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Survey on Machine Learning Approach for Adverse Drug Reactions Classification of Attention Deficit Hyperactivity Disorder

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ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a neurological illness that mostly affects children, while some adults also experience its effects. The symptoms of this condition include hyperactivity, inattentiveness, impulsivity, issues with social interaction, and poor academic achievement. Adverse Drug Reaction (ADR) or drug side effect studies serve an essential part in medication development. Social media users broadcast useful information about their lives, including their health care, making it a useful source of data for identifying previously unknown drug side effects. So, one of the practical pharmacovigilance strategies is the detection of adverse drug effects using social media. With the increasing rise of pharmaceutical and non-pharmaceutical data, Machine Learning (ML) algorithms have emerged as major tools for assessing and classifying ADRs. This analysis provides a comprehensive review of the adverse drug reaction classification of attention deficit hyperactivity disorder using ML techniques. We discuss the benefits and drawbacks of ML-based techniques for classifying adverse medication responses. The most promising ML models are suggested as well as potential future research on the classification of adverse drug effects in ADHD.

Keywords- Attention Deficit Hyperactivity Disorder (ADHD), Machine Learning (ML), Adverse Drug Reaction (ADR)

I. INTRODUCTION

One of the most frequent neurobehavioral illnesses in children is ADHD. This disorder can influence not just academic achievement but also social interaction. If left untreated, this can lead to low academics and social isolation, as well as increased drug misuse and delinquent conduct during adolescence [1]. Pharmacological treatment is extremely successful, and current long-term studies are revealing additional information to assist doctors in determining appropriate therapeutic duration, potential side effects, and more precise outcomes to monitor [2].

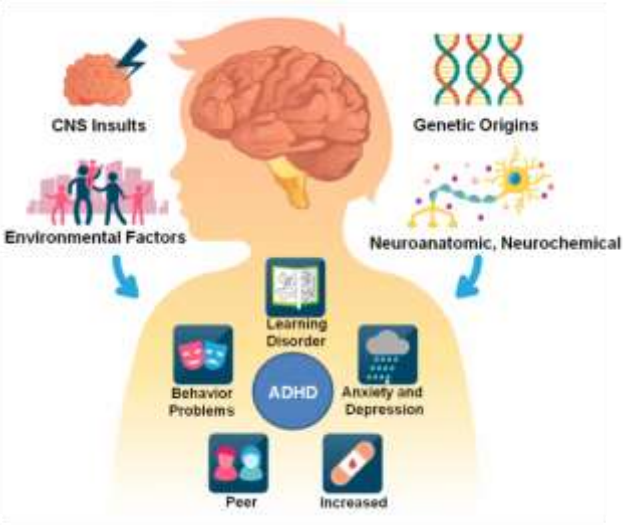

Figure 1: Symptoms of ADHD

Figure 1 depicts the symptoms of ADHD. A negative and unanticipated response to a medication that takes place at levels typically used in human beings is referred to as an ADR or side effect of a drug, according to the World Health Organization [3]. As a result, predicting ADRs is crucial for creating new

medicines and avoiding negative effects. ADR is induced by a typical dosage of medicine when taken normally. ADR does not include drug overdoses. A medicine is deemed safe as long as no adverse responses are observed. Drugs often work to treat illnesses by inhibiting the disease's protein or enzyme pathway, inhibiting the target, or even killing it [4]. Most approaches for forecasting ADRs rely on the assumption that medications with similar adverse effects would always have similar side effects. In addition to other traditional data platforms, social media has therefore become an enabler for the identification and prediction of ADRs to improve pharmacovigilance [5]. Many extant research studies employ various approaches to discover ADRs by examining the relationship between medicine and its ADRs. However, the incidence of ADRs can be linked to a variety of causal factors, making it critical to identify the multi factors that cause ADRs [6]. ADRs are caused by a variety of reasons. The absence of dosage and expert-specific suggestions, drug reactions, symptom severity, lack of integration of drugs, which can depend on race and ethnicity, and most importantly - the patient's characteristics and overall health, are thought to be key contributing to side effects of drugs [7].

This survey is divided into following parts: part II discusses numerous ML classification algorithms for ADR in ADHD; and part III provides a conclusion.

