Explainable machine learning to predict and differentiate Alzheimer's progression by gender

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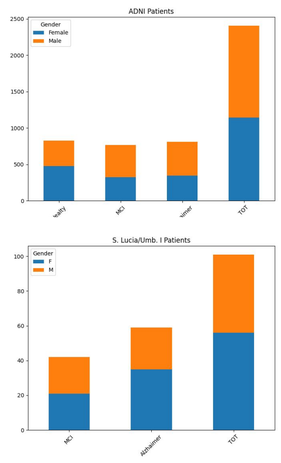
Objectives

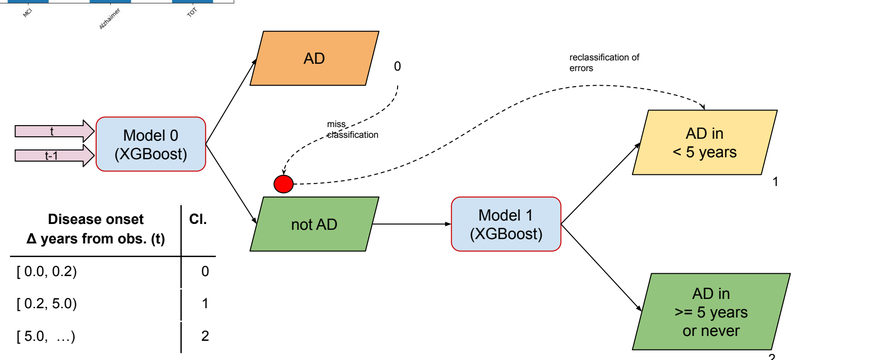
Our primary objective is to develop an explainable Machine Learning (ML) model to support experts in predicting the conversion/onset of Alzheimer's disease (AD) and to explore differences between genders.
Our intention to use only affordable neuropsychological tests.

Data and Models

The data used to train, validate and test ML models were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). We download 11.412 observations of 2407 patients from Sept. 2005 to Jan 2023 including only neuropsychological test results. Patients are grouped in three homogeneous disjoint sets for model training, test and validation.
Observations of 110 patients (March 2013 to March 2023) from Santa Lucia and Umberto Iº are also available to check the portability of the model. Data preparation include features selection based on the amount of non-null values and harmonization with data collected by Fondazione Santa Lucia and Policlinico Umberto Iº. We design a pipeline made up of two cascade classificators: the first detect the AD at present observation (time t), the second (for not-AD observations) predict the AD onset in 5 years or more (potentially never). Pipeline input is made up by two consecutive patient observation: actual (t), and past (t-1). Each model is an optimized XGBoost classificator that use bagging boosting algorithm, which trains multiple decision trees and then combines the results.



	ADNI	S. Lucia/Umb. I
num. of patients	2407	101
num. of observations	11411	318
avg. number of observations	4.74	3.15
std. dev.	3.12	1.12
min number of observations	1	1
max n. of observations	18	7



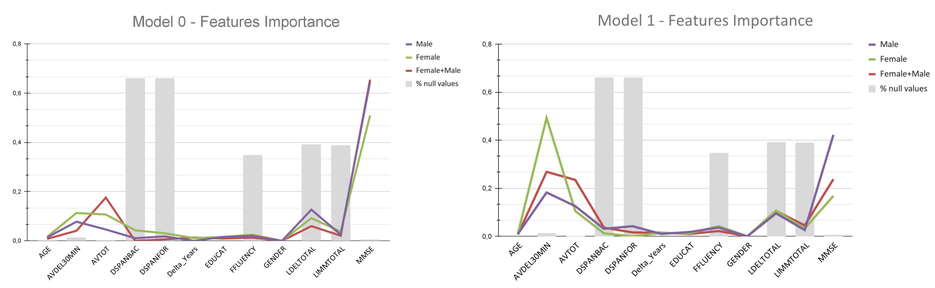
Disease onset Δ years from obs. (t)	Cl.
[0.0, 0.2)	0
[0.2, 5.0)	1
[5.0, …)	2

