Application of supervised learning methods in stratification of autism based on mixed measures of Eye Tracking and Electroencephalogram: Results from the ABC-CT Interim Analysis

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Background

Biomarker discovery in autism research includes a focus on identifying reliable, quantitative measures associated with meaningful subtypes. Standard approaches investigate how specific values extracted from individual experimental paradigms, drawn from methodologies such as eye tracking (ET) and electroencephalography (EEG), relate to clinical outcomes. While powerful, these approaches do not necessarily take advantage of the full spectrum of data measured from different devices on a range of paradigms that, if considered in their fullest, might provide more comprehensive picture of the disorder and its multifaceted aspects.

Objectives

To investigate the feasibility of combining individual measures for ASD biomarker discovery, this study utilizes computational and machine-learning methods to examine how measures extracted from EEG and ET paradigms can be combined to achieve robust predictions of behavioral phenotype.

Methods

This study leverages derived variables from all ET paradigms (Biomotion Preference, Activity Monitoring(AM), Social Interactive(SI) Play, Static Social(SS) Scenes, and Pupillary Light Reflex(PLR)) and EEG paradigms (Visual Evoked Potential (VEP) and Faces vs Houses (ERP)) presented in the interim data set (Summer 2018) of Autism Biomarkers Consortium for Clinical Trials(ABC-CT) formed to investigate promising biomarkers for ASD.

Methods

The dataset contained data from the baseline measurements from 225 children with ASD(n=161) and typical development(n=64). K-nearest-neighbors is used for imputation of missing predictors. Using a variety of machine-learning techniques, with 10-fold 100x-repeated cross validation, this study examines the Pearson's correlation of predictions derived from these 47 potential predictors to ADOS calibrated severity scales(CSS) and IQ. The complete set of predictors, LASSO, principal component analysis(PCA), elastic net(EN) and ridge decision tree(RDT) are used for feature selection; first and second order linear regression models(LM), random forest(RF), support vector machines(SVM) are used for prediction(total of 16 different machine-learning approaches). For comparison, the best single predictor is identified from the set of all predictors

EEG Paradigms

Visual Evoked Potential   **Faces vs Houses**

ET Paradigms

Activity Monitoring   **Social Interactive**   **Static Scenes**
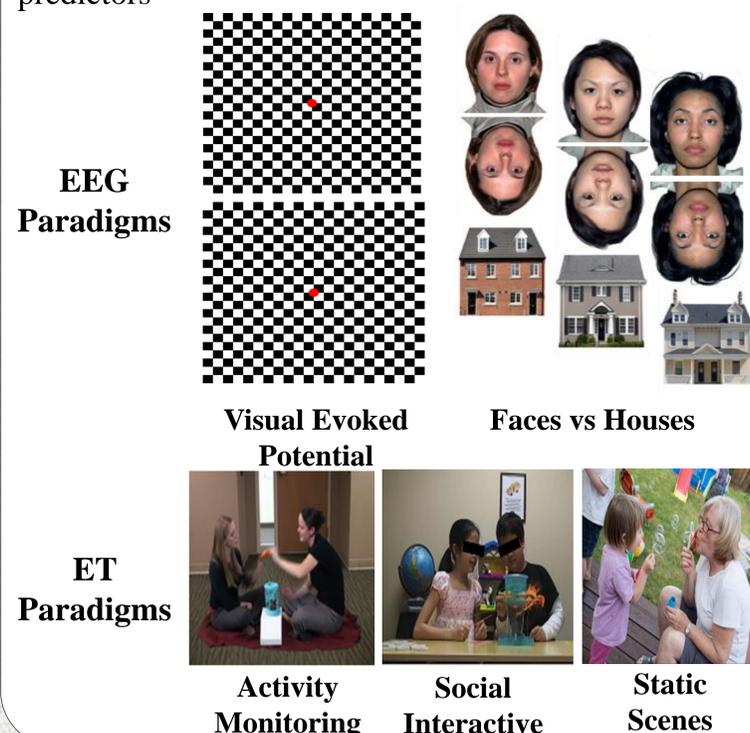
Results

1. As a baseline, correlations between individual variables and outcome variables as examined.
   - *CSS*: the highest correlations were observed in ET %head averaged across AM,SI,SS paradigms, %heads(AM), and %looking(SI), r = 0.548, 0.469, 0.447. The average correlation across all variables was r = 0.282.
   - *IQ*: ET looking % (SI), EEG erp (faces_good) and ET looking % (SS) showed top correlations of r = 0.47, 0.45, 0.43. Similar to CSS, the mean variable correlation was r = 0.280.

2. Using 2nd and 1st order LM,SVM and RF with all derived measures (EEG&ET) achieved:
   - *CSS*: r =-0.000576 (2nd order LM), 0.545(1st order LM), 0.609 (SVM), 0.584 (RF).
   - *IQ*: r = 0.00307 (2nd order LM), 0.549(1st order LM), 0.533 (SVM), 0.484 (RF).

3. Combining PCA, Lasso, RDT, and EN with 1st order LM and SVM achieved:
   - *CSS*:
     - 1st order LM: r = 0.54 (PCA), 0.59 (Lasso), 0.59 (RDT), 0.60 (EN)
     - SVM: r = 0.601 (PCA), 0.602 (Lasso), 0.612 (RDT), 0.594 (EN).
   - *IQ*:
     - 1st order LM: r = -0.54 (PCA), 0.568(Lasso), 0.551 (RDT), 0.564 (EN)
     - SVM: r = 0.574 (PCA), 0.553 (Lasso), 0.504 (RDT), 0.541 (EN).

Conclusions

- These results suggest that a machine-learning approach improves associations above the average single biomarker outcomes and results in minor gains as compared to best single biomarker outcomes.

- However, only limited improvements were observed, relative to straightforward first-order linear regression, by using either variable selection or more advanced machine-learning techniques (SVM, RF).

- This suggests that leveraging complex interactions between biomarkers may not provide substantial gains in matching biomarkers to clinical phenotypes -- a finding that may be expected given that ABC-CT paradigms were all primarily designed to index social-communicative function. Additional nuances of this work, including the different sets of variables identified by machine-learning approaches to best describe different phenotypic relationships, will be discussed in subsequent reports.

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