II. SURVEY ON ADR CLASSICATION USING ML

In the subfield of AI studies known as ML, patterns found in historical data are used to construct prediction models that allow machines to learn and deliver insightful information without the need for human intervention. Pattern identification, diagnostics, planning, automated machine control, prediction, and other activities may all be done using ML [8]. The suitability of several ML techniques for ADR prediction will be investigated. Finally, the current research on ML techniques for ADR outcome prediction will be examined [9]. “Supervised ML Models, Unsupervised ML Models, and Regression ML” Models are the three main categories into which the ML models utilised for the aforementioned tasks can be classified [10]. Figure 2 depicts the different methods for classifying ADR in ADHD.

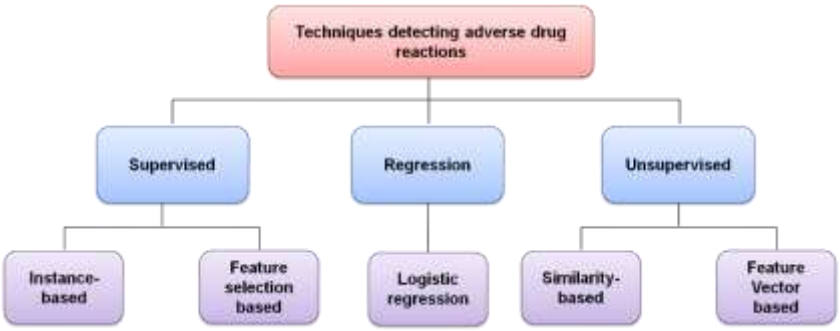

Figure 2: Different ML methods for classifying ADR in ADHD

A. Supervised ML Model

In supervised learning (SL), data is provided to the algorithm in the form of input-output pairs, making it one of the more intriguing approaches for learning a function using ML. This technique requires labeled training data. For ADR classification, SL may be employed. In this strategy, labels play a big part. By training with paired data, the learning model learns to classify drug reactions [11].

i. Instance-based Model (IM)

IM, often known as “lazy learning”, does not require a trainable step. The model attempts to discover a space in which samples distinguish based on their labels. Optimal data representation is difficult to determine, some approaches can be too rapid since they are lazy. The model grows increasingly sophisticated and time-consuming as the input dimension rises. “Nave Bayes (NB) and Support Vector Machine (SVM)” are two approaches utilised in the IM [12].

- **NB**

NB is another ML method that has been used in the information of biomedical for more than 50 years. It is a common way to sort things into groups and make predictions in many fields, including bioinformatics. The probability model that the Naive Bayes method is based on is best described as having features that are statistically independent [13]. A naive Bayesian classifier assumes that the existence of one characteristic for a given class is not affected by the existence of the other characteristics for that class. A classification method that is simple to execute on a computer and works perfectly well, even when compared to more complicated methods. Still, NB, when dealing with a large number of features, is miscalibrated and makes predictions with probabilities that are too close to zero & 1[14]. In [15], sampling techniques were employed to balance the data set to avoid problems like overfitting and poor classifier performance. Classification of ADR data was performed using the NB approach, and when the well-balanced and unbalanced data sets were compared, it was found that the NB classifier achieved very high accuracy. In [16], the authors used NB, a supervised ML classifier, to choose features and classify ADRs. Because of this, the results of supervised learning showed that machine-learning classifiers like Naive Bayes were more accurate than other methods. The NB utilises the sample size to compute probability values for each class, then uses the class with the maximum probability as the test data tag.

- **SVM**

Support vector machine is one of the most recent developments in ML and a subset of supervised learning. Its performance in a variety of applications, especially high-value applications, is outstanding. Because SVM is resource-intensive to compute, its use is restricted. SVM fundamentals have a maximum margin decision boundary that has been mathematically demonstrated to generate a stable and predictable implementation, as well as solid performance in several real-world applications. It has become a well-known classification approach in bioinformatics and chemoinformatics due to its high accuracy in prediction [17]. Using ML-based algorithms, the main goal is to use ML-based algorithms to find and eliminate possible drug-event connections in MEDLINE case reports [18]. Using data from pharmacological databases, the study [19] offers an ML technique for predicting the ADR of a combination medication. Predictions of drug-SE effects using human cell-based tests were accurate. Figure 3 depicts the SVM that predicts drug-target interactions.

