits. Furthermore, most DLmodels arenot interpretable.To address these issues, we developed anovel DL architecture called Time-Aware RNN (TA-RNN) to predict MCI to ADconversion at the nextclinical visit.

Method: TA-RNN comprises of a time embedding layer, attention-based RNN, and prediction layer based onmulti-layer perceptron (MLP) (Figure 1).For interpretability, a dual-level attention mechanism within the RNN identifies significant visits and features impacting predictions. TA-RNN addresses irregular time intervals by incorporatingtimeembedding intolongitudinal cognitiveandneuroimagingdatabased onattention weightsto create apatient embedding. The MLP,trained on demographic data and the patient embedding predicts AD conversion. TA-RNN was evaluated on Alzheimer's Disease Neuroimaging Initiative (ADNI) and National Alzheimer's CoordinatingCenter (NACC) datasets based on F2 score and sensitivity.

Result: Multiple TA-RNN models were trained with two, three, five, or six visits to predict the diagnosis at the nextvisit. In one setup,the models weretrained andtested on ADNI. In another setup, the models were trained on the entire ADNI dataset and evaluated on the entire NACC dataset.The resultsindicated superior performance of

TA-RNNcomparedto state-of-the-art (SOTA) and baseline approaches for bothsetups (Figure 2A and 28). Based on attention weights, we also highlighted significant visits (Figure 3A) and features (Figure 38) and observed that CDRSB and FAQ features and the most recent visithadhighest influence in predictions.

Conclusion: We propose TA-RNN, an interpretable model to predict MCI to AD conversion while handling irregular time intervals. TA-RNN outperformed SOTA and baseline methods in multiple experiments.

