A Machine Learning Approach to Predict Change in Diagnostic Category in Pre-Dementia

Sascha Gill¹, Pauline Mouches¹,², Sophie Hu¹,³, Muhammad Ahmad¹, Nils Forkert¹,², Zahinoor Ismail¹,³,⁴,⁵

¹Hotchkiss Brain Institute, University of Calgary, Calgary, AB, Canada
²Department of Radiology, University of Calgary, Calgary, AB, Canada
³Department of Community Health Sciences, University of Calgary, AB, Canada
⁴Department of Psychiatry, University of Calgary, AB, Canada
⁵Department of Clinical Neurosciences, University of Calgary, AB, Canada

Background

Mild Cognitive Impairment (MCI): is a prodromal stage of Alzheimer’s Disease (AD) associated with an estimated annual progression rate of 10-15%³.

Neuropsychiatric Symptoms (NPS): include symptoms of apathy, mood disturbances, anxiety, agitation, disinhibition and psychosis.

- Associated with higher risk for cognitive decline and dementia³.

Mild Behavioural Impairment: is a neurobehavioral syndrome that describes later-life onset of NPS as an at-risk state for cognitive decline³.

- Symptoms divided into 5 domains including:
  1) Drive/motivation
  2) Emotion dysregulation
  3) Impulse dyscontrol
  4) Social cognition
  5) Abnormal Percepcion

Machine learning classification approaches have been utilized to predict diagnosis of MCI and AD based on different modalities of biomarkers, e.g., clinical, imaging, genetic, and cerebrospinal fluid markers etc.

- However, presence of NPS has been unexplored in these predictive models.

Objectives

The objectives of this study are to use machine learning to:

1. Identify features essential for classifying individuals with Normal Cognition (NC), MCI and AD.
2. Identify features that distinguish the normal vs. abnormal disease group.

We intend to highlight the importance of NPS categorized into MBI domains as features that predict change in diagnostic category in pre-dementia risk states.

Methods

Participants

- Analyzed data collected from the Alzheimer’s Disease Neuroimaging Initiative (ADNI).
- To approximate MBI in the ADNI dataset, we grouped subjects into those sustained with NPS for at least 6 months as MBI+; and those with no NPS as MBI-.

MBI+ sample: n=38 with NC, n=219 with MCI
MBI- sample: n=64 with NC, n=20 with MCI

Measures

Combining the clinical and structural MRI data, a total of 235 variables (features) were considered as potential predictors of change in diagnostic status.

- Clinical features: age, sex, education, domain and total MBI score (transformed NPI-Q score).
- MRI features: FreeSurfer version 4.3 for cortical reconstruction and volumetric segmentation
  - Desikan-Killian Atlas: 34 regions/hemisphere for cortical parcellation (Fig. 1)
  - Segmentation of deep grey matter volumetric structures (e.g. hippocampus)

Figure 1: Key regions labelled in the Free Surfer's Desikan-Killian atlas.

Machine Learning

- Performance of several feature selection methods combined with different machine learning algorithms, including random forest, support vector machine, multilayer perceptron, and decision tree, was compared.

Objectives

1. Identify features essential for classifying individuals with Normal Cognition (NC), MCI and AD.
2. Identify features that distinguish the normal vs. abnormal disease group.

We intend to highlight the importance of NPS categorized into MBI domains as features that predict change in diagnostic category in pre-dementia risk states.

Table 1: Descriptive characteristics of individuals with normal cognition and MCI. All results indicated are based on univariate ANOVAs; group comparisons controlled for seriousness.