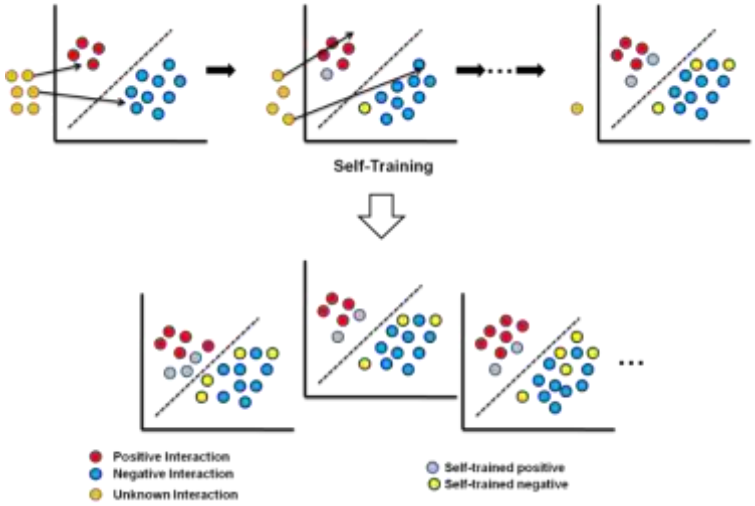

Figure 3: SVM model for drug target interaction

ii. Feature Selection-based

The most important and useful properties for classifying the ADRs are identified by these models using some information theory-based techniques [20].

- **Decision tree**

Decision trees are a prediction method used in learning models. A decision tree normally begins with a single node, from which various outcomes branch out. Each of these scenarios then leads to an additional node which in turn creates branches with a maximum probability. This branching arrangement eventually transforms into a graphic that looks like a tree. In this model, there are three different types of nodes: the random node, which represents the probability of a specific outcome; the decision node, which can be made; and the final node, which refers to the decision tree's outcome [21]. But this technique is highly transparent and understandable because the decision-making process can be easily followed from branch to branch of the tree. Further, unlike with other models, the decision trees do not require any data transformations to work with missing values and discrete numerical or categorical information. The labeled data is used in [22] to teach the Decision Tree algorithm. To categorise the drug-symptom interaction, the DT algorithm is applied. Figure 4 depicts the DT model for ADR

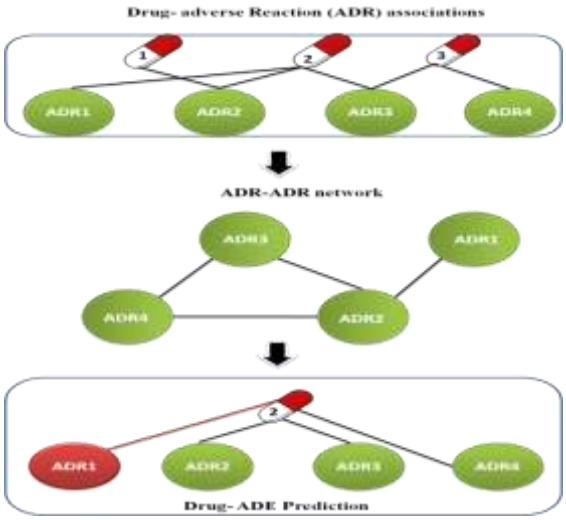

Figure 4: Prediction of ADR using ADR

- **Random forest**

The RF classifier predicts or classifies the dependent variable using the findings from several decision trees. A decision tree must be built around a collection of randomly chosen data points from the training set for the RF classifier. Prior to creating additional or different trees, the number of decision trees must be specified. A category for prediction is given to each of the new trees. An ADR identifier is used in [23] to acquire features utilised in random forests. The RF receives the input to forecast the outcome of the ADR. The RF approach demonstrated great accuracy as a result of RF's excellent performance. It employs a hybrid learning strategy for classification. At each level, they use a tree as a result based on the informational value and it works well for large amounts of data. Study [24] provide a binary classification approach to predict drug, and study [25] use an ML technique (Random Forests) to classify the intensity of the consequence of ADR.

B. Regression

One of the most popular ML techniques, logistic regression, is predicated on the idea that data points may be divided into two separate areas by a linear discriminant using a linear hyperplane [26]. The "logistic regression (LR)" model maximises the average probability of correctly classifying a data point using the maximum probability estimation function. The outcome of LR is the probability that the relevant data point belongs to one of the classes and may be represented as a sigmoid [27]. To classify ADR, a study [28] employed the Logistic Regression technique. For logistic regression, they employed a collection of characteristics comprising word embedding, a semantic feature of semantic and lexicon.

