Mnemosyne: A Decision Support System for Early Detection of Dementia

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Background.

Early detection of dementia improves access to medical services, facilitates symptomatic treatment, and gives patients an opportunity to arrange legal, financial and care plans while still cognitively capable. Many potential predictors of dementia status are readily available in primary care (e.g. socio-demographics and brief cognitive tests), but others are expensive, time-consuming or require specialist input (e.g. neuroimaging, genetics, neuropsychological assessment). Thus, there is an increasing need for non-specialist dementia prognostication tools that recommend whether specialist diagnostic assessments should be undertaken for a given patient based on the patient's individual dementia probability, and then update this probability given the results of these specialized tests. Towards this end, we developed Mnemosyne, a machine learning (ML)-powered decision support engine that predicts a subject's probability of dementia using different combinations of non-specialist and specialist predictors (socio-demographic variables, neuroimaging features and cognitive tests). The underlying ML model used by Mnemosyne is an ensemble of models that are tuned automatically using Bayesian optimization.

Cohorts.

We trained and evaluated our system through 2 separate patient cohorts. The first cohort is the Open Access Series of Imaging Study (OASIS), a cross-sectional study comprising 373 subjects who are more than 60 years old, of which 183 subjects were diagnosed with all-cause dementia (Marcus et. al, 2007). The second cohort was the Alzheimer's Disease Neuroimaging Initiative (ADNI) database, which was made publicly available for participants in the TADPOLE data challenge*. This cohort comprised 1,345 subjects, of which 237 were diagnosed with all-cause dementia. For each subject in both cohorts, predictors included socio-demographic variables, cognitive tests, and imaging features.

Methods.

Mnemosyne is designed to provide clinical guidance in two stages. In the first stage, it provides an initial probability of dementia which informs the decision whether a subject should undergo costly specialist assessments (neuroimaging, genetic, etc) based on her socio-demographic characteristics and brief cognitive test results. In the second stage, it is fed with additional specialist diagnostic assessments, and updates the patient's probability of dementia. The predictions are based on automatically constructed ML pipelines (comprising feature processing and classification stages) using Bayesian optimization with a Gaussian process prior (Alaa & van der Schaar, 2018). Using 5-fold cross-validation, we compared the accuracy of Mnemosyne with that of a widely used brief cognitive assessment (the Mini-Mental State Examination; MMSE), in addition to 10 competing standard ML models. We used the area under receiver operating characteristic curve (AUC-ROC) as a measure of accuracy.

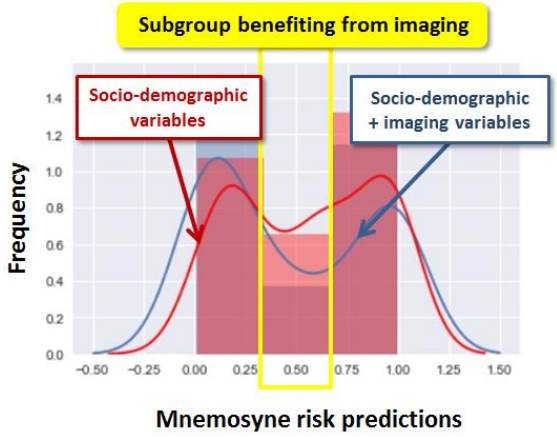

Fig. 1: Impact of imaging features on predictions (OASIS).

Results.

The MMSE brief cognitive assessment was moderately accurate in predicting dementia status in both cohorts (AUC-ROC: 0.782 ± 0.011 on OASIS, 0.725 ± 0.009 on ADNI). The simple Mnemosyne improved accuracy (AUC-ROC: 0.798 ± 0.011 on OASIS, 0.810 ± 0.021 on ADNI) suggesting that conventional primary care decision making could be enhanced. The full Mnemosyne model further improved predictive accuracy (AUC-ROC: 0.851 ± 0.012 on OASIS, 0.861 ± 0.013 on ADNI) demonstrating the value of the additional specialist assessments. This also represented an improvement over the best performing standard ML models: linear discriminant analysis on OASIS and Gradient boosting on ADNI (AUC-ROC: 0.839 ± 0.063 on OASIS, 0.841 ± 0.046 on ADNI). Figure 1 depicts a histogram for the predictions of the simple and full versions of Mnemosyne on the OASIS dataset. The proportion of subjects aged between 60 to 70 years old assigned to the moderate risk group was twice as high as in the overall sample, illustrating the difficulty of predicting dementia status in the young old. The full Mnemosyne model uses the specialist diagnostic assessments to refine predictions for this moderate risk group, thus providing more clinically useful predictions.

Marcus, D. S., Wang, T. H., Parker, J., Csernansky, J. G., Morris, J. C., & Buckner, R. L. (2007). Open Access Series of Imaging Studies (OASIS): cross-sectional MRI data in young, middle aged, nondemented, and demented older adults. *Journal of cognitive neuroscience*, *19*(9), 1498-1507.

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*****https://tadpole.grand-challenge.org