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Predicting Substance Use Disorder in ADHD Patients using Long-Short Term Memory Model

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Abstract

About 20% of individuals with attention deficit hyperactivity disorder (ADHD) are first diagnosed during adolescence. While preclinical experiments suggest that adolescent-onset exposure to ADHD medication is an important factor in the development of substance use disorder (SUD) phenotypes in adulthood, the long-term impact of ADHD medication initiated during adolescence has been largely unexplored in humans. Our analysis of 11,624 adolescent ADHD patients in the Truven database indicates that temporal medication features are the important factors on the health consequences related to SUD and ADHD medication initiation during adolescence.

Keywords

Attention Deficit-Hyperactivity Disorder; Substance Use Disorder; Long-Short Term Memory Model; Big Data

1) Introduction

An estimated 1 out of 13 Americans (20.1 million) over the age of 12 are struggling with a substance use disorder (SUD) [1] and recently, SUD-related overdose deaths surpassed the number of deaths attributed to motor vehicle accidents [2]. One of the potential risk factors for subsequent development of SUD is exposure to medications used to treat attention deficit hyperactivity disorder (ADHD). Given that ADHD is one of the most prevalent neuropsychiatric disorders with 6–10% of children (aged 2–17) having ever received a diagnosis [3], and among them, 62% are medicated [4], it is critical to systematically assess the long-term association of ADHD medication initiated on subsequent risk of SUD [5].

In this article, we address the technical challenges in analyzing temporal medication data [6] and present a long short term memory (LSTM) based framework to predict the long-term

impact of ADHD medication initiated during adolescence. Experimental results show that the temporal medication features of ADHD medication initiation during adolescence are important factors on the health consequences related to SUD.

2) Materials and methods

2–1) Truven Data

We analyzed the large-scale medical records in the Truven MarketScan Commercial Claims database for years from 2009 to 2015. First, we selected all the 254,996 individuals who had an International Classification of Disease (ICD-9) diagnosis of ADHD (ICD-9 code 314.X), among them 136,933 are children (6–12 years) and 118,063 are adolescents (13–20 years) onset exposure to ADHD medication. For each of the ADHD patients, all the ADHD medication records between Jan 2009 and Dec 2015 were extracted. In total, we extracted 11,778,912 records from Truven. To facilitate further study the temporal patterns in the data, we converted the Truven format into a patient-time matrix X(P,T), where P is the complete set of ADHD patients and T is the set of time points between 2009 and 2015 (by month), each cell x_{ij} records the medications a patient pi took at time t_j. Twelve ADHD medications were considered and categorized into four medication groups, i.e. amphetamines, methylphenidate, modafinil, and others, based on the first eight digits of the generic product indicator. Given the monthly subscription records in Truven, the finest temporal resolution of T is by month. Second, we determined if any patient in P had been diagnosed as having a SUD for the first time after he/she had received a prescription for an ADHD medication for at least five months. If this condition is met, the patient was labeled as ADHD-SUD positive (label y_i =1 for patient p_i) and all the ADHD medications after the first SUD diagnosis were removed from X(P,T); otherwise the patient was labeled as ADHD-SUD negative (label y_i =0 for patient p_i). The extracted Truven data include detailed patients-level information over time, ready for assessing the long-term impact of ADHD medications. Note, although the adolescents in the Truven data is much less than children, for those who are ADHD-SUD positive, data of adolescent patients are abundant, whereas the data of children are insufficient for further analysis.

2–2) Temporal Model

We present a LSTM-based framework to predict the long-term impact of ADHD medication initiated during adolescence. LSTMs are deep learning models for processing longitudinal data. We first reduced data sparsity since in the patient medication record matrix X(P,T), 96.6% of medication records are simply 0. Specifically, we removed all 0 before the first ADHD medication record and removed all 0 after the last ADHD medication record. In addition, empty sequences, sequences in which the patient used ADHD medication for less than five months, patients who started using ADHD medication less than five months prior to being diagnosed with SUD were all removed to further reduce noise and remove outliers. After data preprocessing, the data sparsity was reduced from 96.6% to 49.9%. Finally, we adopt the LSTM model to predict SUD using the temporal ADHD medication records in X(P,T).