<table>
<thead>
<tr>
<th>Age(years)</th>
<th>NC (n=102)</th>
<th>MCI (n=239)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>75.64 (5.74)</td>
<td>74.15 (8.06)</td>
<td>.092</td>
<td></td>
</tr>
<tr>
<td>Education(years)</td>
<td>15.97 (2.68)</td>
<td>16.03 (2.74)</td>
<td>.866</td>
</tr>
<tr>
<td>Gender (M:F)</td>
<td>52:50</td>
<td>156:83</td>
<td>.272</td>
</tr>
<tr>
<td>Follow-up period (months)</td>
<td>68.63 (43.36)</td>
<td>53.29 (34.72)</td>
<td>.001</td>
</tr>
<tr>
<td>MBI Drive</td>
<td>0.06 (0.20)</td>
<td>0.34 (0.57)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MBI Emotion Dysregulation</td>
<td>0.30 (0.66)</td>
<td>0.89 (0.92)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MBI Impulse Dyscontrol</td>
<td>0.30 (0.61)</td>
<td>1.22 (1.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MBI Social Cognition</td>
<td>0.02 (0.13)</td>
<td>0.25 (0.50)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MBI Abnormal Perception</td>
<td>0.00 (0.00)</td>
<td>0.03 (0.16)</td>
<td>0.038</td>
</tr>
<tr>
<td>MBI total score</td>
<td>0.69 (1.17)</td>
<td>2.74 (2.47)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Figure 2: Distribution of MBI domain scores in individuals with normal cognition and MCI.

Table 2: Output metrics of the classification experiments with the highest average class accuracy.

<table>
<thead>
<tr>
<th>Objective</th>
<th>Selected features</th>
<th>TP Rate</th>
<th>FP Rate</th>
<th>Precision</th>
<th>Recall</th>
<th>F-Measure</th>
<th>AUCROC</th>
<th>Average per-class accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective 1</td>
<td>5 features selected with an ** accuracy of 60%</td>
<td>0.609</td>
<td>0.220</td>
<td>0.594</td>
<td>0.609</td>
<td>0.597</td>
<td>0.749</td>
<td>59.7%</td>
</tr>
<tr>
<td>Objective 2</td>
<td>2 features selected with an ** accuracy of 80%</td>
<td>0.856</td>
<td>0.291</td>
<td>0.851</td>
<td>0.856</td>
<td>0.852</td>
<td>0.844</td>
<td>78.2%</td>
</tr>
</tbody>
</table>

Table 3: Features selected via machine learning to predict follow up diagnostic status based on baseline inputs. All results indicated are based on univariate ANOVAs.

<table>
<thead>
<tr>
<th>Classification Experiment 1</th>
<th>Features Selected</th>
<th>NC (MCI) (M(SD))</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBI Total Score</td>
<td>0.69 (1.17)</td>
<td>2.74 (2.47)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Volume of Left Hippocampus (mm³)</td>
<td>3596.18 (441.19)</td>
<td>3115.95 (563.86)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MBI Impulse Dyscontrol Score</td>
<td>0.30 (0.61)</td>
<td>1.22 (1.35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cortical Thickness SD of Right Unknown</td>
<td>1.51 (0.10)</td>
<td>1.42 (0.12)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cortical Thickness Average of Left Entorinal</td>
<td>3.38 (0.33)</td>
<td>3.03 (0.51)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Results

- Decision tree algorithm was selected to classify participants based on their diagnostic status using demographics, structural MRI and MBI scores for prediction.
- MBI total score (as approximated by the NPI-Q) has greater prognostic utility than most volumetric variables in predicting diagnostic status.
- Very few variables to make accurate distinction between the classes/groups.

Limitations

- Variability in the follow-up time period.
- MBI domain score approximate by the NPI-Q.
- Focused on data from single imaging Modality (structural MRI).
- No cognitive assessments included → may provide complimentary information and help improve classification accuracy.

Future Direction

- To evaluate the effect of NPS as measured by the MBI-Checklist on AD progression.
- Ensure that time to follow up is controlled for all participants.
- Include multiple imaging modalities and complimentary information from other biomarkers (e.g. CSF, cognitive assessments etc.) which can improve the machine learning model.

Conclusion

This is the first study that combines structural MRI and neuropsychiatric data in a machine learning classification framework to classify individuals based on their diagnostic status. This can be beneficial in a clinical setting and can objectively quantify disease status and progression based on routine neurological data collected in cognitive clinics.

References

5. Pointer M. Machine learning techniques and tools. Morgan Kaufmann.