Personalised Medication Response Prediction for Attention-Deficit Hyperactivity Disorder: Learning in the Model Space Versus Learning in the Data Space

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ABSTRACT

Attention-Deficit Hyperactive Disorder (ADHD) is one of the most common mental health disorders amongst school-aged children with an estimated prevalence of 5% in the global population (1). Stimulants, particularly methylphenidate (MPH), are the first-line option in the treatment of ADHD (2, 3) and are prescribed to an increasing number of children and adolescents in the US and the UK every year (4, 5), though recent studies suggest that this is tailing off, e.g. Holden et al. (6). Around 70% of children demonstrate a clinically significant treatment response to stimulant medication (7, 8, 9, 10). However, it is unclear which patient characteristics may moderate treatment effectiveness. As such, most existing research has focused on investigating univariate or multivariate correlations between a set of patient characteristics and the treatment outcome, with respect to the dosage of one or several types of medication. The results of such studies are often contradictory and inconclusive due to a combination of small sample sizes, low-quality data or a lack of available information on covariates.

In this paper, feature extraction techniques such as latent trait analysis were applied to reduce the dimension of on a large dataset of patient characteristics, including the responses to symptom-based questionnaires, developmental health factors, demographic variables such as age and gender, and socioeconomic factors such as parental income. We introduce a Bayesian modelling approach in a ‘learning in the model space’ framework that combines existing knowledge in the literature on factors that may potentially affect treatment response, with constraints imposed by a treatment response model. The model is personalised such that the variability among subjects is accounted for by a set of subject-specific parameters. For remission classification, this approach compares favourably with conventional methods such as support vector machines and mixed effect models on a range of performance measures. For instance, the proposed approach achieved an area under the receiver operator characteristic curve of 82–84%, compared to 75–77% obtained from conventional regression or machine learning (‘learning in the data space’) methods.