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Deep learning-based prediction of interactions between drugs used by patients with multiple sclerosis

Michael Hecker * [1],Brit Fitzner [1],Niklas Frahm [1],Uwe K. Zettl [1],

[1] *Rostock University Medical Center, Department of Neurology, Rostock, Germany*

Introduction:

Roughly 90% of the patients with multiple sclerosis (MS) take at least two drugs at the same time to modify the course of MS, ameliorate disease symptoms and manage co-existing conditions. A major consequence for a patient taking different medications is a higher risk of treatment failure and side effects. This is because a drug may alter the pharmacokinetic and/or pharmacodynamic properties of another drug, which is referred to as drug-drug interaction (DDI). Computational approaches allow to efficiently test large numbers of drug pairs for potential DDIs.

Objectives/Aims:

We aimed to predict interactions of drugs that are used by patients with MS based on a deep neural network (DNN) framework. We further aimed to identify potential drug-food interactions (DFIs), which can affect drug efficacy and patient safety as well.

Methods:

We used DeepDDI, a multi-label classification model of specific DDI types, to predict changes in pharmacological effects and/or the risk of adverse drug events when two or more drugs are taken together. The original model with ~34 million trainable parameters was updated using >1 million approved DDIs from the current DrugBank database release. Structure data of foods were obtained from the FooDB database. The medication plans of patients with MS (N=627) were then searched for pairwise interactions between drug and food compounds.

Results:

The updated DeepDDI model achieved accuracies of 99.0%, 92.2% and 92.1% on the training set, validation set and testing set, respectively. The patients with MS used 312 different small molecule drugs as prescription or over-the-counter medications. In total, we identified 3748 DDIs in the DrugBank database and 13365 DDIs using DeepDDI. At least one DDI was found for most patients (n=509 or 81.2% based on the DNN model). The predictions revealed that many patients would be at increased risk of bleeding and bradycardic complications due a potential DDI when they would switch to cladribine (n=242 or 38.6%) and fingolimod (n=279 or 44.5%), respectively. Moreover, we identified a total of 55936 DFIs with drug compounds taken by the patients.

Conclusion:

We demonstrate that deep learning techniques can exploit chemical structure similarity to accurately predict unknown DDIs and DFIs in patients with MS. Our study specifies drug pairs that potentially interact, suggests mechanisms causing adverse drug events, informs whether interacting drugs can be replaced with alternative drugs and provides dietary recommendations while taking certain drugs.

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