Machine learning

Current uses in temporal lobe epilepsy

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ABSTRACT

In the era of Big Data, finding patterns amidst large and/or complex datasets is a significant problem, particularly in medical applications, such as in neuroscience and neuroimaging. Machine learning techniques are powerful tools with the ability to develop pattern recognition that, once trained, can be utilized to analyze large datasets in research and possibly clinical settings. Temporal lobe epilepsy is a prominent neuroimaging research subject in which machine learning has been utilized, demonstrating some of its applications in automated labeling of diagnostic imaging, feature classification, and feature extraction.

INTRODUCTION

Medicine is a field with an ever-increasing amount of data needing accurate and timely parsing for diagnoses, making treatment plans, and in clinical research. Pattern recognition is fundamental to this end, and with new and better technology, machine learning (ML) now offers pattern recognition in a digital form, making it a powerful tool that has seen increased use as more information is collected and digitized. High-throughput processing of data with multiple parameters and thousands or even millions of data points ultimately relies on algorithms, whether ML algorithms or those designed by software engineers. Neuroscience is one domain that could benefit from ML, with vast amounts of imaging data, connectomes, and biological pathways. In this paper we will limit our discussion to temporal lobe epilepsy (TLE), a disease with established neuroimaging research in which ML has been used. Examples of such applications include automatic classification and the detection of new imaging features that might give rise to more accurate clinical diagnoses.

MACHINE LEARNING IN BRIEF

ML is a process of iterative optimization, where algorithms form and refine models that can be used to predict an output for a given input. Training data and feedback on the algorithm's output accuracy is used to form models. Models that meet a certain threshold for the desired parameters are kept, modified, and then retested with stricter thresholds. The process is then repeated as needed. ML therefore benefits from having as much training data as possible.

ML is broadly divided into two types: supervised and unsupervised. Supervised ML is characterized by datasets that have inputs with matched outputs for training. For example, a dataset could consist of magnetic resonance imaging (MRI) images

as input data, with each MRI corresponding to an output label of the diagnosis. Unsupervised ML is used for training input data with no matched output. This could be a group of MR images of patients with epilepsy that require the ML algorithm to sort them into subtypes based on patterns found, where the subtypes are not predefined. This is useful for uncovering patterns in the data and its structure, creating a dataset that is more suitable for research and hypothesis generation.¹

Supervised ML can be used for the categorization of discrete data or for regression analysis of continuous data.² There exist a number of supervised methods, with varying benefits and limitations, such as speed of training, accuracy of prediction, suitability for regression versus categorization, and even interpretability as a model.² Supervised ML has applications in automation or assisted labeling of imaging, electroencephalograms (EEG) analysis, and feature extraction that could distinguish pathologies or find novel diagnostic patterns.

Despite the possibilities, the various ML techniques all carry their own limitations. Often, the goal of research is to find models that are not only accurate, but explainable. However, ML does not necessarily generate models that are interpretable.¹ Real-world data is also not perfect, and missing data, noise, and outliers can significantly impact the accuracy of a ML algorithm.³ Even the selection of parameters for input and output can affect the success of a ML algorithm.³

TEMPORAL LOBE EPILEPSY

Of epileptic syndromes associated with recurrent focal seizures, TLE is one of the most common forms and is heavily studied in neuroimaging research, given its association with structural changes such as mesial temporal sclerosis (MTS).⁴⁻⁶ Histopathologic studies have found mesial temporal sclerosis, a primarily hippocampal lesion, is present in 40% of cases of refractory focal seizures.⁷ MTS and other lesions associated with TLE have implications on management options, particularly in cases with refractory seizures where surgery plays a larger role.⁸ Imaging is used to determine whether surgery is appropriate and for postoperative prognosis.^{8,9}

MRI and EEG are two modalities used for the diagnosis of TLE. While EEG is often used initially to distinguish between generalized and focal seizures, its role in TLE is for confirming the diagnosis and sometimes localizing the focus.^{10,11} MRI is useful for identifying structural changes, such as in MTS associated TLE, which can then be used to stratify patients who may benefit from surgery.^{10,11}