3) Experimental results

The LSTM models were deployed on the TensorFlow platform and are trained using eight GeForce GTX 1080 GPUs. Batch size, learning rate, number of hidden neurons and number of epochs were set to be 256, 0.09, 75 and 100, respectively. Two dummy models named All-Negatives and All-Positives, which label all validation samples as negatives or positives, respectively, served as the baseline. Support Vector Machine (SVM) and Random Forest (RF) models were also compared with the LSTM models. For systematic performance testing, we used 90/10 cross-validation and repeated the cross-validation process 20 times. Averaged performance results are reported as the final result. Accuracy, precision, recall, specificity and F1-score are used to evaluate and compare different models.

Performance of the LSTM models, dummy models, and traditional classification models (SVM and RF) are provided in Table I. The LSTM model has the highest accuracy (0.84), precision (0.96), specificity (0.97) and F1-Score (0.82). Recall for this model is on par with that of SVM (0.72 vs. 0.73). The results indicate that LSTM captures important factors in the Truven data providing an increased power to predict the development of SUD, while SVM and RF miss such factors.

The high performance of the LSTM model indicates that the temporal medication records in the Truven data encode critical factors that provide an increased power to predict the development of SUD in adolescent ADHD patients, which are captured by the LSTM model. The LSTM model is also robust. Fig. 1 shows that the performance of the LSTM model on both the training and the validation sets remained stable when different learning rates were applied.

Moreover, we tested how long the medication application patterns could be. Since in the Truven data the longest ADHD medication records span seven years, we generated a batch of new datasets by only considering the ADHD medication records in the first x years (x varies from 1 to 7). Note, all of these new datasets include the same patients. Fig. 2 shows that the performance of the LSTM models steadily increase when longer medication records were used. These results indicate that the medication application patterns is a long-term pattern.

4) Conclusion

SUD is a public health crisis costing the US an estimated $740 billion annually in healthcare, lost workplace productivity, and crime. One of the potential risk factors for subsequent development of SUD is administration of ADHD medications during adolescence. By systematically studying the long-term impact of ADHD medication initiated during adolescence using the LSTM model, we concluded that the long-term temporal medication application patterns appear to be key factors that provide increased power to predict the development of subsequet SUD in adolescent ADHD patients.

References

1. Behavioral health trends in the United States: Results from the 2014 National Survey on Drug Use and Health (HHS Publication No. SMA 15–4927, NSDUH Series H-50). 2015.
2. Murphy SL, X. J, Kochanek KD, Curtin SC, Arias E, National Vital Statistics Reports. 2017.
3. Danielson ML, et al., Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment Among U.S. Children and Adolescents.Journal of Clinical Child and Adolescent Psychology, 2016 47(2): p. 199–212.
4. Centers for Disease Control. Attention deficit hyperactivity disorder Data and Statistics. [cited 2018 April 9]; Available from: https://www.cdc.gov/ncbddd/adhd/data.html.
5. Baskin BM, Dwoskin LP, and Kantak KM, Methylphenidate treatment beyond adolescence maintains increased cocaine self-administration in the spontaneously hypertensive rat model of attention deficit/hyperactivity disorder. Pharmacology Biochemistry and Behavior, 2015 131: p. 51–56.
6. Miotto R, et al., Deep learning for healthcare: review, opportunities and challenges. Briefings in Bioinformatics, 2017: p. 1–11. [PubMed: 26868358]