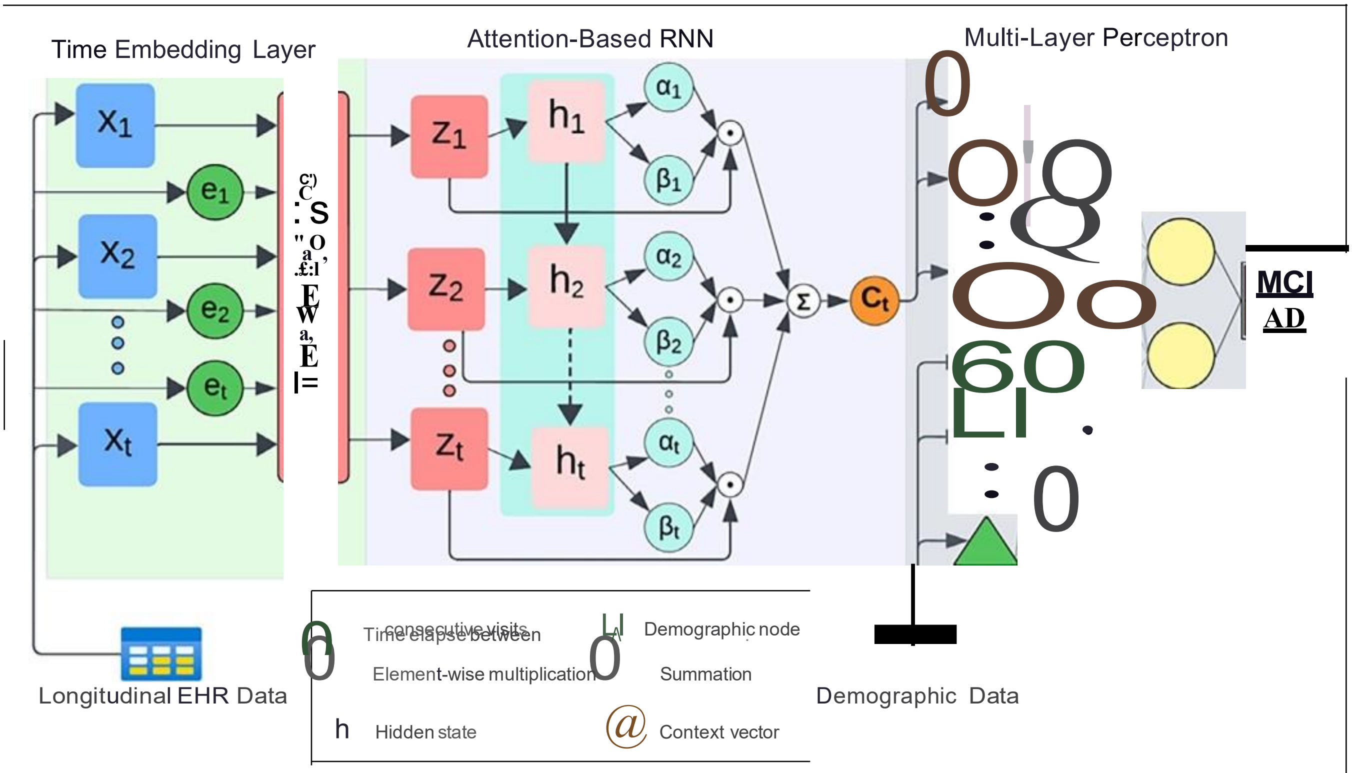

Figure l. TA-RNN architecture for predicting of conversion to AD at the next visit.

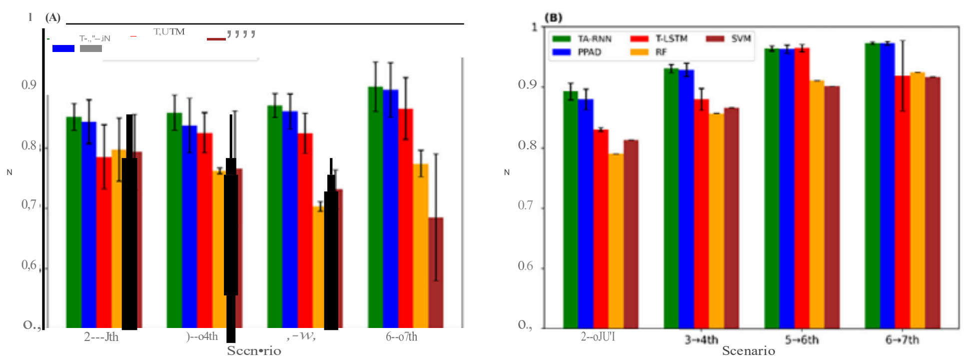

Figure 2. F2 scores for TA-RNN models to predict conversion to AD at the next visit. (A) Models tesled on held-out samples in ADNI after training using two, three, five, and six visits in ADNI, respectively. (B) Models tested on NACC after training using two, three, five, and six visits in ADNI, respectively.

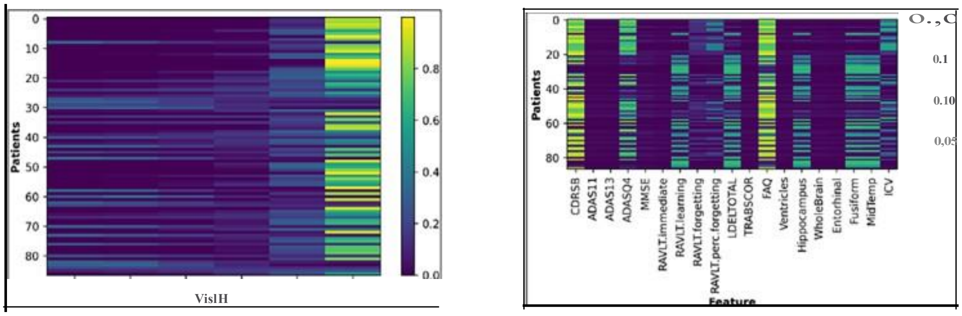

Figure 3. Attention weights (A) Attention weights at the visit level for TA-RNN. TA-RNN evaluated 011 held-out samples in ADNI after training usingsix preceding visits in ADNL (B) Average attention weights at the feature level for TA-RNN. TA-RNN wasevaluated on held-out samples in ADNI after training usingsix preceding visits in AD!"'!.