

Deep Learning to Classify Adverse Events from Patient Narratives



Deep Learning to Classify Adverse Events from Patient Narratives at FDA

Qais Hatim, FDA CDER

Tom Sabo, SAS Institute Inc.

Qais is an expert in industrial engineering, advanced statistical modeling, machine learning, data analytics, and operational research. Qais is a data scientist at the U.S. Food and Drug Administration (FDA), where he performs work that has substantial merit and national importance.

Tom is a principal solutions architect at SAS who, since 2005, has been immersed in the field of text analytics and AI as it applies government challenges. This includes public health analytics, assessing research trends, and counter human trafficking solutions.



Problem Statement

- FDA manual review and coding of adverse events in the FDA Adverse Event Reporting System (FAERS) is hugely time consuming
- This is largely due to the volume of free-text narratives on adverse events occurring to patient/subject
- Automated coding of adverse events will improve postmarket and premarket safety reviews of FDA regulated drugs from a time & quality perspective

Key Points

Question: Can deep learning improve the efficiency of identifying safety signals from patient narratives?

Findings : In this study of 14,976 narrative observations in clinical study reports where 50% of such reports include indications of serotonin syndrome, the most successful deep learning method tested achieved a 98.88% correct classification rate of serotonin syndrome. Furthermore, machine learning methods which provide a layer of interpretability including associated symptoms achieved a 94.4% correct classification rate.

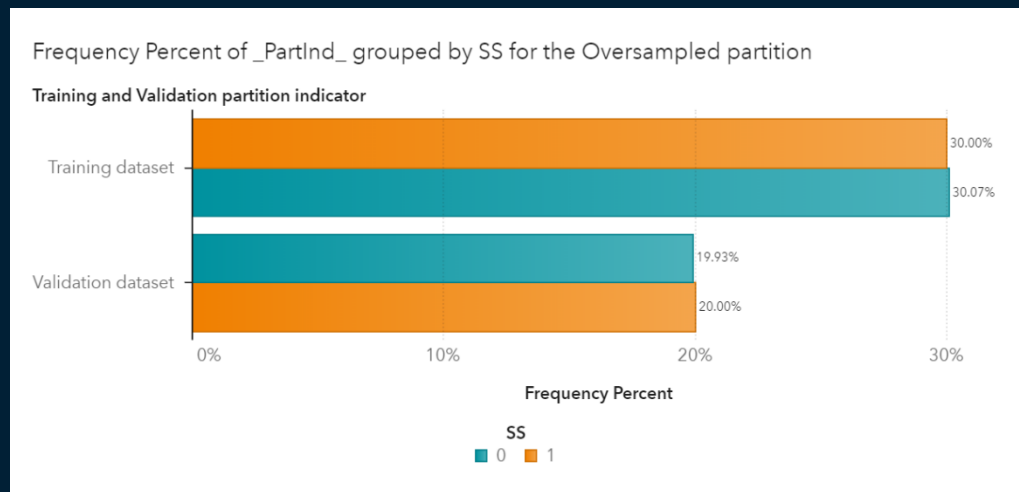
Meaning: Deep learning and machine learning can improve the speed, accuracy, and interpretability of medical coding for adverse events.

Approach

- SAS has applied text analytics and machine learning with FDA in the past with success and presented this work at PhUSE Connect 2018
- This new initiative would leverage Deep Learning to classify one such event, *serotonin syndrome*, and could subsequently be leveraged for many such events
- We leveraged 4 different deep learning methods alongside one machine learning method which provides a layer of interpretability

Data Prep & Pre-Processing

- Extracted drug safety reports from the FDA system
- Flagged narratives with a Serotonin Syndrome flag (SS=1/0)
- Drugs in one of two lists that had some likelihood of serotonin syndrome in the first place
- Oversampled for a 50% SS population, and a 60-40 training validation split



Serotonin Syndrome

Target Variable under focus

Overview



Serotonin syndrome occurs when you take medications that cause high levels of the chemical serotonin to accumulate in your body.

Serotonin is a chemical your body produces that's needed for your nerve cells and brain to function. But too much serotonin causes signs and symptoms that can range from mild (shivering and diarrhea) to severe (muscle rigidity, fever and seizures). Severe serotonin syndrome can cause death if not treated.

Serotonin syndrome can occur when you increase the dose of certain medications or add a new drug to your regimen. Some illegal drugs and dietary supplements also are associated with serotonin syndrome.