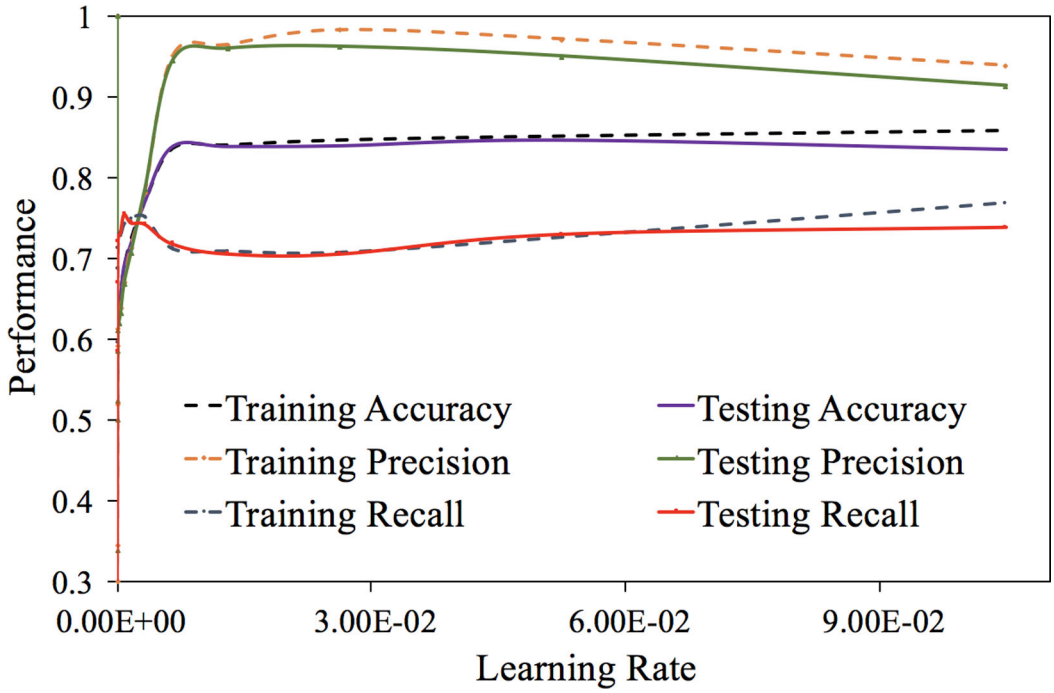

Fig 1).
Impact of the learning rate on the LSTM model.

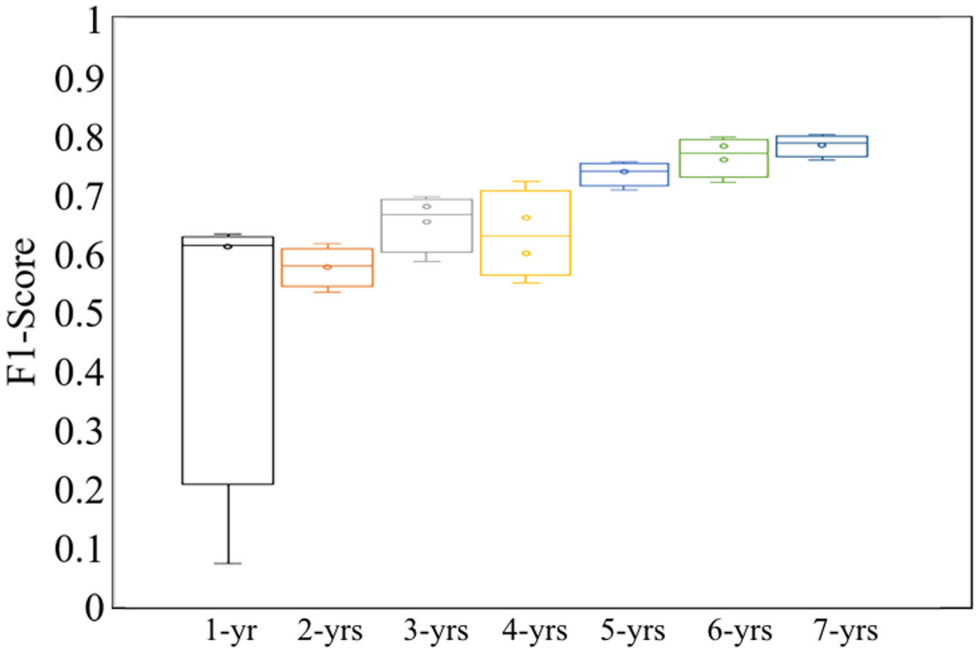

Fig 2).
Impact of the length of ADHD medication records on SUD prediction.

Table 1)

Performance of SUD prediction using traditional classification models and the LSTM model.

Model	Accuracy	Precision	Recall	Specificity	F1-Score
All-Negatives	0.50 ± 0	0.00 ± 0	0.00 ± 0	1.00 ± 0	0.00 ± 0
All-Positives	0.50 ± 0	0.50 ± 0	1.00 ± 0	0.00 ± 0	0.67 ± 0
RF	0.59 ± 0.01	0.59 ± 0.01	0.59 ± 0.02	0.59 ± 0.02	0.59 ± 0.02
SVM	0.58 ± 0.01	0.56 ± 0.01	0.73 ± 0.02	0.42 ± 0.02	0.63 ± 0.01
LSTM	0.84 ± 0.01	0.96 ± 0.03	0.72 ± 0.02	0.97 ± 0.03	0.82 ± 0.01