A Biomarker Panel for Depression Patients: An AI Approach

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ABSTRACT

Background:

- Previous studies have demonstrated links between various biometric features, such as C-reactive protein[1], and major depressive disorder (MDD).
- Studies on the correlation between individual biomarkers and MDD have been unfruitful in terms of clinical utility.

Objective:.

- Develop a panel of biomarkers that effectively clusters people that exhibit MDD-related phenotypes

Clinical Implications:

- Draw insights on the relationship between patient physiology and MDD
- Provide medical practitioners a way to develop more personalized treatment options

Data: UK BioBank

- 502,520 participants, 34 distinct biomarkers

METHODS

1. MDD Classification

- Train a binary classification model to accurately correlate biomarkers with MDD diagnosis
- Identify important features in the model to include in the patient biomarker panel

2. Patient Clustering

- Cluster MDD patients using important features

ACKNOWLEDGEMENTS

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REFERENCES

[1] Howren, M. Bryant, Donald M. Lamkin, and Jerry Suls. "Associations of depression with C-reactive protein, IL-1, and IL-6: a meta-analysis." Psychosomatic medicine 71.2 (2009): 171-186.

[2] Peng, Y.-F. *et al*. The significance of routine biochemical markers in patients with major depressive disorder. *Sci. Rep.* **6**, 34402; doi: 10.1038/srep34402 (2016).

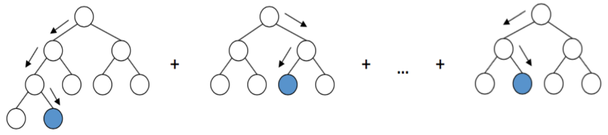
1. MDD CLASSIFICATION

Binary Classification:

- Represent participant as vector of 34 distinct biomarkers
- Use (A) “broad depression” or (B) “probable depression” as classification labels

Gradient Boosting Machine (GBM):

- GBM is an ensemble method that iteratively builds a model using weak prediction models to optimize a loss function (deviance).
- GBM implementations use decision “stumps”, to capture non-linear relationships between input and output.



Preprocessing Experiments:

1. Standardize features values using z-score normalization.
2. Use linear regressions to model the relationship between age and sex, and each biomarker. Store normalized residuals (squared loss) as feature values.
3. Add age and sex as interaction terms per biomarker. (Feature vector of 34*3 values.) Then standardize as in experiment 1.

Hyperparameters:

- step size: 0.25, # predictors: 100, min samples per leaf: 10

2. PARTICIPANT CLUSTERING

Clustering Model:

- Represent participant as vector of top-10 GBM features

DBSCAN Clustering Algorithm:

- DBSCAN is an unsupervised learning algorithm that clusters points based on density.

Experiments:

A. Cluster 198,403 “broad depression” participants

B. Cluster 31,839 “probable depression” participants

Hyperparameters:

A. neighborhood radius: 0.75, min pts in neighborhood: 10

B. neighborhood radius: 0.75, min pts in neighborhood: 10

RESULTS

1. MDD Classification

A. Experiment Accuracy on Broad Depression:

1. Training Set: 66%, Validation Set: 65%, Test Set: 66%
2. Residual values were in the millions (did not proceed with classification step)
3. *Training Set: 78%, Validation Set: 78%, Test Set: 78%*

B. Experiment Accuracy on Probable Depression:

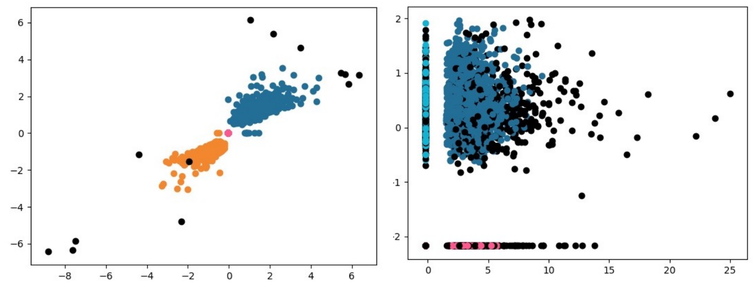
3. *Training Set: 99%, Validation Set: 99%, Test Set: 99%*

Feature Extraction:

- Average most important features among all 100 decision trees

A. Biomarker (Feature)	Importance	B. Biomarker (Feature)	Importance
1. Alanine aminotransferase	2.3956e-01	1. Direct bilirubin	4.5961e-01
2. Creatinine (enzymatic) in urine	1.7443e-01	2. Sodium in urine	2.5803e-01
3. Aspartate aminotransferase	1.4178e-01	3. Cholesterol	1.6709e-01
4. Glycated hemoglobin (HbA1c)	1.3503e-01	4. Apolipoprotein B	3.8848e-02
5. Creatinine	4.5081e-02	5. Apolipoprotein A	1.7687e-02

2. Patient Clustering



(A) Broad Depression (B) Probable Depression

DISCUSSION & FUTURE WORK

- MDD classification was successful after adding interaction terms
- Importance of bilirubin and other significant biomarkers supported by research[2]
- Interesting that top 3-4 biomarkers alone can accurately predict depression (potential for further research)
- Participant Clustering was ineffective (A. male and female clusters, B. single cluster)