Results

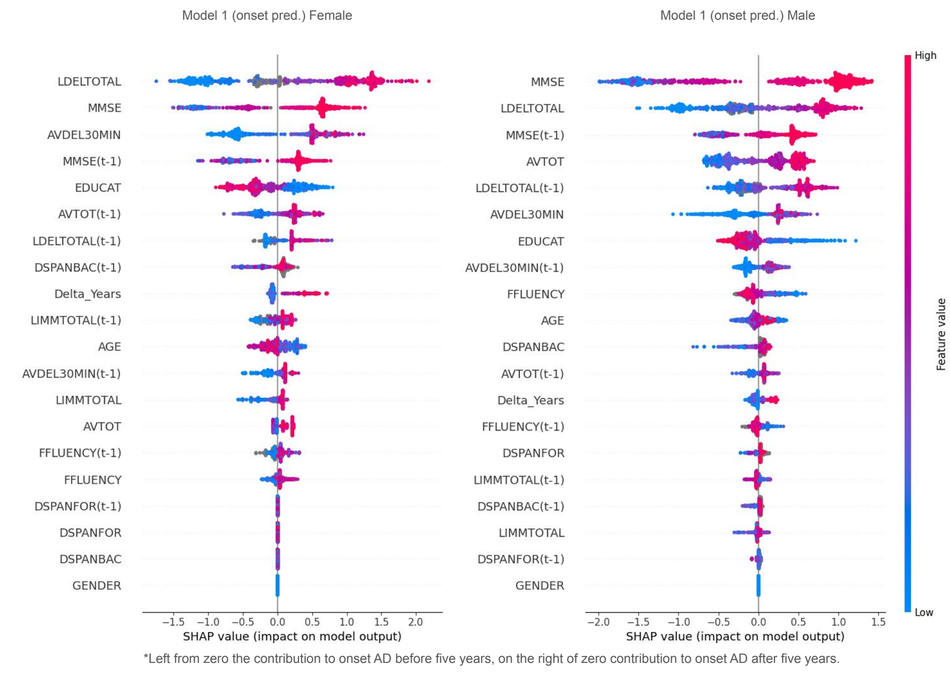
We build three scenarios: one with female and male observations mixed, one only for female and last one only for male. In each scenario we train, optimize, validate and test a specific pipeline. Analyzing models performance over all the scenarios, we have better results by models specialized by gender: female models outperform mixed gender models while male models has quite similar performance as mixed. All models do not use features with highest number of missing values and the aggregated features importance, counted as the number of times a feature is used to split the data across all trees for observation at time *t* plus observation at time *t-1*, shows that Mini-Mental State Examination is the most important features used by both genders to detect not-AD vs AD (Model 0). Other features like Logical Memory - Delayed Recall and Rey Auditory Verbal Learning Test - Delayed become more important to predict the AD onset while Mini-Mental S.E. decrease the importance (Model 1). The results suggest that ML can predict AD progression using a selected number of not-expensive tests, however further efforts are necessary for the integration of data collected with not exactly operational methodology as results on Santa Lucia and Umberto Iº demonstrate.
The study also highlights the importance of considering gender as a variable in predicting AD progression. The use of ML algorithms has emerged as a promising tool for identifying and predicting AD progression. However, their use requires careful consideration of their interpretability to ensure that the results can be trusted and understood. Using explainable approaches allows researchers to gain a deeper understanding of the disease and its progression, ultimately leading to better treatment strategies (Bogdanovic et al., 2022). The integration of multi-cohort data can provide a more comprehensive understanding of the disease assessment (Qiu et al., 2022), while low-expansive tests can improve diagnostic accuracy while minimizing costs and time required for AD management (Merone et al.,2022).

Scenario	ADNI		S. Lucia / Umberto Iº	
	Model 0 healty/AD	Model 1 onset pred.	Model 0 healty/AD	Model 1 onset pred.
Female + Male	0.88	0.90	-	-
Female	**0.92**	**0.93**	0.48	0.87
Male	0.88	0.89	0.74	0.81

f1 score weighted



AVDEL30MIN:Rey Auditory Verbal Learning Test - Delayed, AVTOT: Rey Auditory Verbal Learning Test, DSPANBAC: Digit Span Backward, DSPANFOR: Digit Span Forward, FFLUENCY: Letter Fluency - F, LDELTOTAL: Logical Memory - Delayed Recall: LIMMTOTAL: Logical Memory - Immediate Recall, MMSE: Mini-Mental State Examination.



*Left from zero the contribution to onset AD before five years, on the right of zero contribution to onset AD after five years.

Conclusions

These findings confirm the gender-specific differences in AD progression and the relevance of specific cognitive measures in detecting individual's evolution in AD. In particular the delayed recall of logical and verbal memory as well as MMSE have been shown to be predictive of AD. Further research is needed to confirm and explore these differences, and to develop targeted interventions for individuals at risk for AD. This research demonstrates that explainable ML can effectively predict AD progression trajectories using not-expensive neuropsychological tests as features.

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