Supervised machine learning techniques for the classification of metabolic disorders in newborns

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Background

- Usually blood sample that is collected during the first few days of life to screen for metabolic disorders.

- Test now simultaneously screens the concentrations of up to 50 metabolites to detect more than 20 inherited metabolic disorders .
- **The amount and complexity of the experimental data is quickly becoming unmanageable to be evaluated manually.**

Objective

- Focusing on two representative inborn errors of metabolism—
- phenylketonuria (PKU), an amino acid disorder,
- and mediumchain acyl-CoA dehydrogenase deficiency (MCADD), a fatty acid oxidation defect
- six well-established supervised machine learning techniques were evaluated to determine the ‘best’ screening model

Criteria

- discriminatory performance of the learning algorithm based on pre-classified, selected and clinically validated sub-databases of PKU and MCADD newborns.
- diagnostic prediction of constructed classifiers with optimizing sensitivity and minimizing the number of false positive results considering a large database.

Methods

Used Tandem mass spectrometry (MS/MS)

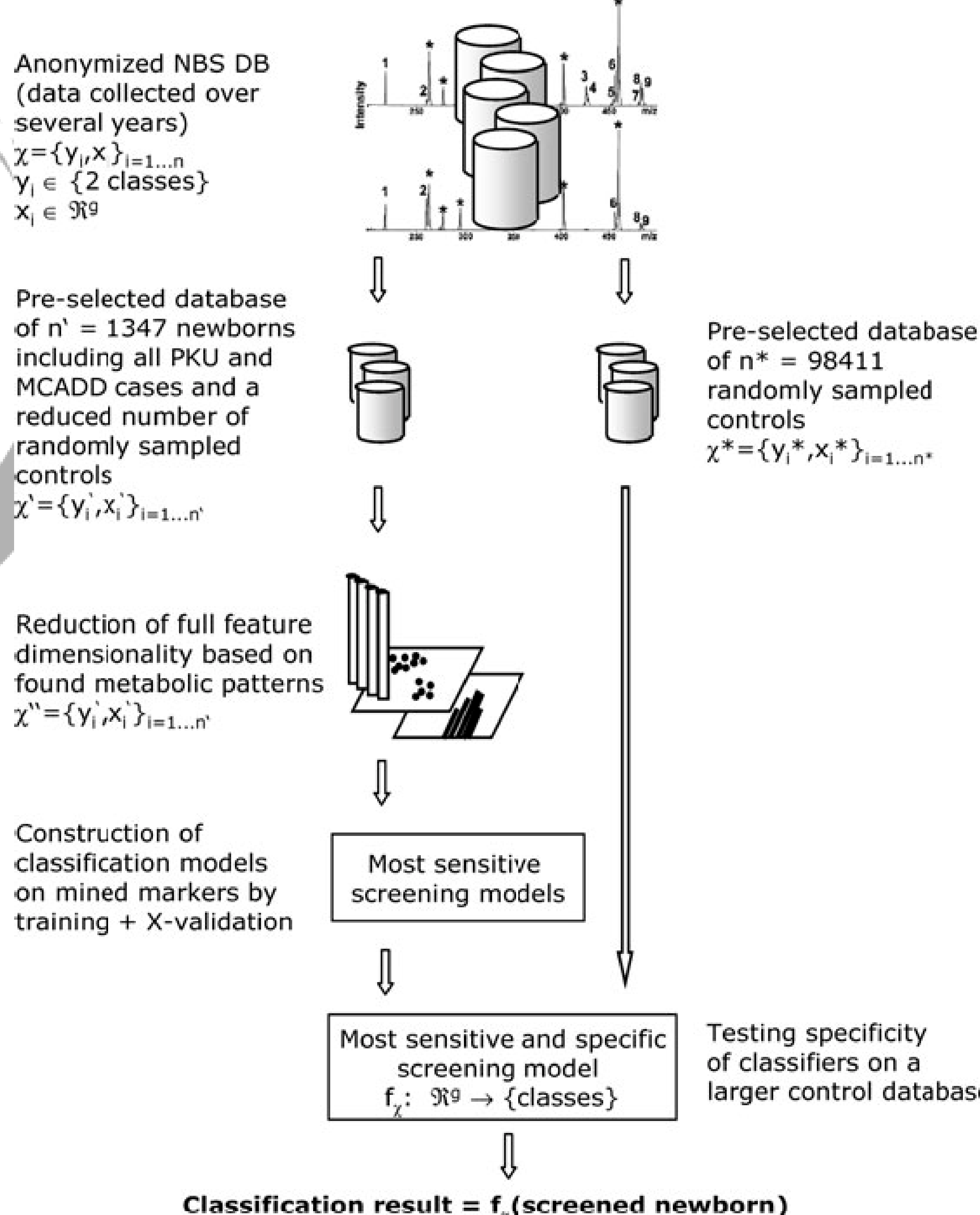
To find

- Phenylketonuria is an amino acid disorder which is caused primarily by a deficiency of phenylalanine hydroxylase
- Medium-chain acyl-CoA dehydrogenase deficieny is a fatty acid oxidation defect which leads to an accumulation of fatty acids and a decrease in cell energy metabolism.

experimental datasets were anonymously provided from the newborn screening program in Bavaria, Germany

- *Discriminate analysis (DA)*
- *Logistic regression analysis (LRA)*
- *Decision trees (DT)*
- *K-nearest neighbor classifier (k-NN)*
- *Artificial neural networks (ANN)*
- *Support vector machines (SVM)*

Fig 1



Anonymized NBS DB (data collected over several years)
$\chi=\{y_i,x\}_{i=1\ldots n}$
$y_i \in \{2 \text{ classes}\}$
$x_i \in \Re^g$
Intensity
m/z
Pre-selected database of n‘ = 1347 newborns including all PKU and MCADD cases and a reduced number of randomly sampled controls
$\chi`=\{y_i`,x_i`\}_{i=1\ldots n`}$
Pre-selected database of n* = 98411 randomly sampled controls
$\chi^*=\{y_i^*,x_i^*\}_{i=1\ldots n^*}$
Reduction of full feature dimensionality based on found metabolic patterns
$\chi``=\{y_i`,x_i`\}_{i=1\ldots n`}$
Construction of classification models on mined markers by training + X-validation
Most sensitive screening models
Most sensitive and specific screening model
$f_\chi: \Re^g \rightarrow \{\text{classes}\}$
Testing specificity of classifiers on a larger control database
Classification result = f_χ(screened newborn)

Use WEKA

- Weka tool set and ADE-4 were used to evaluate results and perform DA and statistical analysis

Winner

- Logistic regression analysis led to superior classification rules (sensitivity>96.8%, specificity >99.98%) compared to all investigated algorithms.
- For the routine clinical screening LRA models proved particularly feasible because of their highly significant prognostic accuracy.

results

- To sum it up, the top three machine learning techniques, LRA SVM and ANN, delivered results of high predictive power
- the DA classifier discriminated worse for both disorders

points

- Machine learning works well in defined tasks.
- LRA and DA work is a similar manner yet one is the best one is the worst. Lesson?
- ANN as labeled the future by many, do you think ANN will become the best