Interpreting the Amnesic Effect of Benzodiazepines using Machine Learning Models

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Introduction

With the recent increase in the prescription of benzodiazepines (BDZs), memory impairment is a crucial component to be evaluated in weighing the risks and benefits of these anti-anxiety medicines. Memory recall, however, varies greatly depending on a person's unique circumstances, making it difficult to predict the amnesic effect of BDZs on a patient using traditional methods of study.

Researchers have recently implemented machine learning in studies of the adverse effects of prescription drugs, which can greatly enhance the accessibility and versatility of healthcare. However, there is a deficit of these machine learning approaches in the research of BDZs, which have been controversial in their alleged side effects due to faulty claims and inconclusive studies. This study attempts to predict the amnesic effect on a particular subject using a machine learning approach.

Methods

The data examined in this study consists of 198 novel islanders of ages ranging from 25 to 82 years old. Each subject was administered one of three anti-anxiety drugs—Alprazolam, Triazolam, or a placebo—at one of three dosage levels. Within each drug group, subjects were divided into three dosage levels to indicate low dosage, medium dosage, and high dosage (over the recommended daily intake). To ensure validity, the number of subjects in each dosage group followed a 1:1 ratio. The islanders were primed with either happy or sad memories ten minutes prior to the memory test to assess how memory recall may be influenced by recent memories. In order to mimic addition, the islanders were tested every day for a week on their performance on a memory test before being administered the drug and after addiction was achieved.

To prepare the data to be interpreted by the models, it was cleaned and standardized. The percent difference in memory score before and after drug administration was assigned to be our label, and the age, dosage, memory score before taking the drug, and primed memory were our selected features. The placebo data were eliminated from the dataset because the correlation between variables was relatively weak, especially for our label, which showed little relationship with any of the features (Fig. 1). For the active drug groups, Fig. 2 depicts a positive correlation between dosage and memory score difference within the active drug group.

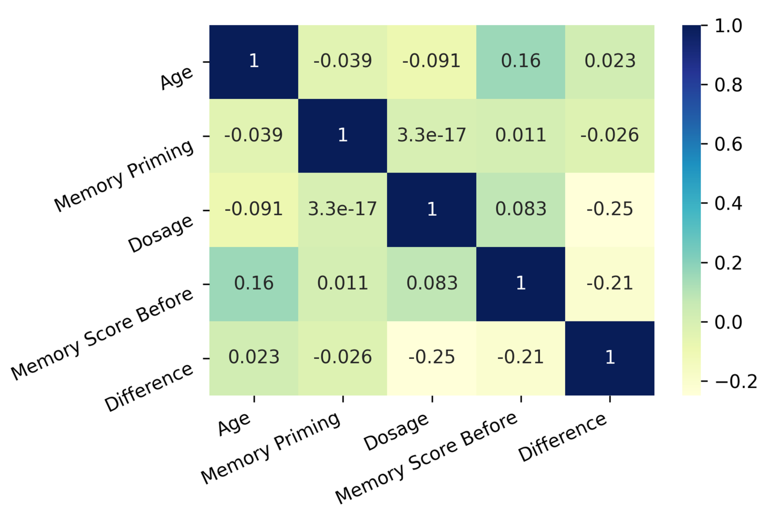

Fig. 1. Correlation heatmap for the placebo group.

Fig. 2. Correlation heatmap for the active drug groups.

Methods

Once preprocessed, the data were split into training and test sets, with eighty percent of it assigned to training and twenty for testing.

Algorithms

Linear regression predicts the dependent variable based on the given independent variables by identifying the best fit linear relationship between the input and output. In this study, multiple linear regression was used with default parameters.

Decision tree learning predicts values based on a sequence of decision rules. GridSearch was applied to tune the parameters, which were changed to max_depth = 4, min_samples_leaf = 4, and splitter = "random", and the rest were set to their default values.

Gradient boosting is an additive model that combines decision trees (weaker prediction models) to create a stronger prediction model in a step-wise manner to predict the dependent variable. Hyperparameter tuning was also applied to this model to reduce the algorithm's error, with the altered parameters being learning_rate = 0.007, max_depth = 3, n_estimators = 400, and subsample = 0.2.

All three models were evaluated using 10-fold cross-validation. To identify the optimal algorithm for predicting the effect of BDZs on memory recall, we compared the root mean square error (RMSE) of each of the models.

Results and Discussion

Upon comparing the performance of the three models, the gradient boosting model consistently yielded a lower RMSE of approximately 15.331 from the 10-fold cross-validation test, relative to the decision tree and linear regression models, which yielded errors of 16.097 and 17.699, respectively. Evaluating the RMSE of the three models revealed that the gradient boosting algorithm predicted values with the least amount of error and was, therefore, the most accurate of the three.

