Genetic Prediction of Clozapine Response by Artificial Neural Network

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Introduction Clozapine is an effective antipsychotic for the treatment-refractory schizophrenia. However, it may cause serious adverse effects. Logistic regression (LR) and artificial neural network (ANN) are the most widely used models in biomedicine [1]. The objective of this study is to construct prediction models of clozapine response with ANN and LR using data of genetic polymorphisms from schizophrenic patients.

Methods Schizophrenic patients who took clozapine were included. Predictor variables included genetic polymorphisms of 5-HT2A, adrenergic α1A, α2A, and β3, and G-protein β3. The outcome valuable is the dichotomous response to clozapine. Multilayer perceptrons were constructed and the training technique was set to back-propagation. Leave-one-out method was used to test the model generalization. The area under the receiver operating characteristic (ROC) curve was calculated for overall performance of each model.

Results 93 schizophrenic patients were included (26 responders) with mean age of 38.4±7.9 years. Forty-nine of them (52.7%) were men. The resultant areas under ROC curves with leave-one-out method were 0.805±0.056 for ANN model and 0.516±0.067 for LR model [2]. ANN model was demonstrated to have significantly higher prediction performance than LR model (difference = 0.289, p < 0.001). It implied an 80.5% chance to discriminate a random clinical responder from a random nonresponder.

Conclusion ANN had better predictive power than LR with data of genetic polymorphisms. Accurate prediction of the response to clozapine before its use may decrease the risk of unnecessary adverse effects.

References

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