Deep-Learning-Based Multi-modal Survival Analysis for Alzheimer's Disease

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Key Takeaway

- ✓ An in-depth examination of the factors that contribute to the progression of DAT can yield an accurate estimate of time-to-conversion for patients at various disease stages.
- ✓ Stratification reveals that different progression groups benefit from different modalities for predicting time-to-conversion
- ✓ Using the current clinical procedure including gathering cognitive test results can outperform survival analysis results produced using costly and invasive genetic or CSF data

Introduction

- Multiple factors contribute to the development and progression of Dementia of Alzheimer's Type (DAT), but the magnitude of each factor's impact on the disease is unknown.
- Recent advances in Deep Learning enable researchers to precisely estimate the underlying relationship between multiple data modalities and DAT and identify the most relevant factors in such complex diseases.
- Using deep learning on multi-modal data, we performed a comprehensive analysis on the prediction of time-to-conversion to DAT on subjects at various stages of the disease, and compared the predictive power of each modality on disease diagnosis and progression.

Methods

Experimental Data

- 401 subjects from ADNI who had MRI, genetic, and CDC (Cognitive tests + Demographic + CSF) data available.
- Subjects were stratified into five subgroups based on clinical diagnosis at the time of MRI image acquisition and longitudinal clinical progression [1].

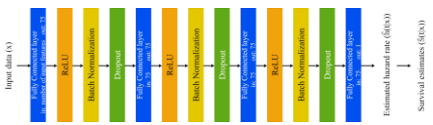
Progression group	Group name	Clinical diagnosis at baseline	Clinical progression	Subjects [M:F]
Non-progressive[b]	sNC: stable NC	NC[a]	**NC** → **NC**	58:51
Non-progressive	uNC: unstable NC	NC	**NC** → MCI	14:8
Non-progressive	sMCI: stable MCI	MCI[a]	**MCI** → **MCI**	65:36
Progressive[b]	pNC: progressive NC	NC	**NC** → MCI → DAT	6:8
Progressive	pMCI: progressive MCI	MCI	**MCI** → DAT	99:56

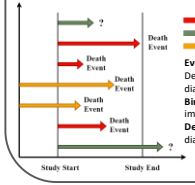
[a] NC: normal control, MCI: mild cognitive impairment,
[b] Non-progressive: censored, subjects who did not receive a DAT diagnosis within the study window, Progressive: uncensored, subjects who received a diagnosis of DAT during the study window,
[c] Clinical diagnosis at baseline is shown in **bold** under the "Clinical progression" column.

Survival Analysis

Survival Analysis: Analysis of the time an individual will experience an event of interest.

Network Architecture





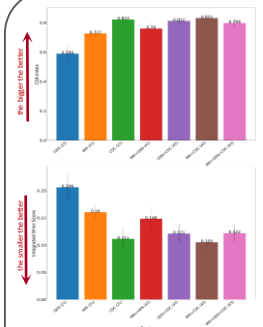
Uncensored (pNC, pMCI)
Right-censored (sNC, uNC, sMCI)
Left-censored (eDAT, tDAT)

Event of interest: Dementia onset (DAT diagnosis)
Birth event: Baseline imaging visit
Death event: DAT diagnosis confirmation

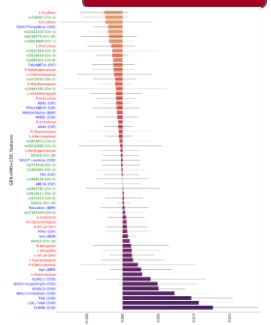
- DeepSurv [2] (non-linear version of Cox regression [3])
- Multilayer Perceptron (MLP) as the base model
- **Input**: subjects' feature vector (x), including MRI, genetic, or CDC features
- **Output**: DAT survival estimate over 10 years

Hyperparameters	Values
Hidden Layers	3
Nodes	75
Dropout	0.3
Wight decay	0.01
Batch size	16

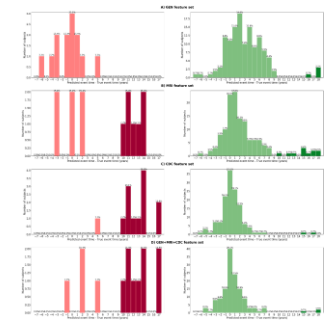
Results



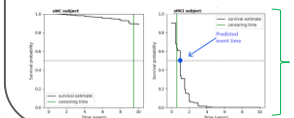
- Performance comparison between different feature sets
- **CDC** works the best amongst single modality feature sets
- Combining **MRI** and **GEN** (**MRI+GEN**) improves the performance
- Adding CDC to any feature set improves the performance over using that feature set



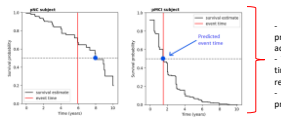
- Feature importance results for the GEN+MRI+CDC feature set **27/36 features** had a positive effect on performance:
  - **6 GEN** **9 MRI** **12 CDC**
- 8 of the top 10 features were from **CDC** including **7 COG** features and **1 DEM**
- The most important feature was **CDRSB**



- Histogram of the difference between the predicted and true event times for **pNC** and **pMCI** groups.
- The predicted event time is the time a subject's survival probability reaches 50%. If a subject's survival probability does not reach 50% by the end of the 10-year period, the subjects is considered a DAT non-converter (shown in **dark red** and **dark green** for **pNC** and **pMCI**).



- Comparison between the predicted survival estimates vs. actual censoring times.
- The predicted event time is the time a subject's survival probability reaches 0.5 (dotted line).
- Filled circle represents the predicted event time.



- Comparison between the predicted survival estimates vs. actual event times.
- The predicted event time is the time a subject's survival probability reaches 0.5 (dotted line).
- Filled circle represents the predicted event time.

Conclusion

- Cognitive test features were shown to have the highest overall predictive power for subjects at early stages of the disease.
- MRI data had less predictive power compared to cognitive test data but was found to be valuable in time-to-conversion prediction for both healthy subjects and subjects at early stages of the disease.
- Although genetic data had the lowest overall predictive power, it was shown to predict the most accurate time-to-conversion for subjects who were healthy at baseline and developed DAT at a later timepoint (pNC subjects)

References

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