C. Unsupervised ML model

There are no labels accessible in unsupervised ML methods. Unprocessed data that has been categorised into groups according to how similar they are to one another is submitted to the algorithm. In huge or complex datasets, this is done in an effort to uncover patterns. This approach starts the analysis with no labels and subsequently finds new label clusters [29]. It is necessary to predetermine the number of available labels, which could be problematic in some circumstances. If there are not enough unique labels, various outputs will be lumped together. Members of the same clusters will be divided into other groups if there are too many labels [30].

iii. Similarity-based Model

Classifiers rely heavily on input features when no labels are available. The input data is transformed into a new feature space, which reduces the disparity between sets of information that are statistically comparable. Clusters of ADRs were visible in the new feature space. [31].

- **k-NN**

This prediction approach involves selecting a certain number of training samples that are physically closest to the present position and then predicting the label from those samples. The sample may be predetermined by the user to be constant, although it occasionally may vary in terms of the local density of points. Typically, the distance can be measured in either metric units or traditional Euclidean distance [32]. The latter is preferred the most. Since neighbors-based algorithms have the capacity to recall all of their training data, they are non-generalizing ML techniques. It is one of the simplest methods for predicting ADR. Utilizing k-NN is based on the principle that medications with identical descriptor vectors are likely to have similar adverse drug reactions [33]. Assume that there is a similarity metric measure sim: $\mathbb{R}^f \times \mathbb{R}^f \to \mathbb{R}$, such as cosine similarity. To forecast drug-ADR association scores g(y), the top l medicines that are the most similar to y are first selected, resulting in a collection of indices of the comparable drugs U(y, l), and then the drug-ADR association scores are derived by

$$g(y) = \left[g_1(y) \dots g_j(y) \dots g_t(y)\right]^U \quad (1)$$

g_k - weighted average function

$$g_k(y) = \sum_{j \in U(y,l)} x_j(y) a_{k,l}, \quad k \in \{1, \dots t\} \quad (2)$$

Here,

weights x_j are obtained from drug similarities

$$x_j(y) = \frac{sim(y, y_j)}{\sum_{j \in U(y,l)} sim(y, y_j)} \quad (3)$$

The “linear neighborhood similarity Method (LNSM)” is one of the KNN extensions that has been used [34]. The similarity weights in LNSM are derived in a way that results in a drug descriptor vector that is a linear combination of descriptor vectors of the neighbouring pharmaceuticals with appropriate similarity weights.

iv. Feature Vector-based Model

In the case of an unsupervised situation, experts pay close attention to the input attributes and utilise them to find a different space where the inputs are grouped according to their differences. “Multi-Layer Perceptron (MLP)“ is an example of a technique utilised in the Feature Vector-based model. The MLP model was employed by the study [35] to train data sets, classify ADRs, and forecast them.

Table 1, shows the classifying of ADRs in ADHD is presented, and several methods are evaluated in terms of their core ideas, benefits, and drawbacks.

Table 1: Merits and demerits of classifying adverse drug reactions

S. No	Approach		Core idea	Demerits	Merits
1.	Unsupervised	Feature vector-based	A classification or clustering operation is carried out using a collection of characteristics that have been defined by the expert.	Selecting the ideal attributes is difficult.	It is feasible to prevent a drug's negative side effects.
		Similarity-based	Utilizing a specified criterion, drug similarity is assessed in order to cluster or classify data.	It is difficult to choose the right similarity criteria. The total amount of data groups is unknown at this time.	Low data dimensionality.
2.	Regression		Regression modelling, which produces a binary output, is used to represent the classification issue.	Classification model training is severely hampered by outlier data.	The feature extraction stage can be eliminated when using deep neural networks to implement.
3.	Supervised	Features selection	The problem of ADR categorization is done by taking into account the most crucial aspects by estimating the information gain of features.	Significant dependence on observed samples.	No training is required. (lazy teaching techniques) It is not necessary to scale and normalise the input data.
		Instance-based	These techniques do not have a training phase; instead, they categorise the data and select the optimal separator depending on where the observations are located in an appropriate space.	The size of the data can be quite huge, which could make computations more difficult.	Data visualisation is very simple. No need to invest time in training.

III. CONCLUSION

In this survey, we have identified one of the finest sources for recognising ADR using ML algorithms as one of the most effective methods. The early detection of adverse drug reactions (ADRs), to reduce financial costs and death, is one of the most critical challenges in the field of medicine. Several methods for extracting characteristics from social media data, as well as classification algorithms for data, were brought forward and addressed. This review has made researchers more aware of the importance to explore this type of adverse drug response prediction, and it has allowed for the examination of some of the most significant machine learning approaches that might be used to predict adverse drug reactions.

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