MRI has been a mainstay in identifying brain lesions, but despite its high sensitivity, up to 30% of refractory TLE are not

detectable on MRI and have heterogeneous histopathology.^{12,13} New evidence does support that 3 Tesla MRI may be powerful enough to reduce the number of false-negative MRIs, accurately distinguishing MTS-associated TLE from non-MTS-associated TLE.¹⁴ EEG has a relatively high rate of detection, up to over 90%, for characteristic epileptiform sharp waves with prolonged interictal monitoring.¹⁰ There is some evidence that EEG may also be used to distinguish paradoxical TLE from MTS-associated TLE, though in general EEG is not able to distinguish MTS-associated TLE from non-MTS-associated TLE.¹⁵ Other imaging modalities, such as PET, are used in conjunction with MRI or in MRI-negative cases to detect other lesions in surgical candidates and may have utility for prognostication.^{16,17}

Given the importance of imaging in the study, diagnosis, treatment planning, and prognosis prediction of TLE, analyses of available and upcoming imaging data using ML could be helpful for a number of tasks.

MACHINE LEARNING IN TEMPORAL LOBE EPILEPSY

ML techniques have been used in the study of TLE in several capacities. Among the first is that of predicting seizures and/or recognizing pre-seizure brain activity. ML has also been used to analyze brain imaging of patients with epilepsy to detect specific features for classification and diagnosis.

Research on utilizing EEGs to predict seizures have been ongoing for over 30 years, and now with signal processing and modeling techniques, ML can be leveraged in analyzing the large amount of EEG data that is becoming available. One example includes work that predicts initiation of preictal states, where ML is used to extract features of EEGs that are important in classifying signals as seizure versus non-seizure events.¹⁸ The researchers were able to predict the start of a pre-ictal state 92% of the time with an average prediction time of 23.6 minutes.¹⁸ ML has also been used to automatically classify EEGs into seizure or non-seizure events with 88% sensitivity and 93% specificity.¹⁹ These developments can help clinicians augment their interpretation and management of EEGs, both by providing automated prescreening as well as increased detection of clinically significant features, allowing for things such as improved medical prophylaxis, monitoring, and even for initial diagnostic workup.

ML has also been used in the analysis of structural images, including MRI, of brains of epilepsy patients. Munsell et al used diffusion-weighted images, which can delineate white matter tracts in the brain, to classify whether individuals were healthy or had TLE with about 80% accuracy.²⁰ They were also able to find a number of white matter network connections that were important for the prediction of surgery outcomes in these patients with similar accuracy to experts.²⁰ A similar study used simple MRIs in an automated processing pipeline to determine which patients had MTS.²¹ They found that specific aspects of certain brain structure such as hippocampal volume, cortical thickness, surface area, volume, and the curvature of inferior frontal and inferior temporal regions of the brain were important in determining which patients

had MTS.²¹ This kind of research not only allows us to categorize images but also investigate the pathophysiology underlying the disease processes that occur in the brain. For example, ML was used by Del Gaizo et al to test a hypothesis that small extrahippocampal structural changes occur in a recognizable and common pattern in the brain of subjects with TLE.²² They were able to compare different MRI techniques and analyze the structural data with ML, confirming that such microstructural extrahippocampal lesions did correlate with the presence of TLE. This research and others like it can, in the future, help augment clinical diagnosis of TLE by delineating other common pathological patterns and characterizing possible subtypes and presentations of TLE, with the ultimate goal of improving treatments.

CONCLUSION AND FUTURE DIRECTIONS

The advances in information technology have brought about more data and with it, more opportunities to expand on research in fields like neuroscience. While the advent of information technology has already brought about an immense number of analytical tools, the flexibility that ML provides in solving problems of pattern recognition has great implications in future research and clinical practice. Within just the scope of TLE, research using ML shows potential in the future for augmenting diagnosis.

As more medical data accumulates, ML may become more commonplace in neuroimaging, personalizing treatment options in targeted therapies, and predicting prognoses of surgical candidates. While ML is already being applied in clinical research, it may take some time before these methods or the results from the research can be translated into clinical practice. However, considering the number of changes brought about by information technology over the past couple decades, one can only imagine how much more the world will transform in the years to come.

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