Milder forms of serotonin syndrome may go away within a day of stopping the medications that cause symptoms and, sometimes, after taking drugs that block serotonin.

Symptoms

Serotonin syndrome symptoms usually occur within several hours of taking a new drug or increasing the dose of a drug you're already taking.

Signs and symptoms include:

- Agitation or restlessness
- Confusion
- Rapid heart rate and high blood pressure
- Dilated pupils
- Loss of muscle coordination or twitching muscles
- Muscle rigidity
- Heavy sweating
- Diarrhea
- Headache
- Shivering
- Goose bumps

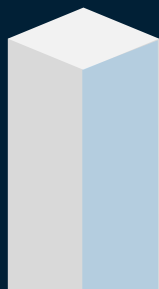
Source: [Mayo Clinic website](#). For informational purposes only

ML Boolean Rules Approach

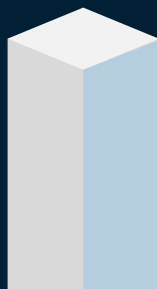
- Rules provided a layer of interpretability and validation around the decision making process

Rule	Target	Average of _F1_	Average of _Precision_	Average of _Recall_
depression & tremor & tachycardia	1	0.930030088	0.892822026	0.970474282
syndrome	1	0.929925698	0.893195521	0.969806279
drug toxicity & venlafaxine	1	0.929803035	0.899875	0.961790247
symptom & hydrochloride & neuroleptic	1	0.929655707	0.899949975	0.961389446
temperature & mydriasis	1	0.929508303	0.900025025	0.960988644
syndrome & hydrochloride & hallucination	1	0.929360822	0.90010015	0.960587842
syndrome & ~attorney & ~site & ~initial information & ~arthritis & ~n	1	0.928899528	0.900526844	0.959118237
monoamine oxidase inhibitor	1	0.917918268	0.96193265	0.877755511
nms	1	0.917767065	0.9619215	0.87748831
suicidal & icu	1	0.917505593	0.962311189	0.876686707
hydrochloride & seizure & selective	1	0.917266942	0.962430291	0.876152305
icu & flush	1	0.917039731	0.962413743	0.875751503
toxicity & flush	1	0.916812426	0.96239718	0.875350701
syndrome & ~attorney & ~site & ~initial information & ~arthritis & ~n	1	0.916585025	0.962380603	0.8749499
syndrome & ~attorney & ~site & ~initial information & ~arthritis & ~p	1	0.91489511	0.963356974	0.871075484
lithium & ~consumer & major	1	0.910649756	0.969523235	0.858517034
linezolid & mental	1	0.910250957	0.969642048	0.857715431
anxiety & hyperthermia	1	0.909941852	0.969623697	0.857181029
anxiety & reaction & tremor & insomnia	1	0.909632572	0.969605323	0.856646627
anxiety & tremor & lorazepam	1	0.909168323	0.969577721	0.855845023
anxiety & jerk	1	0.908781146	0.96955468	0.855177021
escitalopram & disorient	1	0.908238636	0.969522365	0.854241817
toxicity & shake	1	0.907928389	0.969503869	0.853707415
tachycardia & ~attorney & diaphoresis & seizure	1	0.907617965	0.96948535	0.853173013

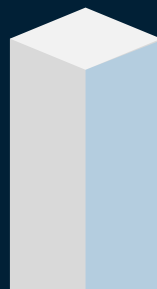
1.12%



1.9%



2.84%



19.37%



RESULTS: Misclassification Rates (%)



tmCoOccur
Averaging



DL on Topic
Weights



tmCoOccur RNN



GloVe 300D

Additional Discussion Points

- This approach can be scalable and is production-ready for health conditions other than serotonin syndrome such as drug induced liver injury and cardiovascular cases
- This approach enables researchers to get deep into the classification of their data – that is – to see how classification of serious events like serotonin syndrome takes place, and to recommend a prioritized set of adverse events for manual review.
- This work has been presented at SAS Global Forum 2021 and the DIA's annual conference 2021. See paper here: https://communities.sas.com/kntur85557/attachments/kntur85557/proceedings-2021/68/1/Hatim_1058.pdf
- This is one of a variety of projects SAS has collaborated with FDA on.



The Future!

- Revisit DILI with these methods – enhance the existing process
- Leverage the latest new “tools”
- Wider simultaneous applicability? Multiple models or one?
- Move these processes one step further to production



Thank you!

Contact Information

Tom.Sabo@sas.com

@mrTomSab

<https://www.linkedin.com/in/tomsabo/>

