The Personalised Medicine Network
Personalised Medicine Research Theme
Center for Genomics and Personalised Medicine

SEMINAR
Approaches to Personalised Medicine at Health

March 15th, 2023 at 15.00 – 16.00

Eduard Biermann (1252-204), The Lakeside Theatres, Aarhus University, Bartholins Allé 3, 8000 Aarhus C

Steve Faraone from SUNY Upstate Medical University, New York

Read more about the speaker here: https://en.wikipedia.org/wiki/Stephen_Faraone

Title: Prediction Modeling of ADHD and its Outcomes using Machine Learning

This presentation provides two examples from our lab describing applications of machine learning to address biological and clinical questions about attention deficit hyperactivity disorder (ADHD). The first study sought to develop a clinically feasible algorithm to predict response to a non-stimulant medication for ADHD (extended release viloxazine (VER)) early in the course of treatment. We used data from 4 phase 3 placebo-controlled trials of 100- to 600-mg/day VER in youth and one in adults. Treatment response was defined as ≥50% reduction in change from baseline (CFB) in ADHD symptoms at Week 6. Predictor variables were: Clinical Global Impressions-Improvement (CGI-I) score at Week 1, 2, and 3; target dose; baseline age, body weight, and body mass index. Five machine learning methods were tested. The Area under the Receiver Operating Characteristic Curve (ROC AUC) analysis found the lasso regression being the best fitting model. ROC AUC for each model increased with increasing the number of weeks of data. Model results were described with an algorithm that can be easily incorporated into clinical practice. The course of clinical improvement two weeks after initiation of treatment can be used to select which patients are likely to benefit from continued treatment with VER. The second study used machine learning to define a set of gene set polygenic risk scores (gsPRS) for phenotypes having a high genetic correlation with ADHD. These gsPRS were added to the standard PRS as input to machine learning models predicting ADHD. For a test subset that had not been used for training or validation, a random forest (RF) model using PRSs from ADHD and genetically correlated phenotypes and an optimized group of 20 gsPRS had an area under the receiving operating characteristic curve (AUC) of 0.72 (95% CI: 0.70 – 0.74). This AUC was a statistically significant improvement over logistic regression models and RF models using only PRS from ADHD and genetically correlated phenotypes. These results show that summing risk at the gene set level and incorporating genetic risk from disorders with high genetic correlations with ADHD improves the accuracy of predicting ADHD. Implications for clinical prediction problems and for understanding the neurobiology of ADHD are discussed.

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Coffee and cake will be served after the seminar