Fig. 3, visualizes the comparison between the measured values and the values predicted by the models and depicts the differences in the regression lines for each model. Gradient boosting has the closest to a perfect correlation between the measured and its predicted values out of the three, suggesting that the percent difference predicted by the gradient boosting model produced results closest to the actual measured values. Furthermore, the regression lines for all three models show a positive correlation between the actual and predicted values, indicating that the predicted values are reasonably close to the actual values in all models. Additionally, the confidence intervals indicate that the predicted values tend to deviate from the measured values as the percent difference diverges from a measured value of approximately 10 percent, which is where the confidence interval seems to be the smallest. Among the three models, the decision tree produced the largest confidence interval, suggesting that there is more variance in its predicted values.

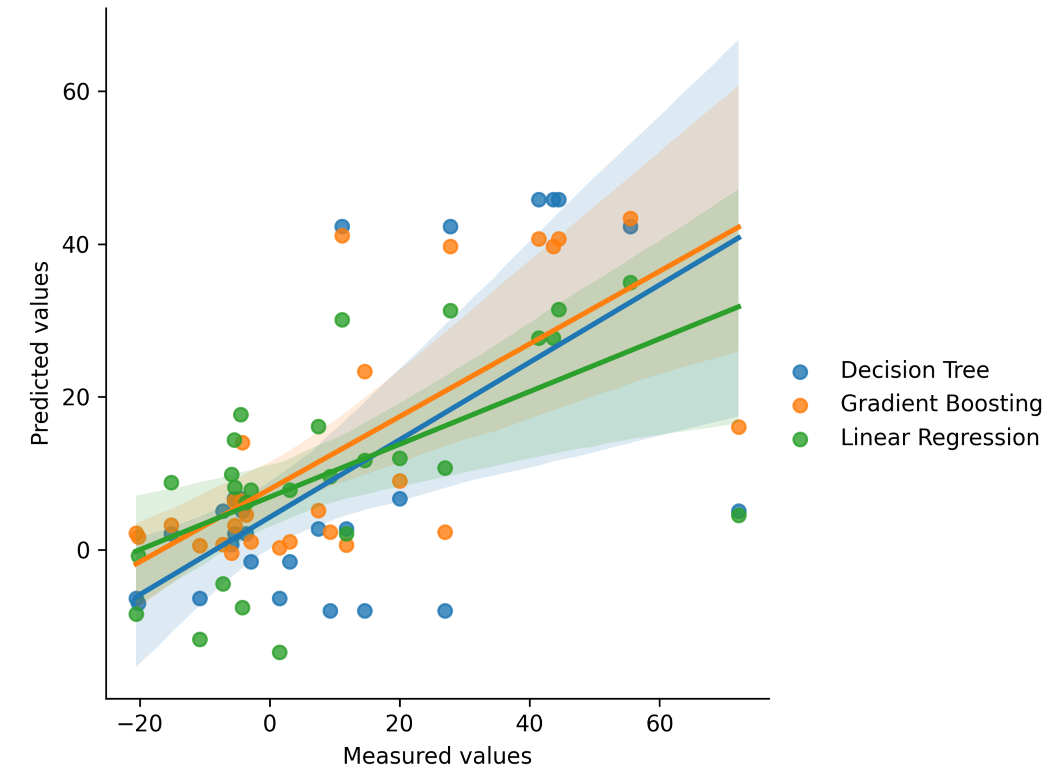

Fig. 3. This plot compares the measured percent difference in memory score from the test set with the percent difference forecasted by each of the three models, as well as the regression lines and the 95% confidence interval.

Results and Discussion

The models presented in this study demonstrate their ability to predict amnesic effect with considerable accuracy and efficiency. Using a machine learning approach to predict the decrease in one's memory can be an efficient tool in prescription processing, a procedure that evaluates the risks and side effects of a prescription that requires a precise filing process. Depending on the drug, this process can be lengthy and tedious when done manually and requires specialized knowledge to properly inform the patient about their prescription. And while machine learning can not replace this traditional method entirely, it can certainly reinforce it by accelerating the process and acting as verification to mitigate the possibility of inaccuracies that come with processing prescriptions manually.

Conclusions

The methods presented in this paper are a proposition for how machine learning can be applied to the study of BDZs and memory impairment, but there certainly is more work to be done before they can become fully functional. For one, because the dataset investigated in this study was somewhat limited in that it comprised less than 200 subjects, our models are susceptible to overfitting. Going forward, we may consider combining multiple datasets to validate our results and produce a more accurate model. Additionally, there are plenty more variables not included in our data that likely affected the difference in memory recall. Working with a more comprehensive dataset with more data points and variables to be considered will greatly enhance the accuracy of the models.

Further experimentation could potentially allow for the application of machine learning techniques in measuring the side effects of prescription drugs, not only limited to anti-anxiety medicine. Not only would machine learning facilitate the prescription process, but it also has the potential to make healthcare more accessible and cost-efficient in the long term. In countries where healthcare is largely inaccessible, machine learning can be a versatile and sustainable method for making medical diagnoses and prescriptions more practical with minimal need for specialized knowledge.

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